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Self-regulation of Slow Cortical Potentials: A New Treatment for Children With Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

OBJECTIVE. We investigated the effects of self-regulation of slow cortical potentials for children with attention-deficit/hyperactivity disorder. Slow cortical potentials are slow event-related direct-current shifts of the electroencephalogram. Slow cortical potential shifts in the electrical negative direction reflect the depolarization of large cortical cell assemblies, reducing their excitation threshold. This training aims at regulation of cortical excitation thresholds considered to be impaired in children with attention-deficit/hyperactivity disorder. Electroencephalographic data from the training and the 6-month follow-up are reported, as are changes in behavior and cognition.

METHOD. Twenty-three children with attention-deficit/hyperactivity disorder aged between 8 and 13 years received 30 sessions of self-regulation training of slow cortical potentials in 3 phases of 10 sessions each. Increasing and decreasing slow cortical potentials at central brain regions was fed back visually and auditorily. Transfer trials without feedback were intermixed with feedback trials to allow generalization to everyday-life situations. In addition to the neurofeedback sessions, children exercised during the third training phase to apply the self-regulation strategy while doing their homework.

RESULTS. For the first time, electroencephalographic data during the course of slow cortical potential neurofeedback are reported. Measurement before and after the trials showed that children with attention-deficit/hyperactivity disorder learn to regulate negative slow cortical potentials. After training, significant improvement in behavior, attention, and IQ score was observed. The behavior ratings included *Diagnostic and Statistical Manual of Mental Disorders* criteria, number of problems, and social behavior at school and were conducted by parents and teachers. The cognitive variables were assessed with the Wechsler Intelligence Scale for Children and with a computerized test battery that measures several components of attention. All changes proved to be stable at 6 months' follow-up after the end of

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Key Words

ADHD, biofeedback, neurobehavioral outcome, EEG, electroencephalogram

Abbreviations

ADHD—attention-deficit/hyperactivity disorder
ES—effect size
EEG—electroencephalogram/electroencephalographic
SCP—slow cortical potential
DSM-IV—*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*

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training. Clinical outcome was predicted by the ability to produce negative potential shifts in transfer sessions without feedback.

CONCLUSIONS. According to the guidelines of the efficacy of treatments, the evidence of the efficacy of slow cortical potential feedback found in this study reaches level 2: "possibly efficacious." In the absence of a control group, no causal relationship between observed improvements and the ability to regulate brain activity can be made. However, it could be shown for the first time that good performance in self-regulation predicts clinical outcome. "Good performance" was defined as the ability to produce negative potential shifts in trials without feedback, because it is known that the ability to self-regulate without feedback is impaired in children and adults with attention problems. Additional research should focus on the control of unspecific effects, medication, and subtypes to confirm the assumption that slow cortical potential feedback is a viable treatment option for attention-deficit/hyperactivity disorder. Regulation of slow cortical potentials may involve similar neurobiological pathways as medical treatment. It is suggested that regulation of frontocentral negative slow cortical potentials affects the cholinergic-dopaminergic balance and allows children to adapt to task requirements more flexibly.

DESPITE THE WIDESPREAD use of stimulant medication for attention-deficit/hyperactivity disorder (ADHD), there is a strong demand for improving treatment of ADHD.¹ A number of concerns accompany the use of stimulant medication. Approximately 25% of children's conditions fail to respond favorably to stimulant medication.² Adverse effects of stimulant medications include reduced growth,³ sleep disorders, decreased appetite, stomach pain, headache, and, in some cases, tics.⁴ There is no evidence of long-term efficacy of stimulants for ADHD. Results from the Multimodal Treatment Study of ADHD^{3,5} show that effect sizes (ESs) of medication management and of combined treatment (medication and behavior therapy) compared with behavior therapy and community care 10 months after the end of treatment are small (0.30 for ADHD symptoms and 0.21 for oppositional defiant disorder symptoms). Children who discontinued medication experienced considerable loss of improvement at follow-up.

Neurofeedback as an additional or alternative treatment is based on pathophysiological changes that are characteristic of ADHD. Children with ADHD, compared with nonclinical controls, show electroencephalographic (EEG) slowing in prefrontal regions⁶ and smaller brain volumes, especially in the basal ganglia and cerebellum.⁷ Since the mid-1970s Lubar and Shouse⁸ have trained children to regulate their brain states through EEG biofeedback to reduce the symptoms of ADHD. They

provided the first published EEG biofeedback (neurofeedback) study and attempted to normalize EEG patterns: Participants were rewarded for increasing the sensorimotor rhythm (12–14 Hz) at motor brain areas and decreasing theta frequency (4–7 Hz). In a series of case studies this method was shown to be successful in improving EEG spectra during cognitive tasks and promoting performance on intelligence tests and scores of attention, academic performance, and social behavior.⁹

Despite these promising results, EEG biofeedback has not been considered a standard therapy for ADHD. Until recently, there were only a few controlled studies of the efficacy of neurofeedback for ADHD, and these studies had methodologic shortcomings such as lack of controls or inadequate controls, no randomization, and no long-term follow-up.^{10,11} Although changes in cognition and behavior are reported to last 10 to 24 months after treatment,¹² these results are difficult to interpret, because no EEG data were presented or data were assessed (often posthoc) in clinical settings. In 2 recently published controlled studies it was shown that neurofeedback leads to the same improvements as medication¹³ and that effects of a combined treatment of medication, parental counseling, and neurofeedback last after washout of medication.¹⁴ In contrast, the effects of a combination of medication and parental counseling did not continue after medication washout.

Whereas the rationale for these studies was based on the modification of oscillatory activity of the brain, there is only 1 study that aimed at deficiencies observed in event-related EEG activity. Heinrich et al¹⁵ were the first to report feedback of slow cortical potentials (SCPs) for children with ADHD and provided preliminary evidence for positive behavioral and specific neurophysiologic effects. SCPs are slow event-related direct-current shifts of the EEG, originating from the upper cortical layer.¹⁶ They last from 0.3 seconds up to several seconds; they are not oscillatory in nature but occur as a consequence of external or internal events. They belong to the family of event-related brain potentials. It has been shown that SCP shifts in the negative direction reflect the depolarization of large cortical cell assemblies, reducing their excitation threshold. In patients with epilepsy, large negative potential shifts have been observed seconds before a seizure and shifts toward electrical positivity immediately after a seizure.¹⁷ In several studies, it was shown that voluntary control of SCPs can be acquired by healthy populations^{18,19} as well as by patients with drug-refractory epilepsy. Suppression of negative SCP shifts significantly decreased seizures.²⁰

In an earlier study, Rockstroh et al²¹ compared children with and without attention problems in their ability to voluntarily control SCP. The children with attention problems were able to modulate SCPs under feedback conditions but were not able to modulate their SCPs without immediate and continuous feedback in transfer

conditions. In addition, children with attention problems had reduced cortical negativity at all electrode positions in anticipation of a task, suggesting that failure to engage specific cortical networks contributes to the performance decrement.

Children with attention disorders may be impaired in the regulation of excitation thresholds of the brain. In the study by Heinrich et al,¹⁵ less impulsivity errors in the continuous performance test, less behavioral signs of ADHD (parents' ratings), and a marked increase in the contingent negative variation was found after 25 sessions of SCP feedback. This result was interpreted as an improvement of mobilization of attentional resources and a neurophysiological correlate of improved self-regulatory capacities. However, no EEG data of the training sessions were reported.

We report here EEG data during learning and relate them to the clinical outcome. In addition, changes in behavioral and academic performance were assessed 6 months after the end of treatment.

METHODS

Patients

Participants were selected according to the following criteria:

- age between 8 and 13 years;
- ADHD inattentive or hyperactive type or combined type according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*;
- no additional neurologic disorder; and
- full-scale IQ >80.

Patients were recruited from the outpatient clinic for psychotherapy at the University of Tübingen and from psychiatric practitioners. Parents and children signed informed-consent forms. ADHD was assessed with several instruments:

- Semistructured questionnaire of developmental and health history;
- DSM-IV questionnaires for parents and teacher;
- Eyberg Child Behavior Inventory²²;
- German translation of Conners' Rating Scale²³;
- Kindl-Questionnaire for Measuring Health-Related Quality of Life in Children and Adolescents, parents' and children's version²⁴;
- Testbatterie zur Aufmerksamkeitsprüfung, version 1.7,²⁵ a computerized test battery that measures several components of attention; and
- German version of the Wechsler Intelligence Scale for Children: Hamburg-Wechsler-Intelligenztest für Kinder.²⁶

With the exception of the above-mentioned ques-

tionnaire for assessment of developmental and health history, all instruments were used after treatment and at follow-up.

The study was conducted in accordance with the convention of Helsinki and approved by the local ethics committee of the faculty of medicine.

Neurofeedback: Training of SCPs

During a training session, the participants' EEGs were recorded at Cz, referred to 2 mastoid electrodes shunted over a 10-k Ω resistance. Electrode positions were prepared with a cleaning paste, and Ag/AgCl electrodes were filled with a conductive paste (Elefix; Bio-Medical Instruments, Inc, Warren, MI). The EEG amplifier (EEG 8, Contact Precision Instruments, Cambridge, MA) used a low-pass filter of 40 Hz, and the time constant was set at 16 seconds. The brain signals were digitized with a sampling rate of 256 Hz. The slow-wave filter consisted of a 500-millisecond interval moving window. The slow-wave amplitude immediately before the active phase of the trial served as a baseline and was set to 0 (see Fig 1).

During the active phase, the slow-wave amplitude was calculated every 62.5 milliseconds as an average of the preceding 500 milliseconds. The position of the feedback signal (cursor, "ball") corresponded to the difference between every 500-millisecond amplitude in the active phase and the amplitude during the baseline. It was corrected online for eye movements (for additional information about signal processing and artifact correction see refs 27 and 28). Weber²⁹ proved that respiration did not influence SCP-shifts.

Participants sat in a comfortable chair ~50 inches in front of a portable computer. As shown in Fig 2, participants saw 2 rectangles (goal boxes) on the top and the

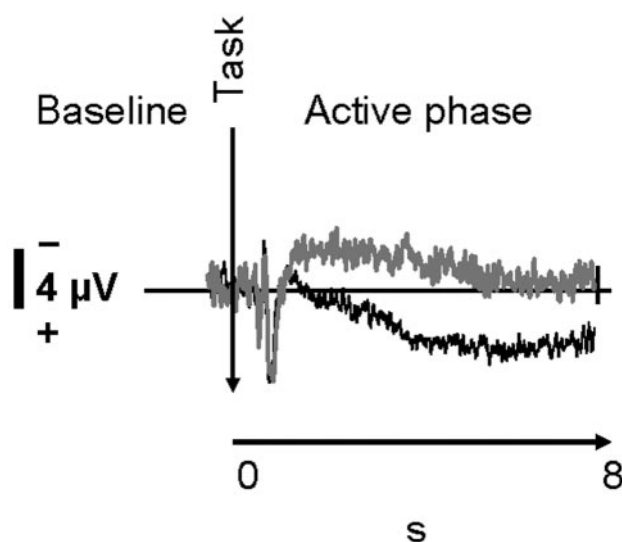


FIGURE 1

Time course of a trial with baseline, task, and active phase. The curves are mean shifts of SCPs for all trials in 1 "run" (39 trials). The upper line indicates negative shifts; lower line, positive shifts.

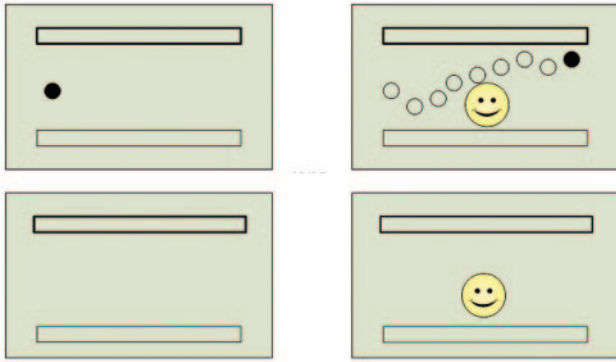


FIGURE 2
Screens: the screen on the left indicates the beginning of a trial, and that on the right indicates the end of a trial. Upper, screen during feedback trials; lower, screen during transfer trials.

bottom of the screen. A highlighted upper rectangle indicated a required SCP shift in the electrical negative direction. A highlighted lower rectangle indicated a required positive SCP shift. Each trial lasted 8 seconds and was divided into a 2-second passive phase and a 6-second active phase. Feedback consisted of a small (1-inch diameter) graphic symbol (“ball”) that moved proportionally to the cortical shift upward (negativity) or downward (positivity). Ball movements started on the left edge of the screen and moved upward or downward to the right edge. After successful trials a smiley face appeared (see Fig 2).

In addition, auditory feedback was given with a high-pitched (negativity trial) and a low-pitched (positivity) tone. A harmonious jingle was introduced as positive reinforcement if the result was correct. As an additional reinforcement at the end of each session, the total number of smiley faces was exchanged for tokens. Whenever a certain amount of tokens was accumulated, they were exchanged for small toys, stickers, or other gifts (valued at ~1.50 Euro). Therefore, the number of available toys was linked to performance.

Each session consisted of 3 to 5 runs, each run comprising 39 trials. Trials with required negativity and required positivity were presented randomly with a 50% probability during the first 15 sessions. Thereafter, the proportion between negativity and positivity tasks was 75% to 25%. To allow generalization to everyday-life situations, trials with feedback were intermixed with transfer trials in which no ball movement was shown (see Fig 2, lower). Although no continuous feedback was presented in transfer trials, the smiley face provided (delayed) information about the success. An entire session lasted ~1 hour, including the time for preparation.

Participants were instructed that the aim of training was to “speed up their brain” to maintain concentration in situations that normally are difficult to attend (listening to somebody else, making plans, and sustained mental effort in tasks such as homework, examinations, etc).

The training was introduced as a computer game in which one can score goals by using one’s brain. No specific instruction was given for how to score points; children were only advised to be attentive to the feedback and to find the most successful mental strategy to move the ball into the required goal. Because there is no unique cognitive strategy for the task,³⁰ examples were given that have been shown to be successful in at least some children. Between runs, therapists asked the subjects to verbalize strategies and encouraged them to try new strategies or stick to the successful ones.

During a session, the trainer sat in a room next-door to the child, connected by an intercom and video monitor. The trainer observed the EEG signals online on a monitor, and a second monitor showed the child. If necessary, the trainer could intervene by either using a 2-way intercom or joining the child.

Thirty training sessions were subdivided into 3 phases of 10 sessions each. As shown in Fig 3, each phase lasted 2 weeks with daily training (5 days per week). The training was scheduled in the afternoon after school classes. Assessment procedures (pretraining/posttraining/6-month follow-up) as well as training sessions took place at the same time of the day.

Parents whose children were on ADHD medication were asked to maintain a constant dose and intake. Between each treatment phase, a 4- to 6-week break allowed the participants to practice the strategies at home and record their daily practice. At the end of training, a 15 × 5-inch picture of a computer screen with the ball and goal box (see Fig 2) was given as memory-aid handout. Participants were instructed to carry it at all times and use it whenever they needed a cue for the self-regulation strategy. During the third training phase children exercised cueing while doing their homework after the end of each training session with the supervision of the trainer. The trainer was instructed to guide the child only in using the cue and not to assist in solving the particular cognitive tasks. Training and assessment procedures were implemented by either a licensed clinical psychologist or graduate students under the psychologist’s supervision.

Data Analysis

EEG Data

For each child, mean differences of SCP amplitudes during both tasks (positivity/negativity) for both conditions (feedback/transfer) were calculated. After testing the normal distribution of data, the difference between the tasks was determined separately for each assessment point (pretraining, posttraining, follow-up) with an independent-samples *t* test. Bonferroni correction was applied to the levels of significance for multiple comparisons. A repeated-measures analysis of variance (first 2 sessions, last 2 sessions, 2 sessions at follow-up) exam-

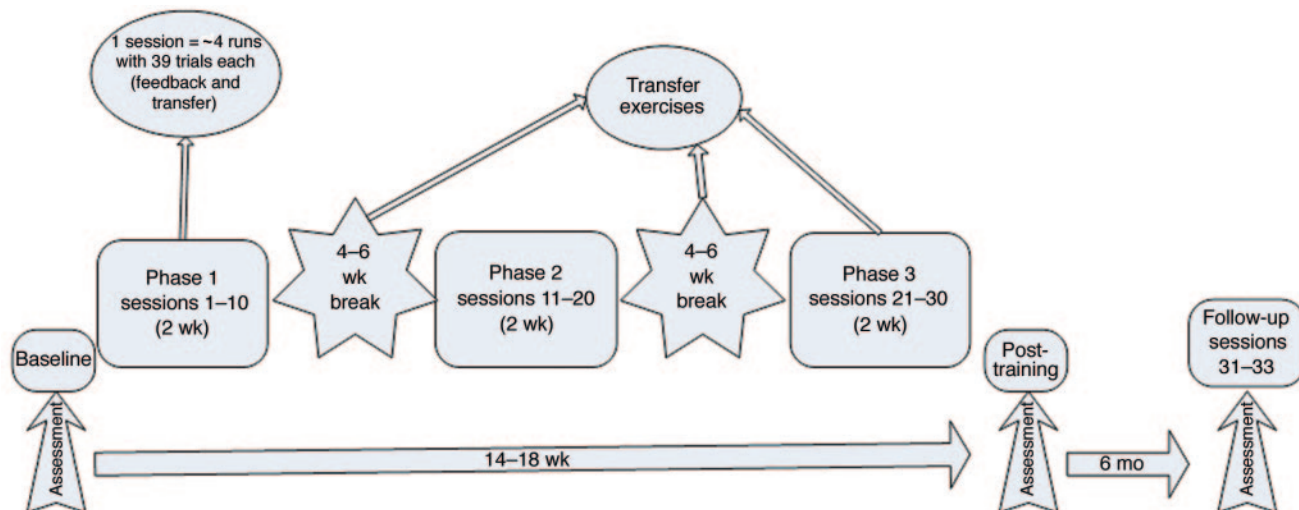


FIGURE 3
Training schedule.

ined effects of time, task, and condition. A posthoc paired-samples test compared measurement times separately in the case of a significant result of analysis of variance. The analysis of variance was corrected with Greenhouse-Geisser, posthoc tests with Bonferroni correction.

Psychometric Test Data

All data were analyzed with the same statistical procedure (repeated-measures analysis of variance) at the 3 assessment points. IQ scores were evaluated only twice (pretraining and follow-up) with a paired-samples test.

ESs

In addition to *P* values, ESs for *P* values of *t* tests were assessed with Cohen's *d*.³¹ ESs measure the magnitude of the effect and vary from ≥ 0.2 (small effect) to 0.5 (medium effect) and ≤ 0.8 (large effect). Cohen's *d* is computed as the difference between the means ($M_1 - M_2$) divided by the pooled SD [$\sigma_{\text{pooled}} = \sqrt{[\sigma_1^2 + \sigma_2^2]/2}$]. ESs in analysis of variance (partial η^2) estimate the proportion of variance in the dependent variable that is attributable to each effect.

Effects of Medication

To ensure a real-life clinical sample, children with and without medication were included. As can be seen in Table 1, 5 of 23 children used stimulants. To rule out possible effects of medication, an analysis of variance was conducted with a mixed model (2 groups: 1 with and 1 without medication with 3 assessment points). Because no differences between groups were found, only data from the entire group are reported.

TABLE 1 Description of Sample

| | |
|--|-----------------------|
| Patients, <i>N</i> | 23 |
| Gender, <i>n</i> | |
| Male | 19 |
| Female | 4 |
| Age, range (mean [SD]), <i>y</i> | 8–13 (9.3 [1.6]) |
| IQ, range (mean [SD]) | |
| Full scale | 83–126 (103.3 [12.2]) |
| Verbal | 87–140 (108 [13.2]) |
| Performance | 76–122 (98 [13.9]) |
| Diagnosis, <i>n</i> | |
| ADHD | 18 |
| ADHD, predominantly inattentive type | 5 |
| Comorbidities, <i>n</i> | |
| Learning disorders | 5 |
| Enuresis | 2 |
| Not otherwise specified | 2 |
| Medication (Ritalin, 18–60 mg), <i>n</i> | 5 |

RESULTS

Patients

Twenty-five children took part, and all of them completed the training. Because 2 children who were not under medication at the beginning of training were placed on medication after the end of training as a result of problems at school, their data were excluded from the follow-up. According to their parents' judgment, one of these children showed no more hyperactivity and the other showed no more symptoms of inattention. Therefore, our data were not biased by this change in treatment. Five children received stimulant medication throughout therapy and follow-up periods. The mean full-scale IQ score (Wechsler Intelligence Scale for Children) was 103, with a 10-point difference between verbal (108) and performance (98) scores.

Regulation of SCPs

Bonferroni-corrected differences between SCP amplitudes for negativity and for positivity tasks were close to significance at the end of training ($t_{42} = 2.133$; $P = .078$; $ES = 0.64$) for the feedback condition and significant at follow-up assessment (sessions 32 and 33) for feedback ($t_{40} = 2.749$; $P = .027$; $ES = 0.85$) as well as for transfer trials ($t_{40} = 2.814$; $P = .024$; $ES = 0.87$). As shown in Fig 4 for feedback conditions and Fig 5 for transfer conditions, children were not able to produce potential shifts according to the task requirement at the beginning of training. Instead, the potentials were negative when positivities were required, and they were negative when a positive shift was asked for. At the end of training and at the follow-up assessment the shifts were as required, and the main effects were caused by responses in the negativity task. A repeated-measures analysis of variance with the factors task and condition for feedback trials revealed a significant effect of time ($F_{2,40} = 4$; $P = .046$; $ES = 0.17$) and of the interaction between time and task ($F_{2,40} = 10.8$; $P = .001$; $ES = 0.35$). For transfer trials a significant effect for the interaction between time and task was present ($F_{2,40} = 4.79$; $P = .016$; $ES = 0.2$). Changes of mean amplitudes were also calculated with a general linear model (repeated measures) separately for negativity and positivity tasks. Although there were no significant effects for positivity trials, amplitudes for negativity trials changed significantly over time ($F_2 = 16.6$; $P = .000$; $ES = 0.45$) in feedback conditions and in transfer trials ($F_2 = 5.9$; $P = .006$; $ES = 0.23$). Posthoc tests revealed that amplitudes differed significantly between sessions 2 + 3 and sessions 29 + 30 (feedback: $t_{21} = 3.5$; $P = .004$; $ES = 0.93$; transfer: $t_{21} = 2.54$; $P = .038$; $ES = 0.73$) as well as between sessions 2 + 3 and follow-up (feedback: $t_{20} = 5.592$; $P = .000$; $ES = 1.1$; transfer: $t_{20} = 3.399$; $P = .009$; $ES = 0.95$).

Behavior

Behavior ratings of parents showed a significant reduction of problems as assessed by the Eyberg questionnaire ($F_2 = 4.478$; $P = .02$; $ES = 0.18$). A paired-samples test revealed that the change was observed between baseline

and the end of training ($P = .018$; $ES = 0.47$). Despite this result, the impact of problems did not change according to the parents' opinion. As shown in Fig 6, the number of problems decreased from 149 to 138. Scores of <127 are considered as normal.

Scores of the Conners' Rating Scale yielded a significant improvement ($F_2 = 3.98$; $P = .03$; $ES = 0.16$) that was attributed to the difference between pretesting and follow-up (posthoc paired-samples test: $t_{22} = 2.56$; $P = .054$; $ES = 0.62$). Mean values decreased from 53.6 to 46.0 to 42.0 (see Fig 7). Scores <45 are considered nonpathologic.

Parents' ratings of DSM-IV criteria were close to significance for inattention ($F_2 = 3.43$; $P = .056$; $ES = 0.14$). The changes in diagnosis for the whole group are shown in Table 2.

Two of 21 children at the end of training and 3 of 19 children at the follow-up evaluation no longer fulfilled the diagnostic criteria for ADHD. Four children with ADHD were diagnosed as having ADHD, predominantly inattentive type only, and four were diagnosed as having ADHD, predominantly hyperactive type only. One of 5 children receiving stimulants reduced medication, and another withdrew from taking the medication. Fisher's exact test revealed a significant difference between pretesting and follow-up in the distribution of children within the diagnostic categories (ADHD, predominantly inattentive type; ADHD, predominantly hyperactive type; and below cutoff) ($P = .033$). The changes between a positive ADHD diagnosis to no diagnosis at all from pretesting to follow-up were close to significance ($P = .06$).

Teachers rated significant improvements in inattention ($F_2 = 4.55$; $P = .032$; $ES = 0.19$), hyperactivity ($F_2 = 7.11$; $P = .003$; $ES = 0.27$), impulsivity ($F_2 = 4$; $P = .034$; $ES = 0.17$), and social behavior ($F_2 = 7.1$; $P = .002$; $ES = 0.26$). No changes were reported for the self-worth, emotionality, or academic-achievement scales. Mean scores and SDs are shown in Fig 8. For all subscales scores, <3 is considered nonpathologic.

Posthoc paired-samples tests revealed significant differences between assessment points: for inattention,

FIGURE 4

Mean amplitudes in negativity trials and positivity trials with feedback during the first sessions, the last sessions, and during the follow-up assessment.

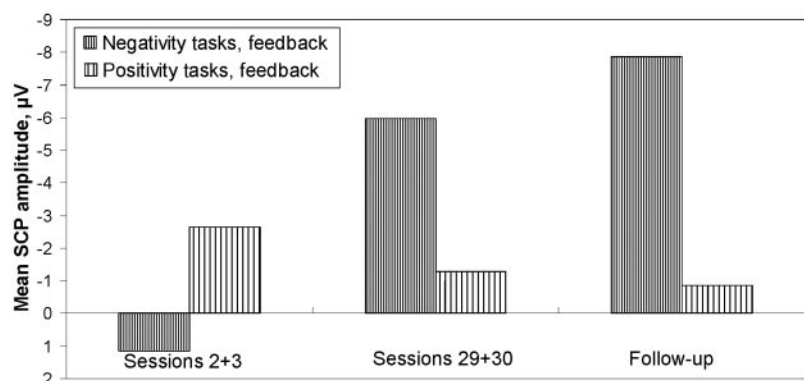


FIGURE 5
Mean amplitudes in negativity trials and positivity trials without feedback (transfer) during the first sessions, the last sessions, and during the follow-up assessment.

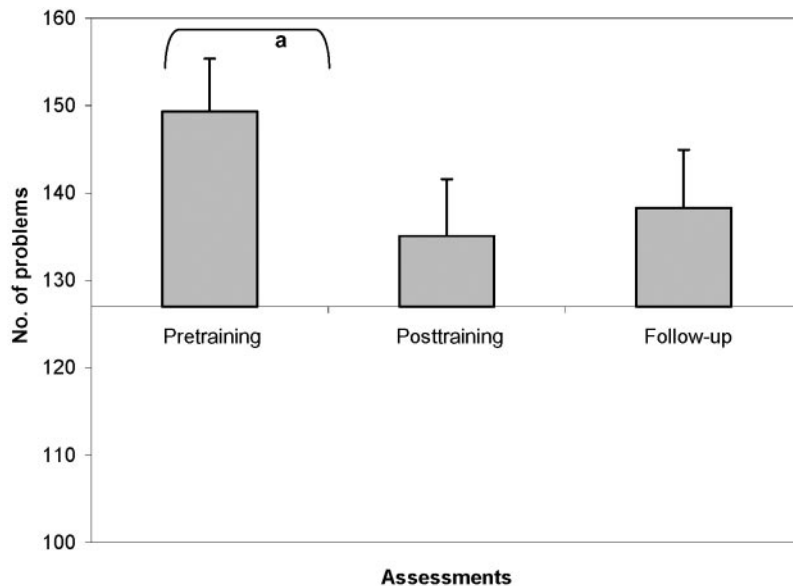
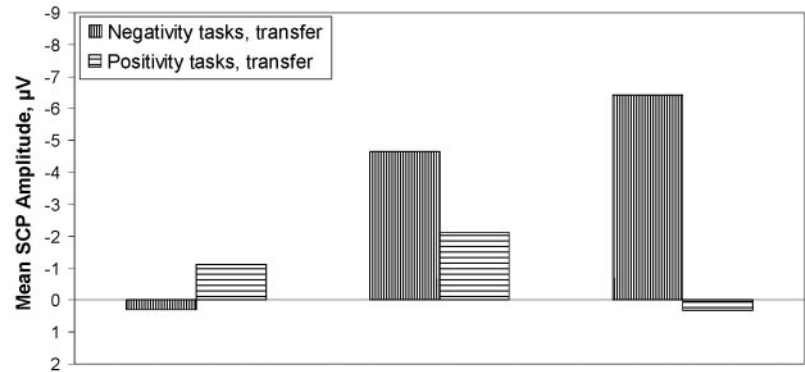


FIGURE 6
Means and SDs of numbers of Behavior problems (parents' ratings). ^a $P < .05$. The clinical cutoff value of the Eyberg questionnaire is 127.

baseline compared with follow-up ($t_{20} = 1.1$; $P = .048$; $ES = 0.55$), for hyperactivity, baseline compared with end of training ($t_{22} = 2.18$; $P = .08$; $ES = 0.28$) and with follow-up ($t_{20} = 4.3$; $P = .000$; $ES = 0.59$), for impulsivity, baseline compared with end of training ($t_{22} = 2.97$; $P = .021$; $ES = 0.36$), and for social behavior, baseline compared with follow-up ($t_{20} = 3.52$; $P = .006$; $ES = 0.64$) and end of training compared with follow-up ($t_{20} = 2.56$; $P = .038$; $ES = 0.45$).

IQ and Attention

Performance IQ scores changed significantly from screening to follow-up ($t_{22} = -2.76$; $P = .011$; $ES = 0.35$), whereas full-scale and verbal IQ changes were not significant.

Measures of attention were assessed with the Testbatterie zur Aufmerksamkeitsprüfung. This test evaluates 12 variables of attention for speed, omissions, and commissions. The data were aggregated for 7 subtests below the 25th percentile and above the 75th percentile. As shown in Fig 9, the number of results below average was significantly reduced ($F_2 = 17$; $P = .000$; $ES = 0.45$).

This improvement was observed from baseline to the end of training ($t_{22} = 5.37$; $P = .000$; $ES = 0.68$) and from the end of training to follow-up ($t_{21} = 5$; $P = .000$; $ES = 0.72$). Test results above average increased significantly ($F_2 = 8.67$; $P = .001$; $ES = 0.29$). Here, improvements were observed from baseline to the end of training ($t_{22} = -4.25$; $P = .000$; $ES = 0.63$) and from baseline to follow-up ($t_{21} = -5.05$; $P = .000$; $ES = 0.85$).

Health-Related Quality of Life

Neither parents nor children showed any changes in their ratings of health-related quality of life. Compared with mean values of healthy children,³² the profile of the patients indicated that they were healthy.

Self-regulation and Clinical Outcome

To determine if clinical outcome can be ascribed to acquisition of self-regulation skills, EEG data from training were correlated with clinical outcome. Children with at least a 2-point reduction in either hyperactivity or inattention criteria of DSM-IV were classified as "improved." Successful acquisition of self-regulation was defined on

FIGURE 7

Means and SDs of Conners' Rating Scale (parents' ratings). ^a*P* < .05. The clinical cutoff value is 45.

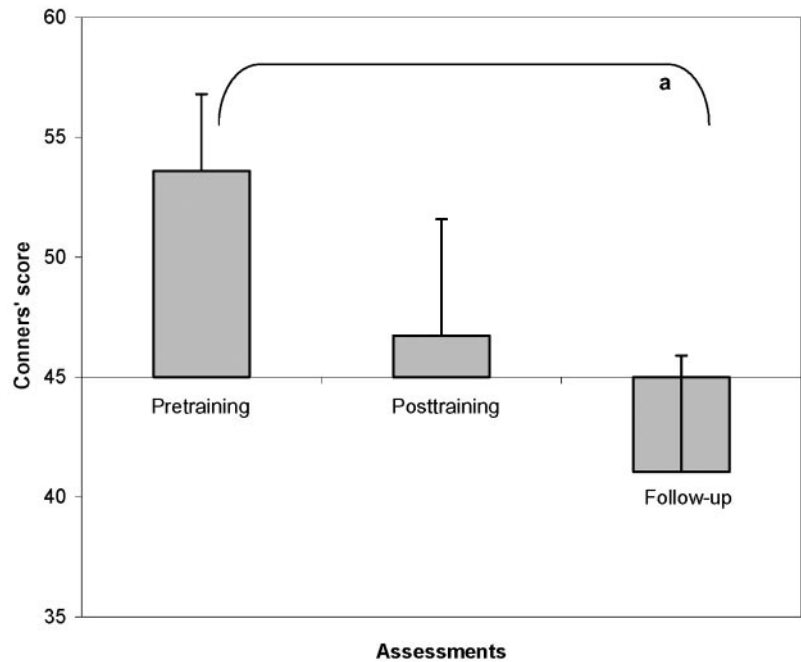


TABLE 2 Diagnosis Pretraining, Posttraining, and at Follow-up Assessment for 23 Children

| | No. of Children | | | |
|--------------|-----------------|--|--|--------------|
| | With ADHD | With ADHD Predominantly Inattentive Type | With ADHD Predominantly Hyperactive Type | Below Cutoff |
| Pretraining | 18 | 5 | — | — |
| Posttraining | 16 | 4 | 1 | 2 |
| Follow-up | 10 | 7 | 2 | 3 |

the basis of negativity trials without feedback during the third training phase. Means of amplitudes were divided by the SE for each child, and the median of these means was used to separate successful from unsuccessful regulators. The difference between group means of amplitudes in negativity trials without feedback (successful regulators = $-5.27 \mu\text{V}$; unsuccessful regulators = $-0.051 \mu\text{V}$) was highly significant (*t* test for independent samples: $t_{12} = -6.58$; *P* = .000). Pearson's χ^2 revealed a significant association between successful self-regulation and clinical improvement at the end of training ($\chi^2 = 5.24$; degrees of freedom = 1; *P* = .022). This association was close to significance at follow-up ($\chi^2 = 2.93$; degrees of freedom = 1; *P* = .087).

DISCUSSION

We report the first, to our knowledge, EEG data during the course of self-regulation of SCPs. There is clear evidence that children learn to control SCPs. Furthermore, this ability remains stable after the end of training without booster sessions. The results of this study show that children with ADHD are able to learn regulation of slow

negative brain potentials (with and without feedback). The assumption that patients with frontal deficits or lesions and ADHD are not able to self-regulate brain activity related to attention was not confirmed.²¹ Because this earlier study did not include as many sessions as our study, the number of sessions might be an important variable. In addition, the transfer exercises between training phases and after training sessions may have contributed to this result.

As can be seen from Fig 4, children did not produce reliably positive potentials; even during required positivity all potentials were negative, although smaller than during required negativity. In the transfer condition (see Fig 5), small positive potentials were produced, but the difference to baseline did not reach significance. In contrast to self-regulation training for patients with epilepsy,²⁰ the children with ADHD controlled negative potentials only. This could be the result of the more extended training of negativity in this study. In a comparison between young (aged 20–28 years) and older (aged 50–64 years) healthy persons, Kotchoubey et al³³ found in both groups potential shifts in positivity trials still negative compared with baseline, although smaller than in negativity trials. Perhaps processing demands of the task itself prevent subjects from producing larger positive potentials. Subjects report that producing positive potential shifts is more difficult and exhausting. Therefore, because they do not need this skill for the treatment of symptoms as in the case of patients with epilepsy, motivation to concentrate on this task might be reduced compared with the negativity task. As in these studies, the children were able to produce electrophysiological differential responses between the negativity (excita-

FIGURE 8
Teachers' rating before training, after training, and at the follow-up assessment. ^a $P < .05$.

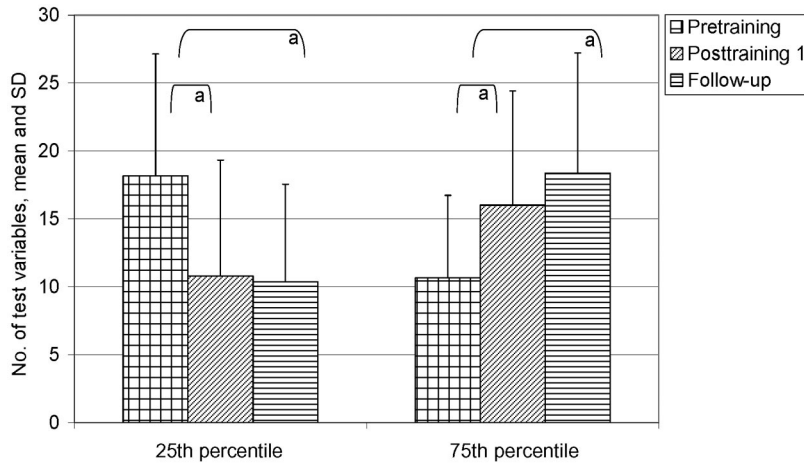
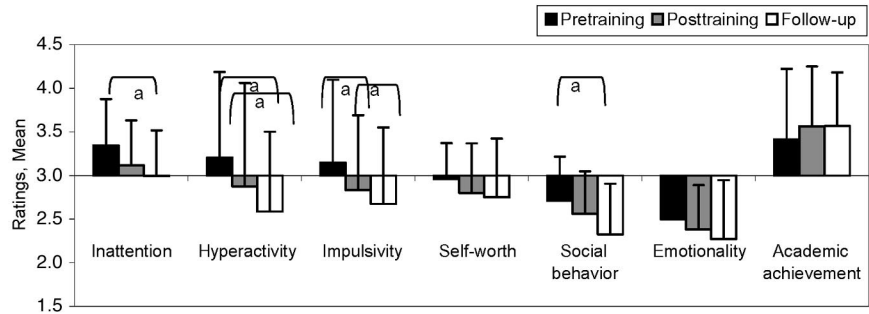


FIGURE 9
Attention scores below the 25th and above the 75th percentile in pretraining and posttraining and at the follow-up assessment. ^a $P = .000$.

tion) and positivity (inhibition) tasks. The limitation is only that positive (supposedly inhibitory) responses did not reach positive values. Thus, the main goal of the training (self-regulation of excitation thresholds and cued increase of excitatory brain activity) was achieved.

After such training, parents and teachers report reduction of behavioral problems, and test data show improvements in cognitive performance. Similar effects have been reported after neurofeedback training in previous studies (eg, refs 13 and 14). In addition we demonstrated that the improvements are stable 6 months after the end of training. ESs of the behavioral changes (between 0.14 and 0.64) of attention (between 0.68 and 0.85) and IQ (0.35) are between medium and large. ESs for pretraining/posttraining data were not reported in previous studies, which makes a comparison of outcomes difficult. The Multimodal Treatment Study of ADHD⁵ reports ESs of 0.30 for the difference between the combined therapy of medication management and behavior therapy compared with behavior therapy and community care for ADHD ratings. Significant differences in outcome were caused by medication. In our study, medication did not affect outcome, but group sizes (5 children with medication, 18 without) were rather small.

Although outcomes in attention, IQ, teachers' ratings, and parents' ratings of Conners' Rating Scale and num-

ber of problems (Eyberg) yielded moderate-to-high ESs, parents' ratings of DSM-IV criteria showed only small positive changes at the end of training, which increased at follow-up.

This mixed picture of parental judgment may reflect some of the problems of using rating scales in the diagnosis of ADHD.³⁴ Obviously, parents' reports differed depending on the scales they used. An ES of 0.62 between pretesting and follow-up was attained for Conners' Rating Scale. Here, parents have to observe their child for 3 consecutive days; ratings are given on 8 items with scores from 0 ("not at all") to 3 ("very much"). On the other hand, the rating scale for DSM-IV criteria contains 40 items, and parents can agree or disagree with each item. According to the Conners' Rating Scale, group data are below the clinical cutoff at follow-up, whereas the categorical judgment with the DSM-IV rating scale yielded much less improvement (ES = 0.14). It may be easier to make a decision that a symptom has weakened than that it has disappeared altogether. It is important to note that the cutoff for the 8 items on Conners' Rating Scale is 15 (for a 3-day observation period: 45).

One could further speculate that the small effects assessed with the DSM-IV scale are related to factors immanent to neurofeedback training. This kind of training may initiate a learning process that needs time and

practice to result in perceivable changes of behavior in complex situations. The same argument might be valid regarding the result that teachers did not see changes in academic achievement, although they rated attention as improved and hyperactivity and impulsivity as reduced. Teachers may hesitate to rate academic improvements before the final examinations, which occurred after the 6-month follow-up. A follow-up ≥ 12 months after the end of training is in progress and should shed light on this hypothesis.

In the absence of a comparable control group, no conclusions of causal relationships between improvement in behavior and cognition and the ability to regulate brain activity can be made. However, it could be shown for the first time that the ability to produce potential shifts in negativity trials without feedback predicts clinical outcome. It was our intention to show in this first experiment that children with ADHD can self-regulate their SCPs and that ESs are substantial and comparable to other types of treatment. Blinding of therapists and patients is unethical in most psychiatric, psychological, and even psychopharmacologic studies. Margraf et al³⁵ demonstrated in a randomized, double-blind comparison of an antidepressant, a minor tranquilizer, and placebo that the great majority of patients as well as their physicians were able to rate accurately whether the active drug or a placebo had been given. Thus, even drug studies cannot be double-blinded in many cases because patients and therapists will perceive positive or negative therapeutic effects. The use of a control group for neurofeedback has comparable limitations: false feedback, for example, is usually detected by patients and leads to adverse effects.³⁶ Even a waiting-list condition does not control for unspecific effects; in expectation of a therapeutic intervention, hope of success may induce changes in behavior. A control group with psychopharmacologic treatment is extremely difficult to compare with an attention-demanding, highly interactive treatment such as the neurofeedback training used in our study. Considering the problems of controlling for unspecific effects, the prediction of clinical outcome by variables of electrophysiology is a viable alternative. The improvements shown are comparable to other effective treatments such as pharmacologic interventions and behavioral treatment, as reported above. Assuming that these studies controlled for placebo effects, the conclusion that our new treatment approach showed comparable efficacy to the reports in the literature seems to be acceptable.

The group in this pilot study was rather heterogeneous regarding gender, medication, and diagnosis. A study with more children should clarify these questions. Moreover, more elaborate control of unspecific effects, medication, gender, and subtypes is needed to confirm the assumption that training to self-regulate SCPs is a viable treatment modality for ADHD. Regulation of SCPs and medication may involve similar neurophysiological

and biochemical pathways; negative potentials of frontal brain areas reflect the balance between cholinergic and dopaminergic activity.¹⁶ Improvement of attentional regulation of frontocentral negative SCPs should affect exactly this balance. With voluntary regulation of SCPs, children may learn to flexibly adjust their cholinergic-dopaminergic balance to task requirements. We assume that the acquired skill becomes automatic and, as a motor skill, is preserved without explicit practice. The children use it flexibly, and success rewards and improves the skill, the behavior, and attention beyond the end of training.

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Self-regulation of Slow Cortical Potentials: A New Treatment for Children With Attention-Deficit/Hyperactivity Disorder

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