Changes in negative and positive EEG shifts during slow cortical potential training in children with attention-deficit/hyperactivity disorder: a preliminary investigation
Junichi Takahashi, Akira Yasumura, Eiji Nakagawa and Masumi Inagaki

We examined the effects of self-regulation of slow cortical potentials (SCP) in nine children with attention-deficit/hyperactivity disorder (ADHD) by focusing on the changes in electroencephalographic (EEG) shifts during SCP sessions. In SCP training, individuals learn to increase and decrease their cortical excitabilities (enhancement of negative and positive cortical shifts). To examine the efficiency of SCP training, we conducted an attention task and measured contingent negative variation, which relates to the attention maintenance ability. Moreover, to assess training effects at the behavioral level, the Japanese ADHD rating scale (SNAP-J) was completed by the parents. In SCP training, we analyzed changes in EEG shifts during 16 training sessions by calculating the peak amplitudes of positive and negative shifts. The results of EEG data showed that peak amplitudes increased in sessions 11 and 12 for negative shifts and in sessions 9 and 13 for positive shifts. Moreover, we found an enhancement of contingent negative variation amplitude in the attention task before and after training, suggesting that the ability of these children to maintain attention could be modified by SCP training. However, significant behavioral improvements were not observed on the Japanese ADHD rating scale. It has been proposed that the number of additional training sessions may affect both physiological and behavioral improvements. Our present results, however, suggest the possibility that even low numbers of training sessions, such as 16, can bring about physiological improvement, whereas greater numbers of training sessions may be needed to have an influence on behavioral changes. NeuroReport 2014, 25:618–624 @ 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Department of Developmental Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan

Correspondence to Junichi Takahashi, PhD, Department of Developmental Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry, 4-1-1 Ogawahigashi, Kodaira, Tokyo 187-8553, Japan
Tel: +81 042 341 2711; fax: +81 042 346 1944; e-mail: j.taka.j@gmail.com

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the best of our knowledge, the mechanisms behind SCP training have not been fully determined. Direct examination of changes in neural activity during training sessions would seem to be the best approach. A previous study [14] has examined the relationship between SCP training (negative and positive SCPs) and functional MRI BOLD signal changes in adults with typical development. The results showed that the generation of negative SCP was associated with widespread neural activation in the central, the prefrontal, and the parietal regions, as well as in the basal ganglia. The generation of positive SCP was accompanied by widespread neural deactivation at several cortical sites, as well as some activation, primarily in frontal and parietal areas, in addition to the insula and putamen. A further study by this group [15] examined the BOLD signal correlates to the CNV amplitude in adults with typical development, in addition to the relationship between SCP training and the BOLD signal changes. They found that there was a significant correlation between neural activation in the left thalamus and the right supplementary motor area and the enhanced CNV amplitude. These investigations contribute to our understanding of the mechanisms behind SCP training in children with ADHD.

In the current study, we examined the effect of SCP training on cortical excitability in children with ADHD. The main purpose of our study was to investigate changes in EEG (negative and positive shifts) in children with ADHD during SCP training. SCP training aims to generate negative (increased excitation) and positive (decreased excitation) SCPs over the sensorimotor cortex [6]. This means that children have to learn to effectively distinguish between negative and positive EEG shifts depending on the training sessions. To examine these changes, we focused on the peak amplitude between baseline and negative EEG shifts and between baseline and positive EEG shifts in each training session: large peak amplitudes for negative (or positive) EEG shifts during SCP training indicated that children effectively generated negative (or positive) SCPs over the sensorimotor cortex.

Methods
Participants
Ten children with ADHD (seven boys and three girls, mean age = 12 years 6 months, range 8 years 5 months to 16 years 7 months) participated in SCP training mainly during their summer holidays. They were recruited from patients who were referred to the outpatient clinic of the Child Neurology Section of the National Center of Neurology and Psychiatry Hospital, Kodaira, Japan. All the participants had normal or corrected-to-normal visual acuity. Written informed consent was obtained from each participant and their parents before participation, after a full explanation of the experiment. The ethics committee of the National Institute of Mental Health, National Center of Neurology and Psychiatry, approved the study protocol. Pediatric neurologists made the diagnoses on the basis of Diagnostic and Statistical Manual of Mental Disorders, 4th ed., text revision (DSM-IV-TR) criteria [1]. No individual’s full intelligence quotient was lower than 80, when tested using the Wechsler Intelligence Scale for Children, 5th or 4th ed. [16,17].

SCP training and analysis
We administered EEG NF training over a period of 10 weeks (July to September, 2013) with two sessions per week during summer vacation (August). The NF system NeuroPrax (NeuroConn, Ilmenau, Germany) was used for SCP training (see also Fumuro et al. [18]). Each session of SCP training lasted for ~12 min, and was composed of 60 trials, of which half were positive condition and the remaining half were negative condition. The target (e.g. a sunfish, a ship, or a plane) moved slowly from left to right and had to be directed upwards (negative condition) or downwards (positive condition). Transfer trials, without contingent feedback, were also administered for 12 trials out of 60 trials (20%), comprising six positive and six negative trials. Each trial lasted about 10 s (the baseline period was 2 s and the feedback period was 8 s). The feedback was calculated from a Cz electrode (reference: right earlobe; ground electrode: forehead; bandwidth: 0.01–30 Hz; sampling rate: 128 Hz) according to the International 10–20 system [19], and impedances were kept below 20 kΩ. The trial was judged successful if the SCP amplitude exceeded a defined level (the levels of negative and positive trials were set to a baseline of −40 and +40 μV, respectively) and lasted more than 2 s (with each successful trial, the sun was presented on the screen as a reward). Two psychologists conducted all the training programs. Each child sat in front of an LED monitor and he/she was asked to enforce attentiveness in the negative condition, or to be relaxed in the positive condition, as in a previous study [13].

We analyzed EEG changes due to SCP training for sessions 1–16 because one 9-year-old boy completed only 16 sessions. We calculated peak amplitude between baseline and negative shifts of EEG. In addition, we calculated peak amplitude between baseline and positive shifts of EEG. We conducted a two-way repeated-measures analysis of variance (ANOVA) using the factors of sessions (16; 1–16) and subtraction (2; baseline and peak amplitude) as within-participant factors in the negative and also separately to the positive condition (excluding transfer trials).

ERP recording and analysis
To examine the effect of SCP training on the CNV component before and after training, we conducted an attention task similar to the MOGRAZ around 2 weeks to a month before and after training (NoruPro Light Systems Inc., Tokyo, Japan) (Fig. 1). The MOGRAZ is suitable in terms of EEG for examining the ability of children to
focus their attention [20]. We used three types of mole images (10° of visual angle) as experimental stimuli, each of which appeared on the screen in one of four quadrants. We used a 17-inch CRT monitor (Trinitron CPD-G220; Sony, Tokyo, Japan) with a 60 Hz refresh rate and a resolution of 1024 × 768 controlled by a personal PC (VAIO PCV-A31N; Sony). In each trial, a cueing stimulus (the mole with sunglasses) was presented for 300 ms. After a blank interval appeared for 500, 1500, or 3000 ms (1500 ms was the experimental condition in 80% of all trials, 500 and 3000 ms for filler conditions in 20% of all trials); and the target or distractor stimulus (the mole with or without glasses) was presented for 300 ms. ISI, interstimulus interval.

The EEG was recorded from four AG/AgCl electrodes (Fz, Cz, Pz, and Oz) according to the International 10–20 system [19], and impedances were kept below 20 kΩ (Alliance Works; VIASYS Healthcare Inc., Madison, Wisconsin, USA). The vertical electrooculogram and the horizontal electrooculogram were also recorded. The ear electrodes were used as reference electrodes. Band-pass filtering was set from 0.05 to 30 Hz. The signals between 100 ms before and 2500 ms after the onset of the cueing stimulus (the mole with sunglasses) were digitized at a sampling rate of 250 Hz.

To compare differences in the CNV amplitudes before and after training, we focused on the Cz electrode in a previous study [6], and ERP data were analyzed using a t-test with the factor of time (2: before and after training), which was performed separately for every 100 ms from 700 to 1800 ms. During ERP data analysis, we used the target mole (with glasses) condition, and on average children had fewer than 16 artifact-free trials out of 32 trials for the target mole condition.

Behavioral data
To examine behavioral changes due to SCP training sessions, we calculated the proportion of successful trials. Because one 9-year-old boy completed only 16 sessions, we conducted a one-way repeated-measures ANOVA.
using sessions (16) as a within-participants factor in the negative and the positive conditions (excluding transfer trials), separately, similar to the analysis of EEG changes.

In addition, the Japanese ADHD rating scale [the Japanese version of the Swanson, Nolan, and Pelham Rating Scale (SNAP-J) [21]] completed by the parents was used to assess training effects at the behavioral level. This questionnaire is composed of 26 items, including three categories: inattention, impulsivity/hyperactivity, and oppositional defiant disorder. The symptom severity of each item is rated on a four-point Likert scale (0: ‘not at all’ to 3: ‘very much’). We conducted a t-test with time as a factor (2: before and after training) in the scores of each and every category individually.

**Results**

**Results of EEG measures**

We excluded the data of one child who declined the SCP training halfway. Thus, data of nine children were included in the final analysis.

For the EEG results (Fig. 2a), the two-way repeated-measures ANOVA was applied to the negative and also separately to the positive condition.

In the negative condition, we found a significant main effect of sessions $F(15,120) = 1.86$, $P < 0.05$, $\eta^2 = 0.19$, and a significant interaction between these factors $F(15,120) = 1.86$, $P < 0.05$, $\eta^2 = 0.19$. In the significant interaction, the simple main effect of sessions was observed $F(15,240) = 3.71$, $P < 0.05$, $\eta^2 = 0.32$, suggesting that the peak negative amplitude in session 12 was larger than that in sessions 2, 3, 5, 7, 8, 10, 13, 15, and 16 $t(240) = 4.49$, $P < 0.05$; sessions 12 vs. 3: $t(240) = 4.55$, $P < 0.05$; sessions 12 vs. 5: $t(240) = 4.19$, $P < 0.05$; sessions 12 vs. 7: $t(240) = 4.29$, $P < 0.05$; sessions 12 vs. 8: $t(240) = 3.63$, $P < 0.05$; sessions 12 vs. 10: $t(240) = 5.13$, $P < 0.05$; sessions 12 vs. 13: $t(240) = 3.97$, $P < 0.05$; sessions 12 vs. 15: $t(240) = 4.02$, $P < 0.05$; sessions 12 vs. 16: $t(240) = 3.69$, $P < 0.05$. In addition, the peak negative amplitude in session 11 was larger than that in session 10 $t(240) = 3.65$, $P < 0.05$. Also, a simple main effect of subtraction was observed in session 12 $F(1,128) = 11.95$, $P < 0.001$, $\eta^2 = 0.09$ and marginal simple main effects of subtraction were observed in sessions 1, 10, and 11 $t(128) = 3.24$, $P = 0.07$, $\eta^2 = 0.02$; session 10: $F(1,128) = 2.78$, $P = 0.09$, $\eta^2 = 0.02$; session 11: $F(1,128) = 3.90$, $P = 0.05$, $\eta^2 = 0.03$. In sessions 1 and 11, the peak negative amplitude was larger than that at baseline. In contrast, in session 10, the peak positive amplitude was larger than that at baseline.

In the positive condition, a significant main effect of sessions $F(15,120) = 1.92$, $P < 0.05$, $\eta^2 = 0.11$ and a significant interaction between these factors $F(15,120) = 1.92$, $P < 0.05$, $\eta^2 = 0.11$ were observed. Regarding this interaction, we found a simple main effect of sessions $F(15,240) = 3.83$, $P < 0.001$, $\eta^2 = 0.19$, suggesting that the peak positive amplitude in session 13 was larger than that in sessions 1, 3, 4, 5, 6, 7, 8, 10, 11, 12, 14, and 16 $t(240) = 4.51$, $P < 0.05$; sessions 13 vs. 3: $t(240) = 4.76$, $P < 0.05$; sessions 13 vs. 4: $t(240) = 3.51$, $P < 0.05$; sessions 13 vs. 5: $t(240) = 3.30$, $P < 0.05$; sessions 13 vs. 6: $t(240) = 3.91$, $P < 0.05$; sessions 13 vs. 7: $t(240) = 5.36$, $P < 0.05$; sessions 13 vs. 8: $t(240) = 4.04$, $P < 0.05$; sessions 13 vs. 10: $t(240) = 3.53$, $P < 0.05$; sessions 13 vs. 11: $t(240) = 5.47$, $P < 0.05$; sessions 13 vs. 12: $t(240) = 4.93$, $P < 0.05$; sessions 13 vs. 14: $t(240) = 3.93$, $P < 0.05$; sessions 13 vs. 16: $t(240) = 3.28$, $P < 0.05$. In addition, the peak positive amplitude in session 9 was larger than that in session 11 $t(240) = 3.57$, $P < 0.05$. Moreover, we observed a simple main effect of subtraction in session 13 $F(1,128) = 15.17$, $P < 0.001$, $\eta^2 = 0.11$ and a marginal simple main effect of subtraction in session 9 $F(1,128) = 3.88$, $P = 0.05$, $\eta^2 = 0.03$. In these sessions, the peak positive amplitude was larger than that at baseline.

**Results of ERP measures**

We excluded the data of one child who could not complete the attention task in pretraining from the data of the nine children who were included in the final analysis of SCP training. Thus, data for eight children were included in the final analysis.

A t-test showed a significant difference in the 800–900 ms time window $t(7) = 2.66$, $P < 0.05$, Cohen’s $d = 0.51$. In this time window, the negative amplitude after training was larger than that before training (Fig. 2b).

**Results of behavioral measures**

For the behavioral changes (Fig. 2c) in the SCP sessions, we performed a one-way repeated-measures ANOVA for each negative and positive condition. There was no significant effect of sessions in the negative $F(15,120) = 1.54$, $P = 0.10$, $\eta^2 = 0.06$ or the positive $F(15,120) = 1.46$, $P = 0.13$, $\eta^2 = 0.15$ conditions.

For the results of the ADHD rating scale, we conducted a t-test with time as a factor of time (2: before and after training) for each category. However, there were no significant differences in any category [all: $t(7) = 0.65$, $P = 0.54$, Cohen’s $d = 0.01$; inattention: $t(7) = 0.13$, $P = 0.90$, Cohen’s $d = 0.01$; impulsivity/hyperactivity: $t(7) = 0.34$, $P = 0.74$, Cohen’s $d = 0.01$; oppositional defiant disorder: $t(7) = 0.86$, $P = 0.42$, Cohen’s $d = 0.05$].

**Discussion**

In the present study, we examined the effects of self-regulation of SCP on children with ADHD by focusing on changes in EEG data during SCP sessions. The SCP training comprised 60 trials (~12 min) including negative and positive conditions. In each training session, a target object moved slowly from left to right and had to be directed upwards (negative condition) or downwards (positive condition).
condition). Children were asked to enforce attentiveness in the negative condition or to be relaxed in the positive condition. Moreover, to examine the efficacy of SCP training, we conducted an attention task and measured CNV, which relates to the ability to maintain attention. Also, the Japanese ADHD rating scale (SNAP-J: [21]) completed by the parents was used to assess training effects at the behavioral level. In the analysis of SCP training, we examined changes in EEG data during 16 training sessions by calculating the peak amplitudes of negative and positive shifts, in addition to behavioral data. The results showed that EEG peak amplitude increased in sessions 11 and 12 for a negative shift and in sessions 9 and 13 for a positive shift. Moreover, in the analysis of the attention task, we found that the CNV amplitude after training was larger than that before training, suggesting that our present SCP training enhanced the attention maintenance ability in these children. However, we found no significant effects in the scores of the Japanese ADHD rating scale before and after training.

The purpose of SCP training is to generate negative (increased excitation) and positive (decreased excitation)
SCPs over the sensorimotor cortex [6]. In this situation, children have to learn to effectively distinguish between negative and positive EEG shifts (enhancement of negative and positive cortical shifts) during the training sessions. We proposed that peak negative and positive amplitudes might become significantly larger with increasing numbers of SCP sessions, if children with ADHD completed SCP training successfully. In line with this consideration, we found that the peak amplitude for a negative shift increased in sessions 11 and 12, whereas the peak amplitude for a positive shift increased in the sessions 9 and 13. On the basis of these EEG results, we found that children with ADHD showed successful training effects during SCP sessions. We also found that the enhancement of these shifts might not be linear during the SCP sessions.

These EEG results might be supported by the ERP results. To compare the amplitude of CNV, which relates to the attention maintenance ability, we conducted an attention task (similar to the MOGRAZ [20]) before and after training. Enhancement of CNV amplitude was observed, suggesting improvements in attention maintenance in children with ADHD. SCP training has been shown to influence functional MRI BOLD signal changes [14], which correlates with the CNV amplitude in adults with typical development [15]. Specifically, because the amplitude of slow negative waves relate to the allocation of attention resources [22], generation of negative SCP may be important for children with ADHD. Consistent with these findings, SCP training in the current study enhanced CNV amplitude, and this amplitude may be a good index for judging the efficacy of SCP training in children with ADHD, whereas SCP training has not previously been shown to modulate the P3 amplitude [6]. Consistent with this finding, our current results also did not show enhancement of the P3 amplitude. Our ERP measurements might be an appropriate method for investigating the effects of SCP training on the CNV component.

One might argue that the number of training sessions in the present study was too small, because previous studies have indicated that the number of training sessions required to modify the ability of attention in children with ADHD might be as many as 30 [7] or 36 [23] (see also Gevensleben et al. [8]). Other studies [24,25] have indicated that a small number of training sessions is sufficient to bring about improvement of this ability. A previous study [24] has reviewed 14 NF studies and calculated that training was given for ~46 min (range = 30–60 min), two and a half times per week (range = 1–5/week), over 32 sessions (range = 18–40 sessions), and during the course of 13 weeks (range = 2–24 weeks). Considering another review [25], the score of inattention at the behavioral level was improved depending on the number of training sessions, whereas no effect of training was observed on hyperactivity or impulsivity scores.

In our present study, we administered only 20 sessions and used 16 sessions of these for analysis. Nevertheless, we were able to observe EEG changes in both the negative and the positive peak amplitude during SCP sessions. Moreover, we found an enhancement of CNV amplitude before and after training. However, we found no significant effects in the scores of the Japanese ADHD rating scale (SNAP-J). These results can be interpreted as follows: even low numbers of training sessions, such as 16 or 20 sessions, might lead to EEG and ERP improvements in children with ADHD. In contrast, low numbers of training sessions might not constitute an intervention generating behavioral improvement in these children. In general, a physiological change may be produced earlier than a behavioral change. Thus, we speculate that even low numbers of training sessions could influence physiological changes, although more training sessions may be necessary to affect behavioral changes. As the problem of the number of sessions necessary to improve disorders in children with ADHD has been considered in many previous studies, future research will be needed to carefully examine the precise relevance of these session numbers.

**Conclusion**

The present results showed changes in EEG shifts (enhancement of negative and positive cortical shifts) during 16 SCP sessions. Consistent with these EEG changes, we also demonstrated enhancement of the CNV amplitude. However, there were no significant behavioral improvements. These results suggest that even low numbers of training sessions can have an influence on physiological changes (EEG and ERP), whereas increased numbers of training sessions may be necessary to have any influence on behavioral changes.

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**Conflicts of interest**

There are no conflicts of interest.

**References**


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