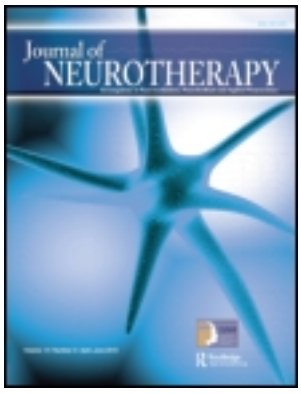

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NEUROFEEDBACK FOR ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: INVESTIGATION OF SLOW CORTICAL POTENTIAL NEUROFEEDBACK—PRELIMINARY RESULTS

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Attention deficit/hyperactivity disorder (ADHD) is characterized by symptoms of inattention, impulsivity, and hyperactivity. Compared to ADHD in children, only a few studies have investigated ADHD in an adult population, and even less have investigated new forms of treatment such as neurofeedback. Neurofeedback has been applied effectively in various areas, especially in the treatment of children with ADHD, and symptom improvements were associated with increased amplitude of the contingent negative variation (CNV). This study investigated if any behavioral and electrophysiological changes reflected in the CNV can be observed after 15 sessions of SCP neurofeedback training. Furthermore, a comparison of CNV amplitude in adults with ADHD and a healthy control group was conducted. Continuous 22-channel EEG was acquired from 10 adults who met *DSM–IV* criteria for ADHD and 8 matched healthy controls. EEG recordings were collected pre/midtreatment and included resting EEG, P300, and CNV tasks as well as ADHD behavioral questionnaires. The adult ADHD group received 15 sessions of SCP training at Cz (referenced to A1, ground A2). The control group only underwent the EEG recording. After 15 sessions of SCP-training a significant improvement in self-ratings of ADHD symptoms was reported. In addition, a trend in increasing CNV mean amplitude was observed after training. A significant difference in baseline CNV between the adult ADHD group and the healthy control group was observed. These results give a promising outlook to the outcome after the completion of 30 sessions of SCP training. The differences in CNV amplitude between the ADHD group and healthy controls are in line with other studies about adult ADHD and CNV. This supports the idea of impaired self-regulation in adult ADHD. The behavioral improvements and increase in CNV after SCP training suggests that SCP training has a positive effect on adult ADHD symptoms and their origin.

INTRODUCTION

This article presents a preliminary analysis of changes in behavior and event-related potentials (ERPs) at the midway evaluation of a slow cortical potential (SCP) training for adult attention-deficit/hyperactivity disorder (ADHD).

ADHD is one of the most common disorders of childhood with a cumulative incidence of 7.5% by 19 years of age (Barbaresi et al., 2004). Furthermore, 30% to 65% of children with ADHD keep their symptoms into adulthood (Faraone, Biederman, & Mick, 2006), which is reflected in a 4% to 5% prevalence rate of adult ADHD in the population worldwide (Goodman & Thase, 2009). The primary symptoms of adult ADHD still include inattentiveness, impulsivity, and hyperactivity, although symptoms of hyperactivity diminish with increasing age (Barkley, 2002). Other

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symptoms of adult ADHD are educational, occupational, and social problems; neuropsychological impairments (Rostain, 2008); and a high risk of unemployment, divorce, and arrest (Barkley, Fischer, Smallish, & Fletcher, 2006; Biederman, Faraone, Keenan, Knee, & Tsuang, 2006). Also, the comorbidity with other psychiatric disorders has been found to be as high as 65% to 89% (for an overview, see Sobanski, 2006).

Despite these problems and the growing need for treatment, only 11% of the adult ADHD group receives treatment (Kessler et al., 2006). The development and evaluation of treatments for adult ADHD is needed as well as basic research of adult ADHD in general.

Similar to childhood ADHD, a reduced orbitofrontal volume in the left hemisphere (Hesslinger et al., 2002), less gray matter in prefrontal areas and in the anterior cingulum (Seidman et al., 2006) have been observed in adults with ADHD. These changes indicate impairments of executive functions like attention, impulsivity, and working memory. Furthermore, electroencephalogram (EEG) differences such as an increased Theta/Beta ratio (Bresnahan, Anderson, & Barry, 1999; Bresnahan & Barry, 2002) and decreased absolute and relative beta power (Clarke et al., 2008) have been found in adults with ADHD compared to healthy controls. These differences suggest processing deficits in adults with ADHD (for an overview see Clarke et al. 2008).

ERPs are useful to investigate the neurophysiological basis of cognitive functions and have been extensively investigated in childhood ADHD (for a review, see Barry, Johnstone, & Clarke 2003) but rather limited in adult ADHD. In adult ADHD early components have been found to differ from healthy controls indicating an enhanced frontal N1, globally enhanced P2, globally diminished N3 (Barry et al., 2009), reduced P300 amplitude (Szuromi, Czobor, Komlósi, & Bitter, 2010), and prolonged P300 latency (McPherson & Salamat, 2004). These differences in early ERP components observed in adult ADHD and differences in late ERP components in children with ADHD (for an overview, see Barry et al., 2003) lead to the assumption that late ERP components like SCPs and contingent negative variation (CNV) could be impaired in adults with ADHD as well.

SCPs are very low electrical shifts in the brain activity (<0.5 s—several seconds after stimulus onset). They reflect the threshold regulation mechanisms of cortical activation (negative shift) and inhibition (positive shift; Birbaumer, Elbert, Canavan, & Rockstroh 1990). SCPs can be described as a phasic tuning mechanism in regulation of attention (Rockstroh, Elbert, Lutzenberger, & Birbaumer, 1993). Negative shifts increase the firing probabilities, whereas positive shifts decrease the firing probabilities of the underlying cell assemblies. SCPs relate to cognitive performance and motor actions, whereas a negativation reflects provision of resources, and planning and initiation of goal-directed behavior and positivation reflects consumption of resources and disfacilitation of excitation thresholds (Strehl, 2009). A strong relationship between SCPs and cognitive and behavioral performance has been observed especially in slow negative shifts and reaction time, stimulus detection, short-term memory, and attention (Birbaumer et al., 1990).

The CNV is a wide and prolonged slow negative potential over central sites. The CNV develops in reaction to a warning stimulus in cue- or go-trials and reflects anticipation and/or or preparation, motor preparation, and attentional behavior (Walter, Cooper, Aldrige, McCallum, & Winter, 1964). It increases with the amount of cognitive energy in anticipation of a task performance, and a decrease has been found in children with ADHD. Compared to healthy controls, reductions of the CNV amplitude during cognitive preparation following a warning stimulus are common in children with ADHD (e.g., Banaschewski et al., 2003, 2004; Perchet, Revol, Fourneret, Mauguière, & Garcia-Larrea, 2001; Sartory, Heine, Müller, & Elvermann-Hallner, 2002; van Leeuwen et al., 1998). Dhar, Been, Minderaa, and Althaus (2010) found a tendency for healthy controls to show larger CNV in the 1550–1650 ms poststimulus interval compared to adults with ADHD. Also, in a study about Gilles de la Tourette Syndrome, patients with additional

ADHD showed an attenuated early CNV compared to healthy controls or Gilles de la Tourette Syndrome without ADHD (Weate, Newell, Bogner, Andrews, & Drake, 1993). The findings of a decreased CNV are in line with dysfunctional regulation of energetical resources in ADHD (Sergeant, 2000) and with negative SCP shifts representing higher neural excitability (Birbaumer et al., 1990). Thus, ADHD, characterized by impaired excitation thresholds, indicates a treatment of self-regulation, which can be achieved with neurofeedback, particularly with SCP training. Neurofeedback is a variant of EEG biofeedback that aims to acquire self-regulation over certain brain activity patterns in an operant conditioning paradigm (Hammond, 2007.) A meta-analysis of the efficacy of neurofeedback treatment in ADHD reported a large effect size on impulsivity and inattention and a medium effect size for hyperactivity for frequency as well as SCP feedback treatment (Arns, de Ridder, Strehl, Breteler, & Coenen, 2009). In a comparison of Theta/Beta frequency training and SCP training for children with ADHD, Wangler et al. (2011) found an increase of the CNV in cue trials for only the SCP training. The long-term behavioral improvements of SCP training for children with ADHD (Heinrich, Gevensleben, Freisleder, Moll, & Rothenberger, 2004; Leins et al., 2007; Strehl et al., 2006), the observed CNV changes (Heinrich et al., 2004; Wangler et al., 2011) and the ability of adults to learn the self-regulation of SCPs (Birbaumer et al., 1990) has led to the idea to investigate the effect of SCP training for adult ADHD.

The objectives for this study were to assess whether SCP training improves core symptoms of ADHD as well as mood and as a neurophysiological measure the CNV mean amplitude. In addition, the CNV mean amplitude of adults with ADHD and matched healthy controls were compared.

METHODS

Participants

This study was approved by the ethics committee of the University of Tübingen, and all participants signed informed consent. The ADHD group and the group of healthy controls were recruited through the University of Tübingen. The healthy controls were matched in age, gender, and IQ to the ADHD group. Inclusion criteria were a full scale IQ of at least 80 and a minimum age of 18 years. The ADHD group had to score above 18 points on the ADHD self-rating scale (described next) and the control group had to score below 18 points.

Procedure

Diagnostics and Questionnaires. The ADHD group underwent the ADHD diagnosis, premeasurements (T1), 15 sessions of SCP neurofeedback, repeated questionnaire as well as EEG measures after 15 sessions of training (T2). The ADHD diagnosis included a demographic and medical history questionnaire, the Structured Clinical Interview for *DSM–IV* Axis I Disorders (SCID-I; Wittchen, Zaudig, & Fydrich, 1997) and the borderline personality disorder section from the SCID-II to rule out comorbid disorders (exclusion criteria: current depression, borderline, anxiety disorders, addiction, personality disorders and any neurological disorders or general medical conditions). As a nonverbal intelligence test we used the Culture Fair Test-20 Revised (Weiss, 2008). Depression and mood were assessed with the German version of the Beck Depression Inventory (BDI-II; Hautzinger, Keller, & Kühner, 2006). ADHD was assessed with parts of the German assessment battery for adult ADHD ''Homburger ADHS-Skalen für Erwachsene'' (Rösler, Retz-Junginger, Retz, & Stirglitz, 2008) from which three tools were used: the self-report questionnaire about childhood ADHD (WURS-K; 25 questions on a 0–4 Likert scale; score higher than 30 must have been met), the self-report questionnaire about the current symptoms (ADHD-SB; 18 questions on a 0–3 Likert scale; score higher than 18 must have been met), and the structured Wender-Reimherr Interview in which seven symptoms are rated on a 0-to-2 Likert scale, with five to 10 questions for each core symptom, held by a trained interviewer (inattention and hyperactivity criteria had to be fulfilled in addition to at

least two other criteria out of temper, affective lability, emotional reactivity, disorganization and impulsivity).

After a short phone screening (demographics, medical history, and current medication or therapy) the questionnaires ADHD-SB, WURS-K, and BDI-II (plus additional ones that are not be specified for this article) were sent to the participants to be filled in at home. If participants fulfilled the inclusion criteria, diagnostics and EEG-recordings were performed on 2 different days. As mentioned, this study is part of a larger project where tasks completed for the whole project included assessment of eyes-closed (15 min) and eyes-open (5 min) resting state, active auditory P300 auditory oddball, passive auditory P300 auditory oddball, and auditory CNV. This article describes only the auditory CNV task.

The controls underwent only part of the diagnostic procedure, including the ADHD-SB, BDI-II, Culture Fair Test-20 Revised, demographic and medical history questionnaire, and the EEG assessment.

Neurophysiological Testing. EEG data were recorded using 22 EEG channels positioned according to the international 10-20 system with the NeXus-32 (Mind Media B.V. with Biotrace+Software). The NeXus-32 is a DC amplifier, in which EEG is sampled at 500 Hz with a range of 263 μV and a bandwidth of DC–70 Hz. EEG activity was recorded at Fp1, Fp2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, Oz, O2, using the NeXus EEG electrode cap with sintered electrodes referenced to common average.

Eye movements were recorded with two horizontal pregelled Ag/AgCl electrodes attached to the outer canthi of each eye and two vertical electrodes attached above and below the middle of the left eye. Impedance levels for all electrodes were below 5 kΩ. Data were stored for offline analysis.

Auditory CNV. The CNV task was an active, auditory, eyes-closed task. A warning stimulus S1 (500 Hz, 50 ms) was followed by an S2, which was either a No-Go low tone (1000 Hz, 50 ms, $N = 350$) or a Go high tone (2000 Hz, 50 ms, $N = 50$) to which the subject needed to react with a press on the space bar. The time between S1 and S2 was 1700 ms, and the time between S2 and S1 varied randomly between 2000 and 2400 ms. The sound pressure level of all tones was 90 dB.

SCP-Neurofeedback Training Sessions. SCP training was conducted with the THERAPRAX® (neuroConn GmbH, Germany). The training protocol was developed by researchers in the lab at the Institute of Medical Psychology and Behavioral Neurobiology and has been used for many years in a variety of studies (Strehl, 2009). SCPs were recorded at Cz referenced against mastoid A1 with a ground electrode on mastoid A2. Eye movements were recorded with two horizontal electrodes attached to the outer canthi of each eye and two vertical electrodes attached above and below the middle of the left eye. Ag/AgCl ring electrodes were used on all sites.

Each SCP-training session consisted of four blocks of 40 trials, with each trial lasting 12 s and consisting of three phases: a baseline phase (seconds 0–2), an active phase (seconds 2–10), and a reinforcement phase (seconds 10–12). The 2-s baseline data were set to zero. At the end of the baseline phase, participants were cued by a triangle directed to the top of the screen to ''activate'' their brain or by a triangle directed to the bottom of the screen to ''deactivate'' their brain. ''Activation'' means to produce a SCP-shift in the electrically negative direction; ''Deactivation'' means to produce a SCP-shift in the electrically positive direction. Trials, which required activation and deactivation, were randomly distributed with a 50/50% rate. In the active phase an object moved from left to right over the screen to provide feedback of the activation or deactivation of the brain activity by moving up or down. In the reward phase, participants received a visual reward if they directed their brain activity in the cued direction for at least 2 s in the second half of the trial. If they could not perform in the cued direction, the screen remained empty.

Participants were trained one to three times per week for a total of 15 sessions. Each session lasted about 1 hr, including preparation time. To generalize newly acquired regulation skills to everyday life situations, 25% of all trials

TABLE 1. Characteristics of the ADHD Group and the Healthy Control Group

	N	Age	IQ	Current ADHD	Childhood ADHD	BDI-II
ADHD	10	28.4 (3.83)	112.5 (13.03)	29.9 (5.89)	33.9 (8.74)	10.05 (7.89)
Control	8	26.71 (2.87)	115 (6.56)	4.5 (3.55)	X	1 (1.29)

Note. Standard deviations are in parentheses. ADHD = attention deficit/hyperactivity disorder; BDI = Beck Depression Inventory; X = data not collected.

served as ''transfer trials'' in which no visual feedback was presented during the active training phase. The level of success was indicated with the visual reward system only. Participants were also instructed to use their self-regulation in everyday life situations. These 15 sessions constitute the first phase of the training. After a break of about 3 weeks patients will return for another phase of 15 sessions.

Analysis

Dependent Variables. As primary outcome the changes in core symptoms were assessed by the ADHD-SB (self-report). Variables of secondary outcome included mood (BDI-II) and changes in CNV (mean amplitude and area).

Independent Variables. For the pre–post evaluation the independent variable is the treatment. In addition, for the comparison of the neurophysiologic and cognitive data the health status (healthy and ADHD subjects) constitutes another independent variable. Training data are reported elsewhere as soon as all patients have completed all 30 sessions.

Statistical Analysis

Behavioral Data. A paired sample *T* test for the ADHD-SB and the BDI-II was calculated for the baseline (T1) and the assessment after 15 sessions of SCP training (T2) for 10 participants. For all comparisons the effect size Hedges's *d'* was calculated using the mean average, standard deviation, and sample size using the program MetaWin 0.2.

CNV Analysis. The EEG data were filtered (low cutoff: 0.5 Hz, high cutoff: 30 Hz, notch: 50 Hz), 100 ms prior S1 baseline corrected and averaged for all Go-events with a correct response. The mean activity was calculated 1300–1600 ms post S1. A paired sample *T* test was performed to compare T1 and T2. Also the CNV data from the control group were compared to the T1 assessment of the ADHD group with an independent *T* test. Due to one corrupted file only nine data sets were included for the ADHD group.

RESULTS

Participants

The descriptive data of the ADHD group of 10 patients (four female) and a group of eight age, gender, and IQ matched healthy controls (three female) is shown in Table 1. Two of the ADHD adults were medicated with a daily dose of Ritalin (20 mg). For the EEG assessment they were asked to not take the medication 12 hr prior to the measurement. However, they were allowed to take the medication parallel to the SCP training but were asked to not change the dose rate or report any changes in medication. Two participants from the ADHD group and two from the control group were left-handed. For ADHD and BDI-II differences between the ADHD group and the control group, see Table 1.

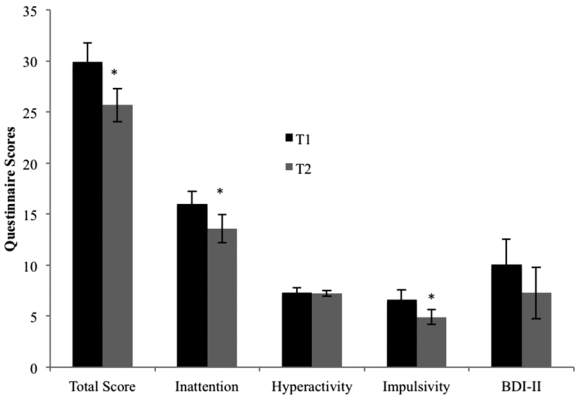

FIGURE 1. Comparison of the attention deficit/hyperactivity disorder questionnaire data before training (T1, black) and after 15 sessions of SCP training (T2, gray). BDI = Beck Depression Inventory. $^{*}p < .05$.

TABLE 2. Effect Size Hedges's *d′* and Variance for the Behavioral Data Pre–Post 15 Sessions of SCP-Training

	ADHD-SB	Impulsivity	Inattention	Hyperactivity	BDI-II
Effect size	–0.73	–0.60	–0.56	–0.08	–0.33
Variance	0.21	0.21	0.21	0.20	0.20

Note. ADHD = attention deficit/hyperactivity disorder; BDI = Beck Depression Inventory.

Behavioral Data

Behavioral data of T1 and T2 are shown in Figure 1. The paired sample *t* test comparing T1 and T2 data revealed a significant reduction in the total score of ADHD symptoms, $t(9) = 2.653$, $p < .05$; in inattention, $t(9) = 3.597$, $p < .05$; and impulsivity, $t(9) = 2.395$, $p < .05$. A trend in a decreased hyperactivity score was observed. Effect sizes *d′* are shown in Table 2.

Contingent Negative Variation

ADHD versus Healthy Controls. An independent *t* test showed a significant difference

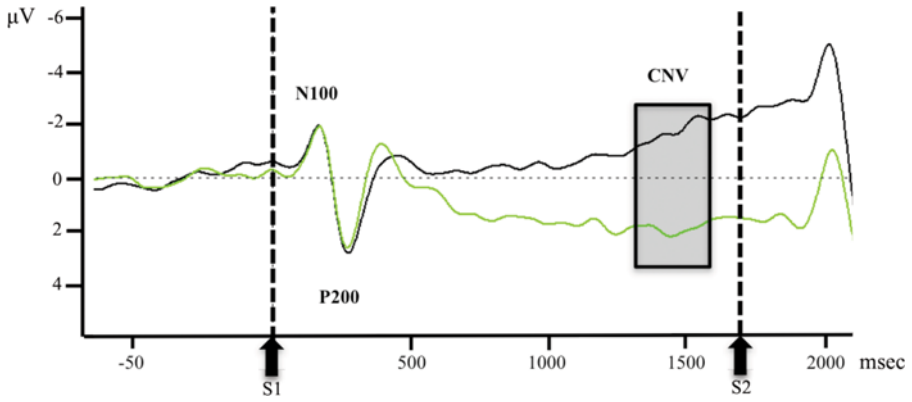

FIGURE 2. Grand average event-related potentials at Cz for the auditory contingent negative variation (CNV) task for the control group (black line) and the attention deficit/hyperactivity disorder group at T1 (green line). *Note.* Early components and the CNV are labeled. The warning stimulus (S1) and the Go-stimulus (S2) are indicated and they gray window indicates the 1300–1600 ms analysis window of CNV post S1. (Color figure available online.)

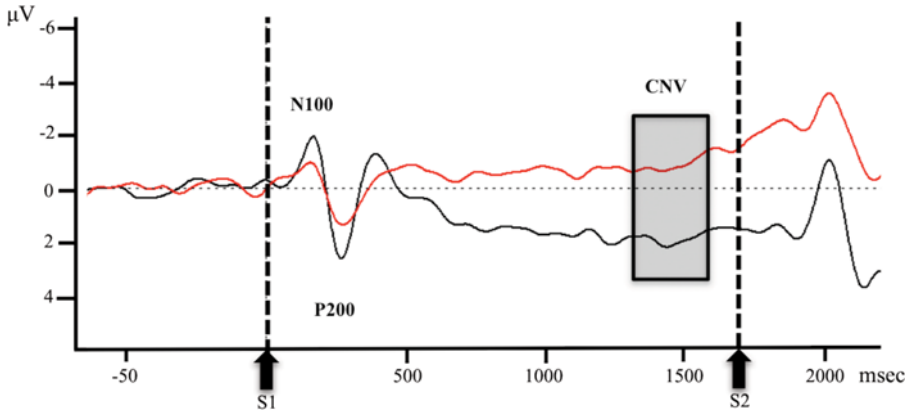

FIGURE 3. Grand average event-related potentials at Cz for the auditory contingent negative variation (CNV) task for the attention deficit/hyperactivity disorder group at T1 (black line) and the attention deficit/hyperactivity disorder group at T2 (red line). *Note.* Early components and CNV are labeled. The warning (S1) and the Go-stimulus (S2) are indicated and they gray window indicates the 1300–1600ms analysis window of CNV post S1. (Color figure available online.)

between controls ($M = -1.89$, $SE = 1.84$) and the ADHD group ($M = 1.78$, $SE = .49$), $t(15) = 1.821$, $p < .05$, $d' = -0.84$) in CNV mean amplitude at Cz. Figure 2 shows the ERPs with labeled components for the control group compared to the ADHD group at T1.

Pre versus Post 15 Sessions of SCP-Training. After 15 sessions of neurofeedback there is a trend toward an increase of the CNV mean amplitude from T1 ($M = 1.78$, $SE = 1.84$) to T2 ($M = -.95$, $SE = .72$, $d' = -0.62$) in mean activity. Figure 3 shows the ERPs with labeled components for the ADHD group at T1 and T2.

DISCUSSION

In this article, preliminary data on 10 adults with ADHD before and after 15 sessions of SCP neurofeedback training are presented as well as data of the adult ADHD group compared to eight matched healthy controls.

A positive effect of the SCP training is reflected in behavioral as well as electrophysiological data. A significant decrease in the total score of ADHD symptoms, and more specifically for inattention and impulsivity scores, was observed in the self-assessed behavioral data with a medium effect size. Hyperactivity showed a marginal decrease with a small effect size. These decreases over all symptoms after just 15 sessions of neurofeedback are promising for a positive outcome after 30 sessions and a total of 20 patients. The observed improvement in mood as reflected in the decreasing BDI-II score is also an indicator for the effects of SCP-training.

The behavioral improvements are also reflected in the electrophysiological data. We observed a nonsignificant increase of the CNV amplitude after training but with a medium effect size. This result after only 15 sessions of SCP training considering the small sample size is promising as to the further project.

The significant difference between the control group and the ADHD group in CNV mean amplitude showing a decrease for the ADHD group with medium to large effect size confirms the trends observed in adults (Dhar et al., 2010; Weate et al., 1993). This supports the observations already reported in childhood ADHD (e.g., Banaschewski et al., 2003, 2004; Perchet et al., 2001; Sartory et al., 2002; van Leeuwen et al., 1998).

Overall, these preliminary results give a promising outlook for the outcome of the whole project and support the possible efficacy of SCP training for adult ADHD.

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