

If-then planning modulates the P300 in children with attention deficit hyperactivity disorder

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Children with attention deficit hyperactivity disorder have difficulties with tasks that require response inhibition. We measured electroencephalographic data of nonmedicated children with attention deficit hyperactivity disorder and control children in two conditions: (a) a neutral condition without a self-regulation strategy and (b) a condition that involved the making of if-then plans (i.e. 'If situation X is encountered, then I will perform the goal-directed behavior Y'). If-then

plans improved response inhibition and increased the P300 in children with attention deficit hyperactivity disorder compared with the neutral condition. The present results encourage the application of self-regulation using if-then plans in addition or as an alternative to common medical therapy. *NeuroReport* 18:653–657 © 2007 Lippincott Williams & Wilkins.

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Introduction

Children with attention deficit hyperactivity disorder (ADHD) are impulsive [1]. They have difficulties waiting their turn, they are more likely to interrupt another person speaking, or they might not finish reading a problem in a math exam. Likewise, children with ADHD have difficulties performing Go/NoGo tasks [2], that is, tasks that require a response to one kind of stimulus, but the inhibition of a response to another.

ADHD is typically treated with methylphenidate (MPH) – an amphetamine, acting on the dopamine system [3] – that has positive effects on the core symptoms inattention, hyperactivity, and impulsivity [4]. MPH, however, is a controversial drug as its long-term effects are unclear [5,6]. Despite concerns, over the past decade the prescription of MPH has increased comparatively more than the increase in prevalence would predict [7,8].

The performance of children with ADHD on Go/NoGo tasks is improved by MPH [9,10]. A similar effect can be achieved by teaching children the self-regulation strategy of implementation intentions [11,12], that is making 'if-then' plans, which facilitate the translation of task goals into effective goal-directed action, thereby helping these children to achieve better executive control [13]. Implementation intentions alleviate the need for conscious executive control by delegating control to prespecified critical environmental cues. Implementation intentions take the format of 'If situation X is encountered, then I will perform the goal-directed behavior Y' and thus link a critical anticipated situation (if part) to a goal-directed behavior (then part).

Implementation intentions have proven to be an effective self-regulatory tool in various domains [14].

Go/NoGo tasks typically invoke the P300 component in the electroencephalogram (EEG). P300 occurs when selective attention is paid and a response decision is required [15]. NoGo stimuli evoke higher amplitudes than Go stimuli, reflecting the endogenous evaluation of response control or conflict monitoring. In children with ADHD the amplitude increase in response to NoGo stimuli compared with Go stimuli is less pronounced [16].

The NoGo P300 has been localized to the anterior cingulate cortex (ACC, [16,17]). Owing to the fact that the ACC tends to be coactivated with the dorsolateral prefrontal cortex in neuroimaging studies, it is viewed as an important route for frontal brain regions to regulate motor behavior [18]. The ACC is also strongly activated when a response conflict occurs and, therefore, seems to be involved in error detection, conflict monitoring, and behavioral adjustment after erroneous responses [19]. Most importantly, the ACC was found to be influenced by the mesencephalic dopamine system [18] – a system that is altered in children with ADHD [3].

In this study, we investigated the influence of the self-regulation strategy of making if-then plans on the P300 component in a Go/NoGo task. We compared nonmedicated children suffering from ADHD with control children in (a) a neutral condition not involving a self-regulation strategy and (b) a planning condition that involved the making of if-then plans (i.e. implementation intentions, [11,12]).

Methods

Participants

Thirteen (one female) children diagnosed with ADHD and 16 (one female) age-matched control children (12.4 ± 0.37 and 12.9 ± 0.33 years, respectively) participated after giving informed consent. The study was approved by the research ethics committee of the University of Konstanz and is compliant with the World Medical Association Declaration of Helsinki. Children with ADHD were recruited through a collaborating child psychiatric outpatient center in Konstanz. The children were selected by the head child psychiatrist as diagnosed with ADHD combined type [1] only. None of the children with ADHD had been prescribed medication within the previous 12 months. Control children were contacted through the participant record system of the University of Konstanz. Each child underwent two EEG measurements on separate days, approximately 4 weeks apart and was rewarded with 20¢ after finishing the second session.

Task

The Go/NoGo task consisted of 360 stimuli (50% colored drawings of transportation vehicles and 50% colored drawings of animals) that were presented on a computer screen (Samsung Samtron 96 BDF 19", Schwalbach, Germany) approximately 60 cm away from the children's eyes using E-Prime. Stimuli lasted 1000 ms and were presented with an ISI of 1500 ms. At 500 ms before each stimulus, a fixation cross was shown in the middle of the screen. The children were asked to respond to animals and vehicles by pressing one of two colored buttons, respectively. The correspondence of stimulus type and response-button was reversed after the first half of the experiment to prevent the task becoming too easy. Thirty training trials that were excluded from further analysis introduced each half of the experiment to ensure that children understood the task. At 150 ms before 33% of the trials, a stop sign was presented for 150 ms. The stop sign was a white sprawled-out hand on a circular purple background. The stop sign indicated that no response was to be given on the following trial. The trials following stop signs were treated as NoGo-trials; all other trials were Go-trials.

Instructions

Children received either a regular instruction of how to perform the task (neutral condition) or they were given an instruction involving an if-then plan (planning condition). The neutral instruction contained information concerning the task (e.g. pressing one button for animals and the other for vehicles and not pressing a button at times the hand was shown). The if-then plan in the planning condition was formulated as follows. If I see a hand, then I will not press any button. The planning condition did not involve more instructions than the neutral condition; the conditions only differed in the nature of the phrasing. Instructions in both conditions were standardized and did not differ between children.

Procedure and electroencephalogram recordings

At the first session, all children were given the neutral instruction on how to perform the Go/NoGo task. At the second session, all children were assigned the if-then plan. This was not counterbalanced to make sure that children

would not utilize the self-regulation strategy in both sessions. Whilst the children performed the Go/NoGo task, their EEG was recorded using a high-density 257-channel cap (Geodesic Sensor Net 200, Eugene, Oregon, USA) chosen to fit optimally each child's head. Data were recorded continuously with a sampling rate of 250 Hz and an online band-pass filter of 0.1–100 Hz after making sure that impedance values did not exceed 30 k Ω .

Electroencephalogram data analysis

All EEG data analysis was performed using BESA (Graefeling, Germany). EEG data epochs (–100 to 800 ms in relation to stimulus onset) for correct Go-trials (trials followed by a correct button press) and correct NoGo-trials (trials correctly followed by no response) were averaged per participant and condition (neutral, planning), excluding epochs containing other artefacts (signal amplitudes $>250 \mu\text{V}$). NoGo–Go difference waveforms were created by subtracting Go-trials from NoGo-trials. Data were low-pass filtered at 30 Hz. Grand average waveforms were computed by averaging Go, NoGo, and NoGo–Go epochs across participants within group and condition. A prominent P300 in NoGo trials, and respectively NoGo–Go difference waves were found at electrode Cz and nine surrounding channels.

For statistical analysis (using Statistica, Tulsa, Oklahoma, USA), mean amplitudes were computed for the NoGo–Go difference wave per participant and condition in two consecutive time windows (160–312 and 312–452 ms) after averaging the waveforms of Cz and nine surrounding electrodes. Within the time windows, mean amplitudes were compared between groups using repeated measures analyses of variance with within-participant factor CONDITION (neutral, planning). Planned comparisons were computed in case of statistically significant interactions. For the grand average NoGo waveforms, a regional dipole was fitted in a time window comprising the P300 component per group and condition. The first component of a preceding principal component analysis of the grand average signal explained $>99\%$ of the variance of the signal, suggesting that a single source would be an adequate characterization of the underlying activity. It is very unlikely that a single underlying source can account for the variance in the NoGo–Go grand average waveforms. Therefore, a distributed source model (minimum L2 norm) was computed per group and condition. The minimum-norm approach is a common method to estimate a distributed electrical current image in the brain at each time sample [20]. The sources are evenly distributed using 1426 standard locations 10 and 30% below the smoothed standard brain surface. As the number of sources is much larger than the number of sensors in a minimum norm solution, the inverse problem is highly underdetermined and must be stabilized by a mathematical constraint, the minimum norm. Out of the many current distributions that can account for the recorded sensor data, the solution with the minimum L2 norm, that is the minimum total power of the current distribution, is displayed.

Behavioral data analysis

Behaviorally, the number of correct responses following Go trials, the number of correctly inhibited responses following NoGo trials, and reaction times in Go trials were analyzed. Reaction times of three children with ADHD could not be

included in analyses for technical reasons. None of the data was normally distributed; therefore, Wilcoxon tests for paired samples were computed for within-group differences between conditions. For between-group comparisons, Mann-Whitney *U*-tests were used.

Nonparametric Spearman correlations were calculated between NoGo-Go mean amplitudes and behavioral performance in the individual groups and conditions. The significance level of all statistical analyses was 5%. Standard errors are reported.

Results

Behavioral results

Behaviorally, children with ADHD inhibited their response less efficiently after NoGo trials than control children in the neutral condition ($87.3 \pm 2.8\%$ vs. $94.5 \pm 2.5\%$, $z=2.01$, $P<0.05$). This group difference was not present in the planning condition ($90.1 \pm 2.4\%$ ADHD vs. $95.3 \pm 2.2\%$ control). Children with ADHD also had significantly slower reaction times than children without ADHD in the neutral (606 ± 22 ms vs. 509 ± 17 ms) and the planning condition (625 ± 23 ms vs. 490 ± 18 ms, $z=2.79$, $P<0.01$ and $z=3.43$, $P<0.01$, respectively). Interestingly, this effect was more pronounced in the planning condition as reaction times slowed compared with the neutral condition in the ADHD group whereas they increased in the control group.

Within the ADHD group and only in the planning condition, a significant correlation was found between NoGo performance and NoGo-Go amplitude difference [$r=0.79$, see Fig. 1b; for display reasons, one outlier in the ADHD group is not shown. If the outlier ($x=4.49$, $y=50.83$) is excluded from the correlation computation, the correlation coefficient changes from $r=0.79$ to $r=0.76$]. The better the ADHD children inhibited their responses after NoGo trials, the bigger the NoGo-Go amplitude difference was. This correlation was not present in the neutral condition ($r=0.19$). It was not significant in the control group in any of the conditions either ($r=0.44$ and $r=0.17$ for the neutral or planning condition, respectively).

P300

In the time window between 160 and 312 ms following the onset of a stimulus children with ADHD showed a significantly smaller NoGo-Go amplitude difference than control children [$F(1,27)=5.22$, $P<0.05$] interaction GROUP \times CONDITION [$F(1,27)=4.8$, $P<0.05$, see Fig. 1a] in the neutral condition, whereas there was no difference between the groups in the planning condition [$F(1,27)=0.07$, $P=0.80$]. Furthermore, children with ADHD had a significantly smaller NoGo-Go amplitude difference in the neutral condition compared with the planning condition [$F(1,27)=4.33$, $P<0.05$], whereas there was no difference between conditions in the control children [$F(1,27)=0.93$, $P=0.34$].

In the consecutive time window of 312–452 ms, control children and children with ADHD had comparable NoGo-Go amplitude differences in the neutral condition [$F(1,27)=0.003$, $P=0.96$] interaction GROUP \times CONDITION [$F(1,27)=4.22$, $P<0.05$, see Fig. 1a]. In the planning condition, however, ADHD children had a significantly larger NoGo-Go amplitude difference than control children [$F(1,27)=6.67$, $P<0.05$]. The NoGo-Go amplitude difference did not differ between conditions in the ADHD group [$F(1,27)$, $P=0.57$, $P=0.46$]. It was significantly smaller in the planning

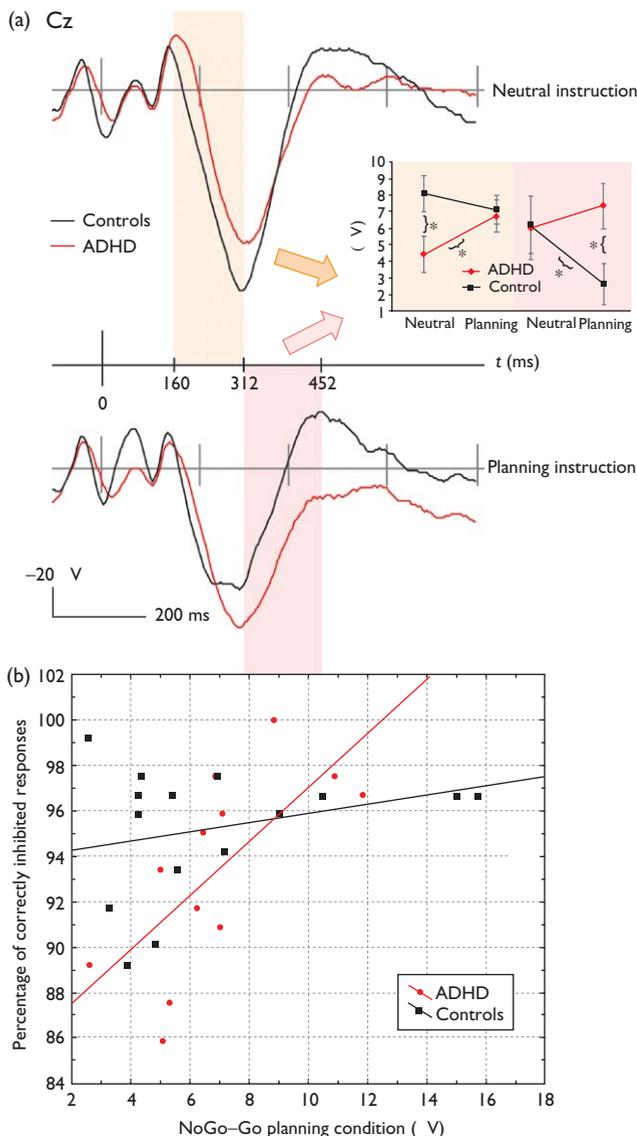


Fig. 1 (a) Grand average waveforms of the NoGo-Go difference at electrode Cz. Control children had a larger NoGo-Go difference than children with ADHD in the early time window (160–312 ms) when they were given the neutral instruction. No difference between the groups was present when children were given the planning instruction. In the later time window (312–452 ms) no difference was found between the groups when the children were given the neutral instruction. In the planning condition, children with ADHD had a more pronounced NoGo-Go difference than control children. Significant differences are marked with an asterisk. Vertical lines represent standard errors. (b) Correlation between the NoGo-Go difference and inhibition performance in the early time window (160–312 ms) of the planning condition. ADHD, attention deficit hyperactivity disorder.

condition compared with the neutral condition in the control group [$F(1,27)=4.99$, $P<0.05$].

Source localization

A regional source was fitted for the grand average NoGo waveforms per group and instruction condition (Fig. 2a, b). Localization was performed in a time window comprising the P300 component. Estimated Talairach coordinates of the sources corresponded to the ACC in all cases (Talairach

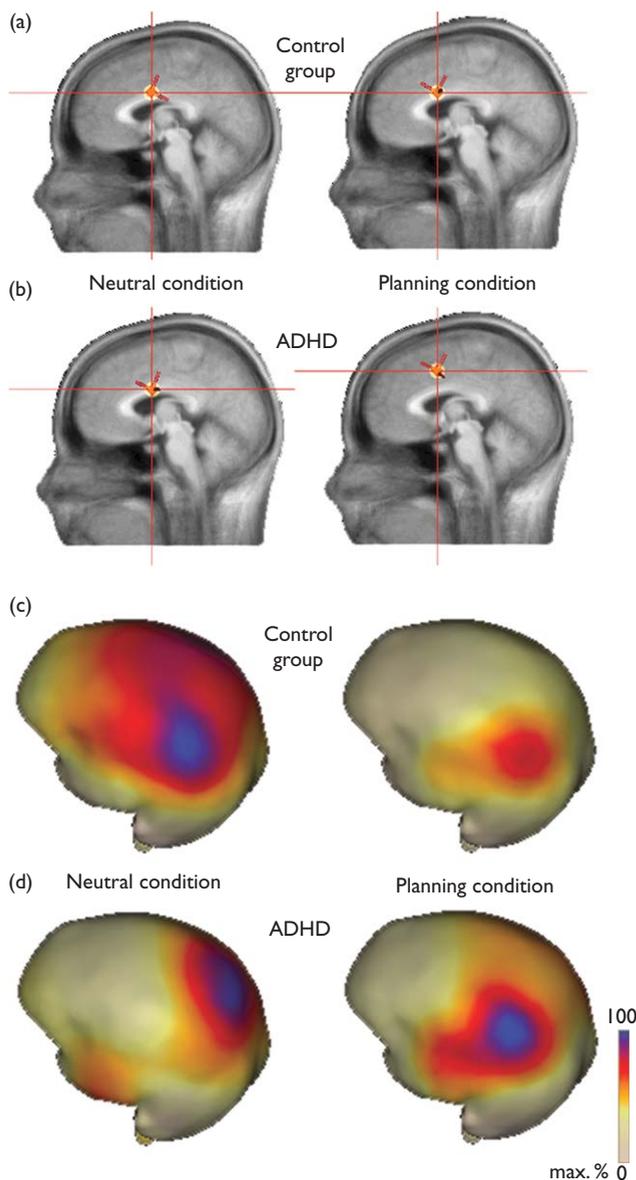


Fig. 2 (a, b) Localization of regional sources at the NoGo peak. All sources were fitted to the ACC. (c, d) Minimum L2 norm output at the global field power peak latency (308 ms). Whereas control children are characterized by a temporoparietal source in both conditions (c), children with ADHD show a more posterior source in the neutral condition and resemble the control children in the planning condition (d). ACC, anterior cingulate cortex; ADHD, attention deficit hyperactivity disorder.

coordinates in mm: controls neutral condition $-2, 1, 29$; controls planning condition $4, -8, 26$; ADHD neutral condition $-3, 0, 26$; ADHD planning condition $-2, -4, 41$). A single source cannot account for brain activation differences in response to NoGo and Go stimuli, as the NoGo and Go P300 most likely have different underlying generators [21,22]. Thus, a distributed source solution was computed at the global field power peak latency (308 ms) of the grand average NoGo-Go difference waves for children with and without ADHD in the neutral and planning conditions, respectively. Control children were characterized by a temporoparietal activation focus in the neutral and

the planning instruction conditions, although the activation strength seemed to be weaker in the planning condition (Fig. 2c). Children with ADHD, on the other hand, showed a more posterior-central focus in the neutral condition and resembled the children without ADHD in the planning condition (Fig. 2d).

Discussion

For the first time it was demonstrated that the self-regulation strategy of making if-then plans alters both behavioral and electrophysiological indices of performance in a Go/NoGo task among children with ADHD. Without this self-regulation strategy, children with ADHD made more inhibition errors following NoGo trials and had a significantly smaller NoGo-Go amplitude difference than control children during the first half of the P300 component. No difference was observed between the control and ADHD groups when the children were given the self-regulation strategy. As the NoGo-P300 represents the endogenous evaluation of response control and conflict monitoring, our results suggest that these processes become more pronounced when ADHD children are given a self-regulation strategy. The high correlation between successful inhibition performance on NoGo trials and the NoGo-Go amplitude difference in children with ADHD suggests that response control itself becomes more efficient. Children with ADHD had slower reaction times than control children. This was more pronounced in the planning condition. This result indicates that the self-regulation strategy of making if-then plans helped the children with ADHD to respond less impulsively (slower), but more correctly.

Although control children did not display an increased NoGo-Go amplitude difference in the planning condition the self-regulation strategy might have had a facilitating effect as the data from the second half of the P300 component suggest. Children with ADHD had a greater NoGo-Go amplitude compared with controls in the planning condition. The reason for that was not an amplitude increase within the ADHD group, but a decrease of NoGo-Go amplitude in the control group. Behavioral performance remained the same, however, suggesting that the self-regulation strategy facilitated response control in children without ADHD and was associated with less activation of related cortical structures, which might be interpreted as less processing effort.

The ERP results are complemented by the result pattern of the minimum condition solutions. Children with ADHD in the planning condition looked strikingly similar to control children in the neutral instruction condition. Although control children exhibited the same activation focus under both conditions, it was weaker in the planning condition. This finding supports the hypothesis that less activation of relevant cortical structures was needed to perform at the same behavioral level within the control group. Children with ADHD showed a more posterior activation focus in the neutral condition compared to the planning condition and to the control children under both conditions. It has been shown that the Go-P300 has maximal amplitudes in more posterior areas than the NoGo-P300 [21,22]. Thus, it might be the case that activation during go-trials dominated the NoGo-Go difference wave under the neutral condition causing the activation focus to be more posterior than in the planning condition.

A candidate structure involved in response control is the ACC [18,19]. The source of the NoGo-P300 was fitted to the ACC in both groups and conditions. The ACC is influenced by the mesencephalic dopamine system [18] that is altered in ADHD [3]. Therefore, ACC functioning may be altered in children with ADHD as well. This might explain why the NoGo-Go amplitude difference was diminished in the neutral condition in the ADHD group despite the fact that the NoGo-P300 was localized to the ACC.

The present findings support the hypothesis that implementation intentions are beneficial for children with ADHD. This might be due to the creation of a strong mental link between the specified critical situation (if part) and the intended goal-oriented behavior (then part). Forming such if-then links delegates the control to prespecified critical environmental cues. In other words, by explicitly specifying when, where, and how a goal has to be transformed into action, implementation intentions disencumber executive functions. Thereby action initiation becomes immediate, efficient, and no longer needs conscious intent [23–25]. Demonstrating that control children need less activation in the planning condition to perform on the same level as in the neutral condition further strengthens this view.

Conclusion

The results of this study suggest that the development of treatment strategies involving if-then planning might be beneficial to children with ADHD and a desirable alternative to medication with psychogenic drugs.

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