

**Title:** Altered proactive control in adults with ADHD: Evidence from event-related potentials during cued task switching

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## **Abstract**

Cognitive control has two distinct modes – proactive and reactive (Braver, T. S. (2012). The variable nature of cognitive control: a dual mechanisms framework. *Trends in Cognitive Sciences*, 16(2), 105–112). ADHD has been associated with cognitive control impairments. However, studies have mainly focused on reactive control and not proactive control. Here we investigated neural correlates of proactive and reactive cognitive control in a group of adults with ADHD versus healthy controls by employing a cued switching task while cue informativeness was manipulated and EEG recorded. On the performance level, only a trend to generally slower responding was found in the ADHD group. Cue-locked analyses revealed an attenuated informative-positivity – a differential component appearing when contrasting informative with non-informative alerting cues – and potentially altered lateralisation of the switch-positivity – evident in the contrast between switch and repeat trials for informative cues – in ADHD. No difference in target-locked activity was found. Our results indicate altered proactive rather than reactive control in adults with ADHD, evidenced by less use of cued advance information and abnormal preparatory processes for upcoming tasks.

**Key words:** proactive control, cued task switching, ERP, ADHD

### **General Scientific Summary**

This study suggests proactive rather than reactive control difficulties in adults with ADHD, evidenced by lesser usage of the information carried by cues as well as by indications of problems with task-specific rule activation in preparation of switching. This new insight adds significantly to our understanding of cognitive control deficits in ADHD with potential clinical implications.

## Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent, early onset neurodevelopmental condition with symptoms of impaired attention, and/or excessive hyperactivity-impulsivity, interfering with functioning or development. Many of the ADHD-related problems have been linked to impairments in cognitive control processes, associated with structural and functional anomalies in the prefrontal cortex (Nigg & Casey, 2005; Tamm, Menon, Ringel, & Reiss, 2004).

Cognitive control is conceptualised as an ability to flexibly adapt to changing circumstances by regulating behaviours so that inappropriate ones are suppressed and required ones are facilitated in response to environmental demands (Braver, Reynolds, Donaldson, & Louis, 2003). Existing models of ADHD (Barkley, 1997; Nigg, 2005; Sergeant, Geurts, Huijbregts, Scheres, & Oosterlaan, 2003) and experimental evidence, implicate abnormalities in cognitive control as a factor significantly contributing to ADHD symptomatology (Durstun, 2003; Durstun, de Zeeuw, & Staal, 2009; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Children as well as adults with ADHD often perform poorer than their healthy counterparts on tasks probing cognitive control (e.g., Cepeda, Cepeda, & Kramer, 2000; Dibbets, Evers, Hurks, Bakker, & Jolles, 2010). Neuroimaging studies provide further evidence for the deep-seated nature of these cognitive control deficits persisting into adulthood by implicating activation, functional connectivity, electrophysiological and structural abnormalities, in brain areas underlying these functions (Bush, Valera, & Seidman, 2005; Castellanos & Proal, 2012; Cortese et al., 2012, 2013; Dickstein, Bannon, Castellanos, & Milham, 2006; Fried et al., 2014; Valera, Faraone, Murray, & Seidman, 2007; Weyandt, Swentosky, & Gudmundsdottir, 2013).

Braver's (2012) model postulates cognitive control as a dual mechanism operating via two distinct control modes – proactive and reactive. Proactive control is a form of active goal-relevant information activation and maintenance that helps us to prepare for cognitively challenging events and primes the attentional and response systems for a required reaction. Reactive control, in contrast, involves transient goal-relevant information reactivation upon the detection of interference and its resolution (Braver, 2012; Braver et al., 2003). Hence, proactive

control represents anticipatory preparation, triggered by contextual cues, prior to the occurrence of an event, while reactive control relates to the detection and resolution of conflict or interference after its onset. In the context of ADHD, studies probing cognitive control, have primarily focused on the reactive control mode, i.e., target-related disturbances. However, event-related potential (ERP) studies suggest that in individuals with ADHD inferior task performance and target-related aberrant brain activity may be preceded by altered preparatory processing during the cue-target phase in paradigms where a cue precedes the target, e.g., cued-CPT, which may reflect altered proactive control. These studies performed in adults and children with ADHD demonstrated a reduced cue-locked P3, reflecting reduced attentional orienting to cues, and diminished contingent negative variation (CNV) amplitudes, indicating less motor preparation or stimulus anticipation in ADHD (Albrecht et al., 2013; Banaschewski, Yordanova, Kolev, Heinrich, et al., 2008; Hauser et al., 2014; Kenemans et al., 2005; McLoughlin et al., 2010; Valko et al., 2009). Adult and child functional magnetic resonance (fMRI) studies have revealed abnormal signal patterns (mostly hypo-activation) during stimulus anticipation (Cubillo et al., 2010; Dibbets et al., 2010; Fassbender, Krafft, & Schweitzer, 2015; Plichta & Scheres, 2014; Sidlauskaite, Sonuga-Barke, Roeyers, & Wiersma, 2015a; Ströhle et al., 2008). While these findings provide clear indications of deviant ADHD-related preparatory processes, there is little systematic research on proactive control in ADHD. In a simple cued paradigm, it is hardly possible to differentiate between cue-related preparatory alerting effects, priming the subject for upcoming events in a bottom-up fashion, and proactive cognitive control, which refers to an active use of cue information in order to prepare for future stimuli in a top-down manner.

A way to systematically study proactive control processes is to manipulate cue-informativeness, hence the load on proactive control. Without manipulating cue-informativeness, it is difficult to tell whether the reduced preparation reflects proactive control impairments or it is the result of reduced general alerting in ADHD, as cues may convey advance information about the task and also have a general alerting property. Manipulating cue-informativeness, especially in combination with ERPs, has been shown to be very

successful for distinguishing proactive and reactive control processes in healthy and clinical populations (Jamadar, Hughes, Fulham, Michie, & Karayanidis, 2010; Jamadar, Michie, & Karayanidis, 2010; Karayanidis et al., 2009; Barcelo & Cooper, 2016; Czernochowski, 2015; Kiesel et al., 2010; Whitson et al., 2014; Wylie, Murray, Javitt, & Foxe, 2008), but surprisingly has not yet been applied in ADHD. In the current study, we therefore followed this approach in order to disentangle the processes implicated in proactive and reactive control and to examine their modulation in a sample of adults with ADHD and healthy controls. We measured ERPs during a cued task switching paradigm, based on the work of Jamadar and colleagues (Jamadar et al., 2010).

Task switching paradigms are frequently used as proxies to investigate cognitive control processes involved in cognitive flexibility (Kok, Ridderinkhof, & Ullsperger, 2006; Ruge, Jamadar, Zimmermann, & Karayanidis, 2013). In such paradigms, participants have to repeat or switch between tasks. Typically, participants respond more slowly on switch versus repeat trials – referred to as the switch cost. In cued task switching paradigms, the switches or repeats can be indicated at the cue level, enabling investigation of proactive control processes. As in previous research (e.g., Jamadar et al., 2010), in the current study we included informative as well as non-informative alerting cues. Informative cues indicate a repeat or switch target, rendering advance anticipatory preparation, while non-informative cues act as an alerting signal, signalling that the target is about to appear without specific task information (a repeat or a switch) at the cue level. By studying cue- and target-locked ERPs, one can investigate covert proactive and reactive control processes, which is not possible with behavioural measures alone (reaction time or switch cost), that represent the cumulative endpoint of all these processes.

Within cued task switching paradigms, proactive control is reflected by the usage of informative cues to prepare for an upcoming task. Research applying such paradigms has revealed two cue-locked ERP components linked to the usage of cue information. Both components have a parietal scalp distribution but have been shown to have distinct temporal and functional characteristics. First, the informative-positivity (~300 ms post cue) – is linked

to the information content of a cue, appearing as a difference ERP component in the contrast between informative and non-informative alerting cues. Hence, the informative-positivity has been argued to index early task-goal related activation processes (e.g., perform the colour, not the shape task), as well as the orienting of selective attention (e.g., attend to the colour, ignore the shape) (Jamadar et al., 2010; Karayanidis et al., 2010a, 2010b; Swainson et al., 2006). This component is followed by the switch-positivity (~450 ms post-cue), reflecting differential switch-related activity (greater for switch than repeat trials), specifically for informative cues. The switch-positivity has been argued to be an index of anticipatory task-set reconfiguration and specific response rule activation (e.g., colour task, blue stimulus – press left button; yellow stimulus – press right button) (Jamadar et al., 2010; Karayanidis et al., 2010a, 2010b; Swainson et al., 2006).

Target-locked ERPs, related to reactive control, also show differential switch-related activity. A decrease in parietal positive activity has been observed for switch relative to repeat trials, referred to as the switch-negativity. This component reflects the effort to overcome interference due to task-set inertia that cannot be initiated until stimulus onset (Karayanidis, Provost, Brown, Paton, & Heathcote, 2011).

In keeping with the hypothesis of impaired proactive control processes, we expected adults with ADHD to show a smaller cue-locked informative-positivity (comparing informative to non-informative alerting cues, as in Jamadar et al., 2010) and/or smaller switch-positivity (comparing informative cue switches to informative cue repeats, as in Jamadar et al., 2010). The target-locked switch-negativity amplitude was also examined to explore potential group differences in processes related to reactive control. Finally, we also included no-cue trials in our paradigm, in which switch or repeat targets were not preceded by any cue. This manipulation allowed us to additionally test for potential group differences in general alerting.

## Method

### Participants

Twenty-three adults with a clinical diagnosis of ADHD (9-inattentive type; 14-combined type) and 23 healthy control individuals participated. Each participant gave their written informed consent prior to the study and received a monetary reward for participation. The study was approved by the local ethics committee. Both groups of participants were recruited via advertising in local magazines, social websites, word-of-mouth, or from the lab's pool of participants who had agreed to be contacted in the future. Each ADHD participant met the lifespan criteria for the disorder and had an official clinical diagnosis, obtained in a clinical setting, as well as a research diagnosis obtained using DSM-IV-based structural clinical Diagnostic Interview for Adult ADHD (DIVA 2.0; Kooij & Francken, 2010). In addition, ADHD participants also scored above the cut-offs on childhood and adulthood ADHD symptom self-report questionnaires: The Wender Utah Rating Scale (WURS; Ward et al., 1993;  $M = 60.91$ ;  $SD = 17.46$ ; cut-off for childhood ADHD – a score higher than 46) and a DSM-based self-report questionnaire gauging problems of inattention and hyperactivity in adulthood and childhood (Kooij & Buitelaar, 1997) (adults with ADHD had to exhibit at least 4 symptoms in the inattentive and/or hyperactive/impulsive domain to meet the adulthood ADHD criteria). Additionally, ADHD symptom severity was measured with the DSM-oriented ADHD scale of the Adult Self-Report (ASR;  $M = 75.81$ ,  $SD = 10.06$ ; Achenbach & Rescorla, 2003). All of the control participants scored below clinical cut-offs on the ADHD questionnaires (WURS:  $M = 26.13$ ,  $SD = 12.70$ ; ASR:  $M = 55.00$ ,  $SD = 5.97$ ). Based on ASR ratings, 4 ADHD participants qualified for comorbid depression, 3 ADHD participants for anxiety disorder and 2 ADHD participants for substance use disorder. Participants had a normal or above normal estimated full scale IQ ( $>80$ ) derived from a seven subtests version of the Wechsler Adult Intelligent Scale (Ryan & Ward, 1999). Groups did not differ on IQ (controls:  $M = 113.21$ ,  $SD = 12.40$ ; ADHD:  $M = 113.26$ ,  $SD = 14.44$ ;  $p = 0.991$ ), sex ratio (controls: 11 females; ADHD: 12 females;  $\chi^2(1) = 0.087$ ,  $p = 0.768$ ) or age (controls: age range 18–38 years;  $M = 23.30$ ,  $SD$

= 3.97; ADHD: age range 19–48 years; M = 26.30, SD = 8.68; p = 0.139). ADHD participants on stimulant medication (7 - methylphenidate and 1 - dextroamphetamine), refrained from their use for 24h prior to testing. The overall exclusion criteria were neurological or psychiatric disease (other than ADHD) and history of brain damage.

### **Task design**

We used a variant of a cued task switching paradigm. On each trial geometric shapes of circle or triangle in blue or yellow were presented as target stimuli on a black computer screen. Participants had to respond to either the shape or the colour of the stimulus, as indicated by a preceding cue. There were three types of cues that could precede the target. First, the informative cue consisted of the word “shape” or “colour” (indicating the task type) which appeared 800 ms before stimulus onset. Secondly, the non-informative alerting cue consisted of only two hyphens, - -, presented on the screen 800 ms before the stimulus alerting that the target is about to appear, but providing no task-specific information. On these trials, the task information (-shape-/colour-), was inserted between the hyphens and appeared on the screen simultaneously with the target. Thirdly, the no-cue condition – no advance cuing was presented and the task information, (-shape-/colour-) appeared on the screen together with the target and prompted participants to respond without any advance preparation. While participants do not see a cue stimulus in this condition, there is a trigger programmed in the task at the time when the no-cue would appear (i.e., 800 ms before target stimulus) granting no-cue-related ERP analyses. Participants were instructed to respond as fast as they could without sacrificing accuracy. There was a total of 576 trials divided into 4 blocks of 144 trials, which were completely randomised (1:1 switch/repeat ratio). This resulted in a total of 192 trials per each cue condition. At the end of each block there was a short break of 30 seconds before the next block began. The experiment took around 35 minutes. An outline of the experimental paradigm is provided in Figure 1.

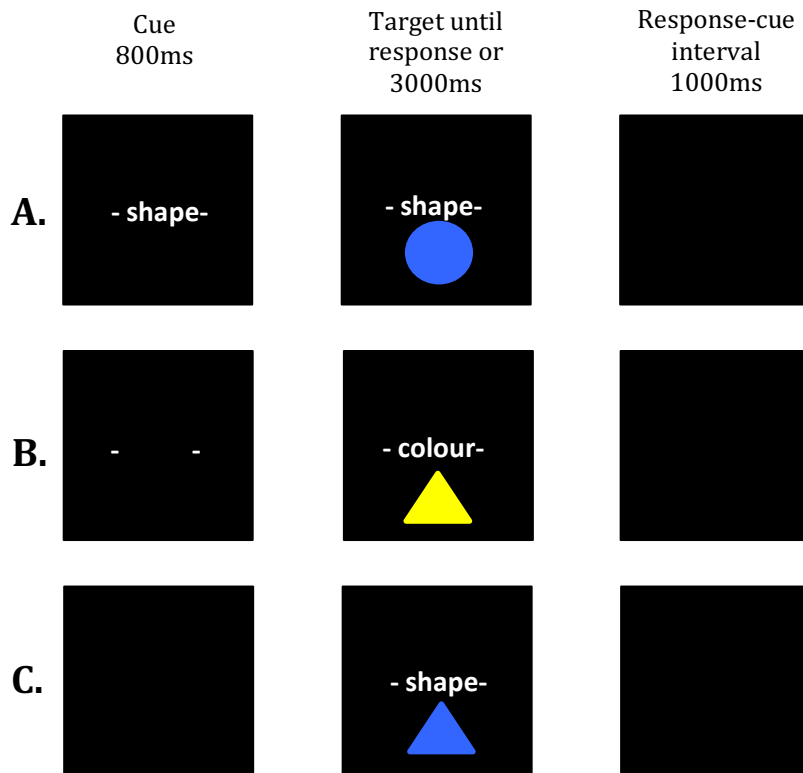


Figure 1. A schematic representation of the experimental paradigm. **(A)** Informative cue trial – the cue contains all the information about the task. **(B)** Alerting cue trial – an alerting signal (-) is presented during the cue phase and exact task information – together with the target. **(C)** No-cue trial – no-cue is presented and all task information is displayed simultaneously with the target. Cue – target interval is kept constant (800ms). Target stays on the screen until the response is executed or for maximum 3000ms. All stimuli were presented on a black screen which did not change during the task presentation.

### EEG data acquisition and processing

EEG data were recorded using a Biosemi Active Two System, with 64 electrodes, while participants performed the cued switching task. The EEG signal was sampled at 2048 Hz and referenced online to the CMS-DLR electrodes. Vertical oculograms were recorded via electrodes positioned above and below the left eye and in line with the pupil. The EEG data were offline rereferenced to the average reference. A 0.1 Hz high-pass filter and a low-pass filter of 70 Hz was applied to the recorded data, together with a notch-filter of 50 Hz.

The data were segmented relative to the onset of cues and targets with epochs of 900 ms. To correct for eye blinks the standard Gratton and Coles algorithm implemented in Brain Vision Analyzer 2.0 was used. The epochs were baseline corrected using a 100 ms pre-cue and pre-target interval. A 100-ms baseline is considered acceptable (Luck, 2014) and used by other researchers employing similar paradigms (e.g., Karayanidis, Coltheart, Michie, & Murphy, 2003; Nicholson, Karayanidis, Bumak, Poboka, & Michie, 2006; Kamiyo & Masaki, 2016; Kapanci et al., 2019). Segments with amplitudes exceeding  $\pm 100 \mu\text{V}$  were considered to be artefacts and hence were rejected from further analyses. A spherical splines procedure was used for interpolating noisy channels. After the data were pre-processed, averages of each trial type were calculated and a low-pass filter of 30 Hz was applied. The averages were based on the three cue conditions, i.e., informative, alerting, no-cue, as well as switches and repeats. Groups did not differ in the number of segments left after artefact rejection for either of the cue conditions, all  $p$ 's  $> 0.05$  (informative cue: M controls = 152.86, SD = 24.39; M ADHD = 149.43, SD = 18.21; alerting cue: M controls = 151.86, SD = 22.63; M ADHD = 145.43, SD = 23.41; no-cue: M controls = 152.69, SD = 25.83; M ADHD = 142.65, SD = 18.92). What is more, the number of ERP epochs remaining after artefact rejection for switch and repeat trials did not differ in informative (M\_switch: 73.43 (SD = 2.12); M\_repeat: 75.78 (SD = 1.73);  $p = 0.122$ ) and alerting (M\_switch: 72.76 (SD = 1.83); M\_repeat: 74.17 (SD = 1.81);  $p = 0.214$ ) cue conditions. Only in the no-cue condition, there were slightly more repeat than switch trials left (M\_switch: 72.43 (SD = 1.89); M\_repeat: 75.28 (SD = 1.67);  $p = 0.017$ ). Error trials were removed from ERP analyses.

Based on similar previous studies by Jamadar and colleagues (2010a,b), we were interested in the following ERP components: the early cue-locked informative-positivity, emerging as an early positivity in the informative-uninformative difference wave; the later cue-locked switch-positivity, reflected in the switch-repeat difference wave for informative cues; and the target-locked parietal switch negativity, with reduced positive activity for switch versus repeat trials. Mean amplitude windows were extracted using the mean area information export function in Brain vision analyzer.

The choice of electrodes and time windows for all the comparisons was based on previous research and maxima within stable across-group topographies. In accord with the studies by Jamadar and colleagues (2010a,b), all the studied ERP components showed posterior topographies (see figures 3, 4, 5; also supplementary material figures 1, 2, 3). Based on these topographies, analyses for the informative-positivity and switch-positivity were done at POz. Because the topographical maps (see figure 4) showed lateralised effects for the switch-positivity, lateral electrodes were additionally included in the analysis of this component (PO3, PO4). The target-related switch-negativity component was quantified at Pz. The informative-positivity was calculated as the average mean amplitude in the window of 300 – 500 ms post cue. The switch-positivity was defined as the average amplitude in the 400 – 700 ms window post cue. Important to note is that the components are established from different contrasts: the informative-positivity is based on the comparison between informative and non-informative cues, while the switch-positivity is based on the comparison between switch and repeat trials, specifically for informative cues. The switch-negativity was quantified as the mean amplitude within a 200 – 500 ms time window post target.

### **Statistical Analysis**

Behavioural data were analysed using repeated measures ANOVAs for response times (RTs) and errors with cue type (informative, alerting, no-cue) and switch (switch, repeat) as within-subject factors and group (control, ADHD) as a between-subjects factor.

Repeated measures ANOVAs were also applied to test our a priori hypotheses regarding our ERP data (i.e., smaller informative positivity and/or switch-positivity in ADHD) and to explore potential group differences in processes related to reactive control (i.e. target-locked ERPs).

To address the hypothesis of a smaller cue-locked informative-positivity in ADHD, a repeated measures ANOVA was employed with cue type (informative, alerting) as within-subject factors and group (controls, ADHD) as a between-subjects factor. Although not

hypothesized, to test for potential group differences in general alerting, we repeated the above analyses, but now for the alerting versus the no-cue condition.

To test our hypothesis of a smaller switch-positivity in ADHD, we applied a repeated measures ANOVA specifically for informative cues with the within-subject factors switch level (switch, repeat) and electrode laterality (PO3, POz, PO4), and group (control, ADHD) as a between-subjects factor.

Potential group differences in the target-related switch-negativity were analysed via a repeated measures ANOVA with cue type (informative, alerting, no-cue), switch level (switch, repeat) as within-subject factors and group (control, ADHD) as a between-subjects factor. All cue types were included in this analysis because of their potentially differential preparatory effects on target processing and because we did not have specific predictions. In doing so, we could explore potential group differences in reactive control as a function of the level of opportunity to prepare in advance (no-cue, cue as a general alerting signal, cue with advance information about the upcoming task).

## Results

### Behavioural data

Figure 2 depicts RTs per cue type and switch/repeat condition. There was a main effect of cue type on RT ( $F(1.46, 64.34) = 674.64, p < 0.001; \eta^2 = 0.939$ ) – participants responded fastest during informative cue trials ( $M = 692.09$  ms), followed by alerting ( $M = 952.74$  ms) and no-cue ( $M = 995.30$ ) conditions (all conditions differed significantly from each other, all  $p$ 's  $< 0.001$ ). Switch and repeat conditions also differentially modulated RT ( $F(1, 44) = 79.82, p < 0.001; \eta^2 = 0.645$ ) – participants were generally faster to respond on repeat trials irrespective of cue type (within each cue condition, switch and repeat RTs differed significantly, all  $p$ 's  $< 0.001$ ). There was a cue type x switch interaction ( $F(2, 88) = 4.72, p = 0.011; \eta^2 = 0.097$ ) indicating the smallest difference between switch and repeat trials in the informative cue condition. Lastly, there was an overall tendency for the ADHD group to respond more slowly irrespective of cue or switch/repeat condition ( $F(1, 44) = 2.86, p = 0.097; \eta^2 = 0.061$ ). Groups did not differ in terms of the percentage of errors ( $F(1, 44) = 0.003, p = 0.955; \eta^2 = 0.000$ ) and performed the task with a very high degree of accuracy ( $>95\%$ ).

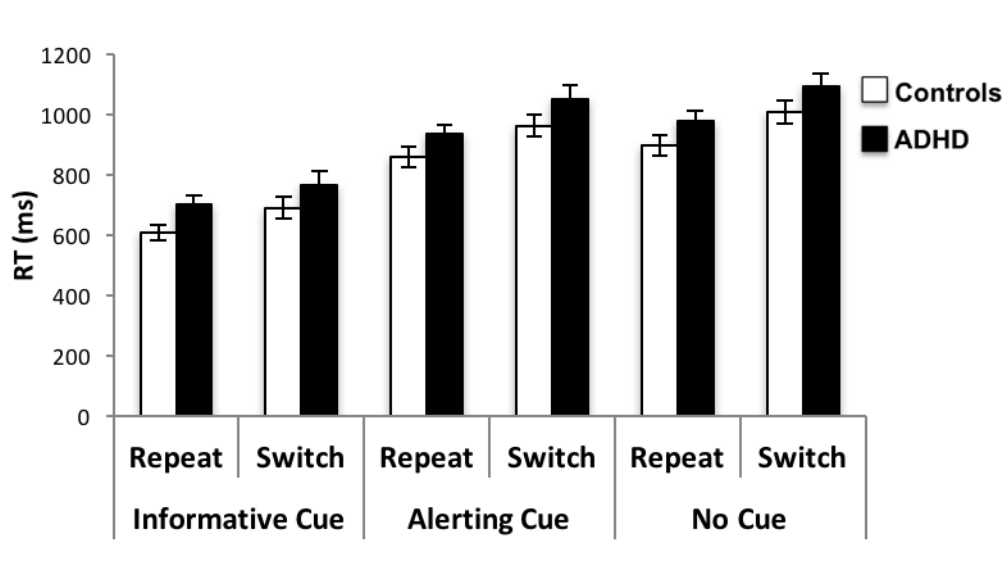


Figure 2. Response times (RT) ( $\pm$ SE) for each cue type and switch/repeat condition in controls and adults with ADHD.

### ERP data

## Cue-locked

As depicted in the difference waves in Figure 4A (raw cue-locked ERPs are shown in Figure 3; for topographies please see Supplementary material), there is an early difference in cue-related activity between informative and alerting cues, referred to as the informative-positivity, 300–500 ms post cue at POz (see also Jamadar et al., 2010).

The repeated measures ANOVA showed a main effect of cue type ( $F(1, 44) = 58.13, p < 0.001; \eta^2 = 0.569$ ), i.e., amplitudes were more positive for cue-locked informative- informative cues than alerting cues. There was no main effect of group ( $F(1, 44) = 0.187, p = 0.667; \eta^2 = 0.004$ ); however, a significant cue type x group interaction ( $F(1, 44) = 4.40, p = 0.042; \eta^2 = 0.091$ ) emerged indicating that the informative-positivity was reduced in the ADHD group, see also Figure 4B (for raw ERPs – Figure 3).

To explore group differences in general alerting effects, we repeated the analysis but now comparing trials with alerting cues to trials with no-cues. There was a main effect of cue type ( $F(1, 44) = 35.95, p < 0.001; \eta^2 = 0.450$ ), indicating that also alerting cues induced positive activity in the time window of the informative positivity, which was not apparent in the no-cue condition. However, there was no main effect of group ( $F(1, 44) = 0.725, p = 0.399; \eta^2 = 0.016$ ) nor a group x cue type interaction ( $F(1, 44) = 0.064, p = 0.801; \eta^2 = 0.001$ ), indicating no difference between groups in general alerting effects.

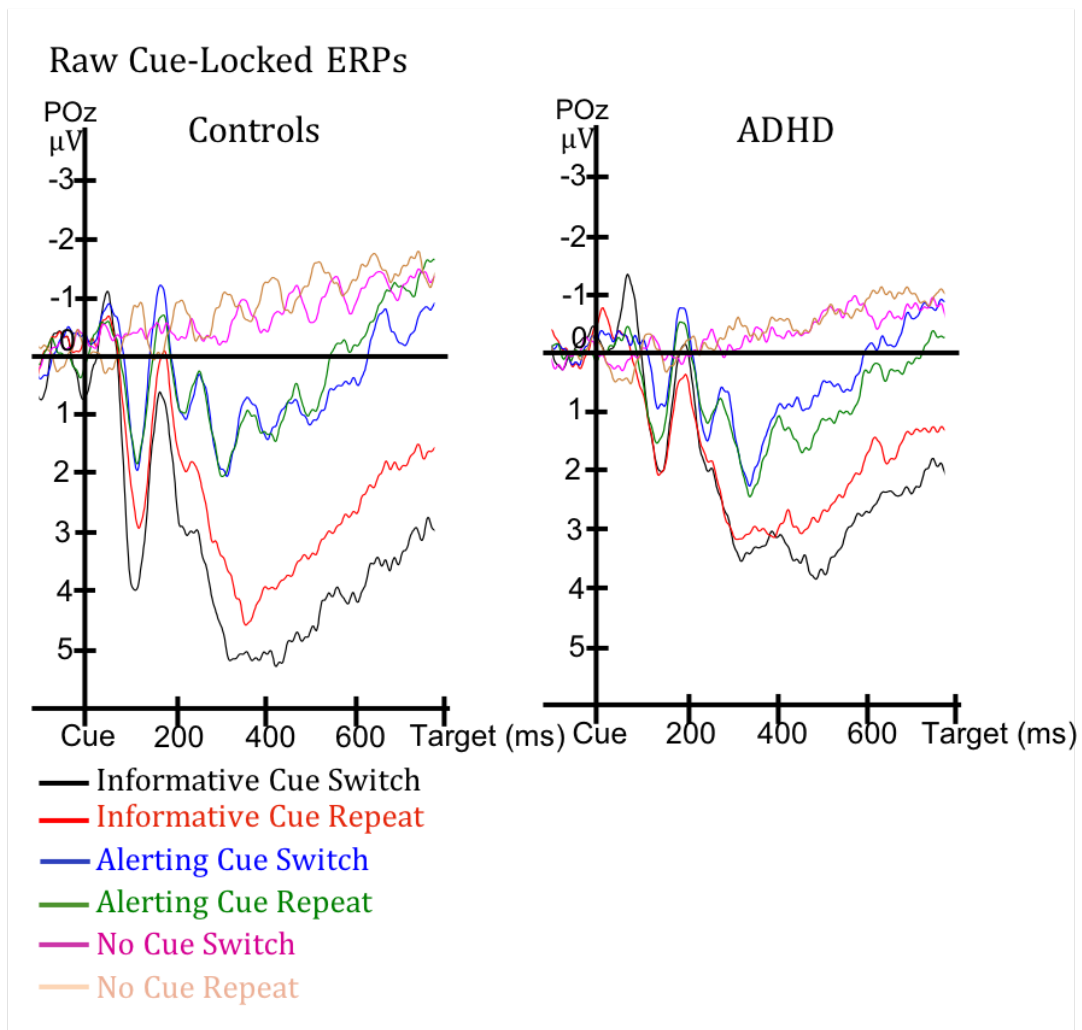


Figure 3. Raw Cue-locked ERPs for informative, alerting and no-cue conditions in controls and individuals with ADHD.

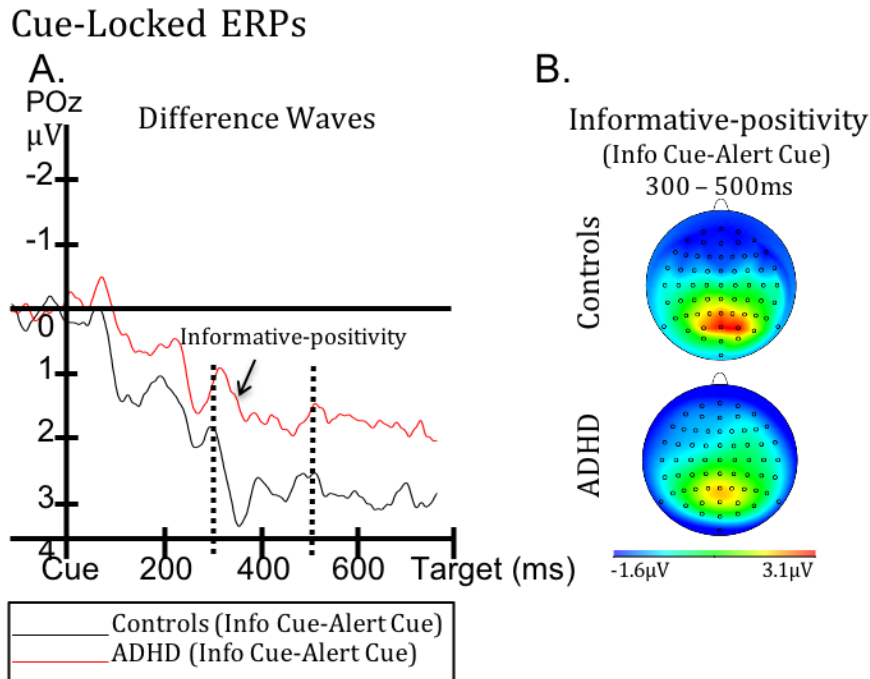


Figure 4. Cue-locked ERPs – informative-positivity. The figure (A) displays the difference waves depicting the informative-positivity at POz and topographic maps (B) for adults with ADHD and control subjects.

We also observed the switch-positivity – a switch-related parietal component following informative cues between 400–700 ms post cue, as can be seen in Figure 5 (see Figure 3 for the raw ERPs; for topographies please see Supplementary material). There was a main effect of switch ( $F(1, 44) = 15.22, p < 0.001; \eta^2 = 0.258$ ), indicating, as expected, that the switch-positivity was observed in the switch versus repeat contrast for informative cues. No main effect of group was observed ( $F(1, 44) = 2.04; p = 0.160; \eta^2 = 0.044$ ). However, we did observe a trend towards a switch x laterality x group interaction ( $F(2, 88) = 2.25, p = 0.086; \eta^2 = 0.054$ ), tentatively suggesting a group difference in lateralisation of the informed positivity (see also figure 5B). However, it has been argued that an ANOVA may not be suitable to test for differences in topography, since the interaction with electrode location can be originating from an enhanced global underlying activation of differences in source. We therefore performed a vector scaling procedure on our data (McCarthy & Wood, 1985). We repeated the above

analyses on the scaled data and it showed an effect for this interaction of  $p = 0.053$ . We tend to believe therefore that the effect may reflect a genuine laterality effect, although results should be interpreted carefully as the effect is only marginally significant, warranting replication.

### Cue-Locked ERPs

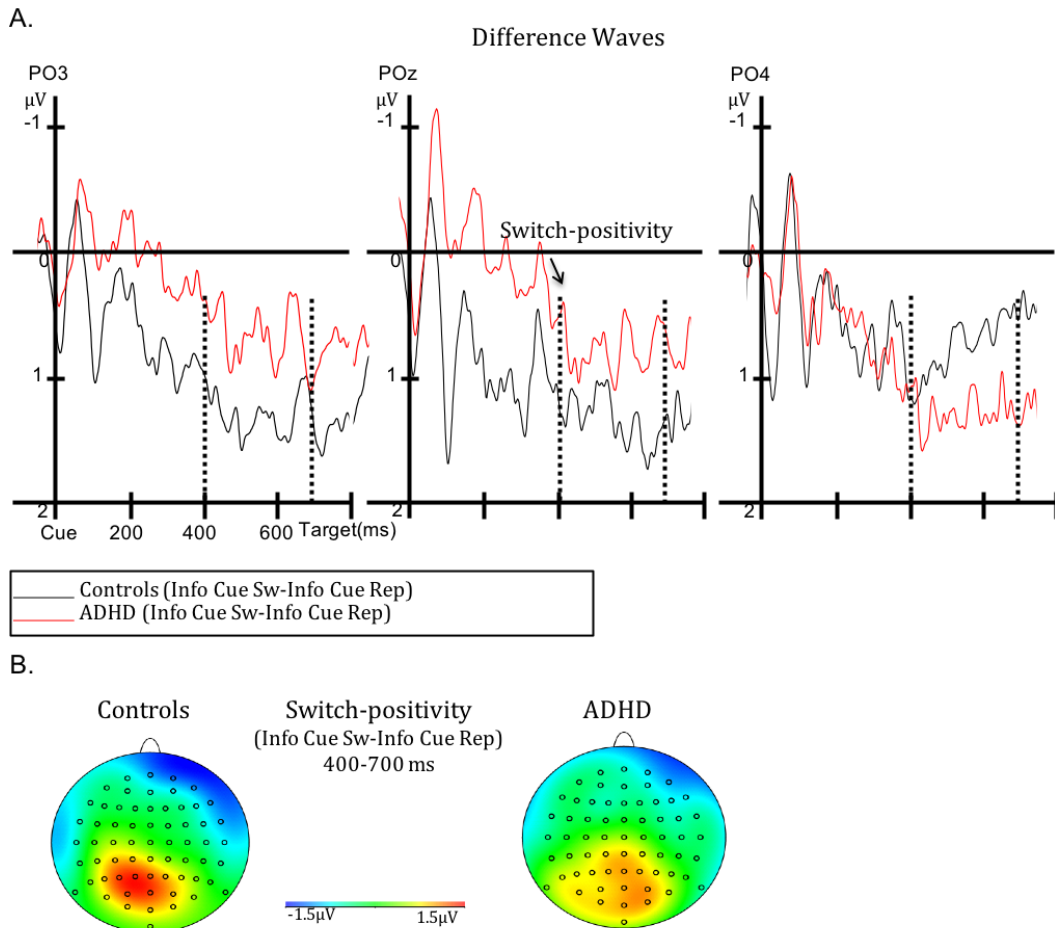


Figure 5. Cue-locked ERPs – switch-positivity. The figure (A) displays the difference waves depicting the switch-positivity (tentatively suggesting the potential laterality effect) and topographic maps (B) for individuals with ADHD and control subjects.

We also explored the relationship between ERPs and behavioural measures with correlational analyses. While the direction of the effects was as predicted (negative association between cue-related ERP difference scores (for informative-positivity: informative – alerting cue; for switch-positivity: informative cue switch – informative cue repeat) and response time difference scores (for informative positivity: informative cue RT – alerting cue RT; for switch-positivity:

informative switch cue RT – informative cue repeat RT) i.e., higher ERP activity was associated with smaller response times), none of the correlations were significant.

### **Target-locked**

There were main effects of cue type ( $F(2, 88) = 26.05, p < 0.001; \eta^2 = 0.372$ ) and switch ( $F(1, 44) = 19.32, p < 0.001; \eta^2 = 0.305$ ) as well as a cue type x switch interaction ( $F(2, 88) = 8.64, p < 0.001; \eta^2 = 0.164$ ). Follow-up analyses showed that the switch-negativity (the decrease in posterior positivity for switch relative to repeat trials) was only apparent for informative cues ( $F(1, 44) = 16.53, p < 0.001; \eta^2 = 0.273$ ). There was no significant difference between switch and repeat trials; either for the alerting cue ( $F(1, 44) = 0.09, p = 0.758; \eta^2 = 0.002$ ), or for the no-cue condition ( $F(1, 44) = 0.10, p = 0.745; \eta^2 = 0.002$ ). Most importantly however, neither the main group effect ( $F(1, 44) = 0.40, p = 0.527; \eta^2 = 0.009$ ), nor any of the interactions with group were found to be significant (all  $p$ 's  $> 0.05$ ) (Figure 7; please see Figure 6 for raw ERPs; for topographies please see Supplementary material).

### **Additional exploratory analysis**

Of note, the EEG data seem to indicate a differentiation of informative vs. alerting cues already at an earlier stage than the informative positivity, namely around 100 ms post cue (P1, see raw ERPs in Figure 3). Although this was not hypothesised, we decided to explore this further. Analyses indeed showed a main effect of cue type ( $F(1, 44) = 18.56, p < 0.001; \eta^2 = 0.297$ ) indicating a larger P1 for informative cues. However importantly, groups did not differ in this effect ( $F(1, 44) = 1.22, p = 0.275; \eta^2 = 0.027$ ). Larger P1 amplitudes to informative vs. alerting cues in our study may be explained by differences in stimulus features, opposed to previous studies (e.g., Jamadar et al., 2010). We further elaborate on this in the discussion section.

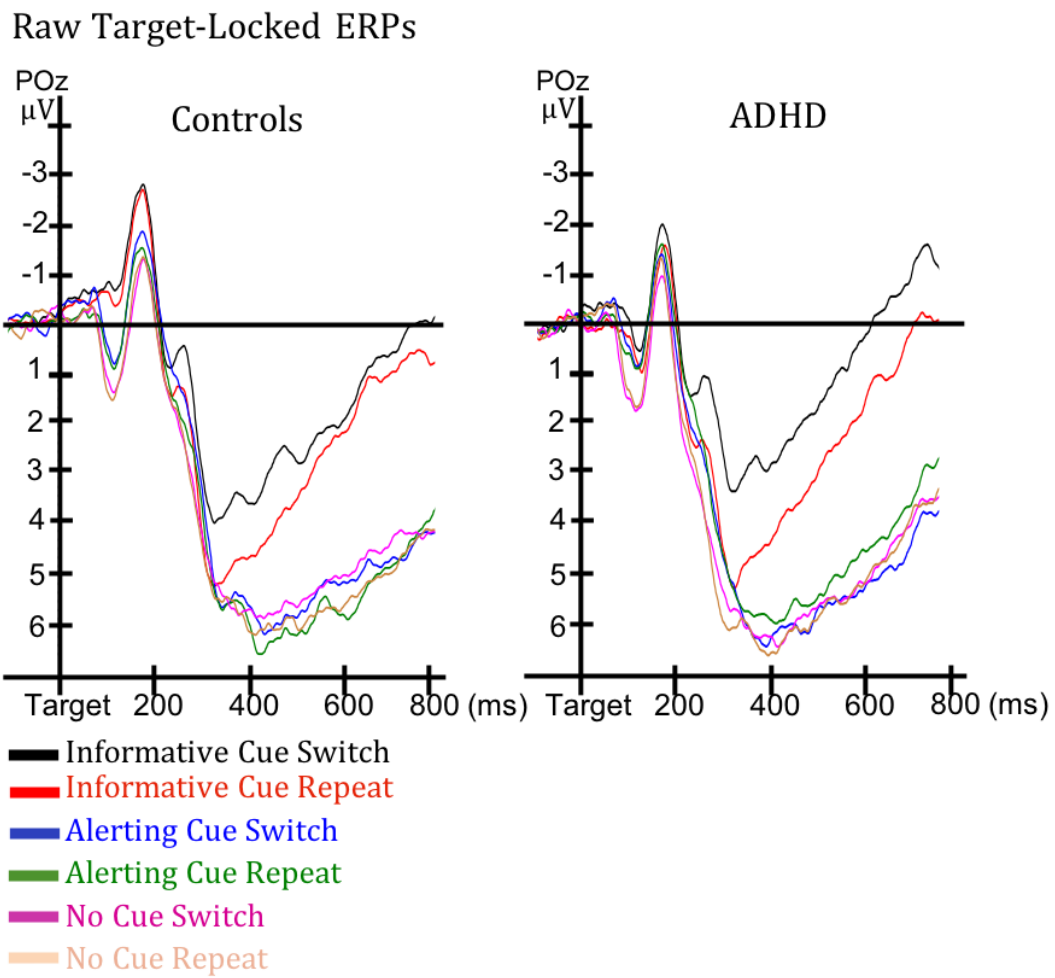


Figure 6. Raw Target-locked ERPs for informative, alerting and no-cue conditions in controls and individuals with ADHD.

## Target-Locked ERPs

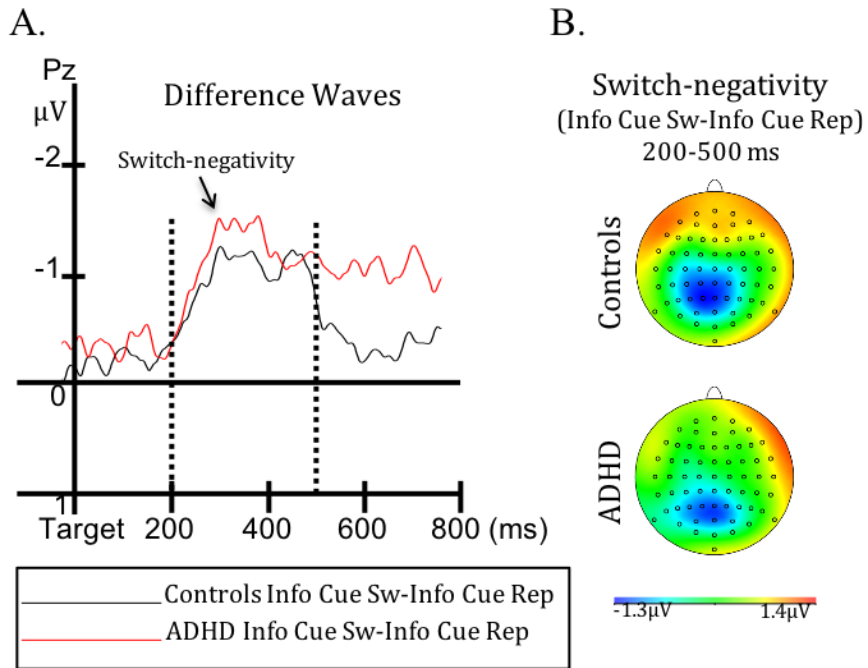


Figure 7. Target-locked ERPs. The figure (A) displays the difference waves depicting the “switch-negativity” (only present for informative cues) and topographic maps (B) for individuals with ADHD and control subjects.

## **Discussion**

In the current experiment, we tested for ADHD-related proactive and reactive control impairments by measuring EEG during performance on a cued task switching paradigm, in which cue-informativeness was manipulated. In accord with previous studies, we observed the cue-locked informative-positivity and switch-positivity, and the target-locked switch-negativity (Jamadar, 2010a,b). Groups did not differ for task-switching at the performance level; adults with ADHD tended to respond slower than controls irrespective of condition and no group difference was detected for switching performance. However, there were two EEG findings of note that point towards potential proactive control abnormalities in adults with ADHD. First, while the informative-positivity was present in both groups it was significantly reduced in adults with ADHD. Secondly, the reduced informative-positivity was followed by a potentially altered (marginally significant) lateralisation of the switch-positivity in adults with ADHD.

### **Cue-locked informative-positivity & switch-positivity**

Informative in contrast to alerting cues enable anticipatory task preparation, hence, task goal reactivation and initiation of attentional priming while alerting cues are only signals rendering the most basic preparatory processes without task-specific rule reactivation (Jamadar et al., 2010; Karayanidis et al., 2010a). The fact that the cue information-related informative-positivity was diminished in adults with ADHD suggests abnormalities in the early anticipatory processing of external cues announcing task rules. This means that adults with ADHD did not properly use the information provided by the cue to efficiently reactivate the associated task rules and initiate the relevant attentional bias to execute the task at hand. This finding is in line with the cardinal symptom of distractibility and not being able to efficiently allocate and engage attention to task-relevant stimuli in ADHD (Aboitiz, Ossandón, Zamorano, Palma, & Carrasco, 2014; Bush, 2010; Hasler et al., 2016). Therefore, this could signify a failure of the cognitive control system during early stages of cue processing, which in turn may relate to the commonly reported preparatory or anticipatory deficits in ADHD (Banaschewski et al., 2008; Barry,

Johnstone, & Clarke, 2003; Johnstone & Clarke, 2009; Plichta et al., 2009; Scheres, Milham, Knutson, & Castellanos, 2007; Smith, Taylor, Brammer, Toone, & Rubia, 2006). Our finding is in accordance with frequent observations of reduced brain activity to cues in fMRI and ERP research (Carrasco, Ortega, Lo, Anillo-vento, & Aboitiz, 2013; Durston et al., 2007; Fassbender et al., 2015; Furukawa et al., 2014; Hasler et al., 2016; Mazaheri et al., 2014; Plichta & Scheres, 2014; Scheres et al., 2007; Sidlauskaite, Sonuga-Barke, Roeyers, & Wiersma, 2015b).

It is worth discussing that exploratory analyses showed that differentiation between informative and alerting cues was already noticeable at an earlier stage than the informative-positivity (around 100 ms) post cue, which was not reported in previous studies (e.g. Jamadar et al., 2010). This may be due to differences in task design. In our case, the informative and alerting cues did substantially differ in stimulus features (i.e., words for informative cues and two hyphens for alerting cues), whereas in Jamadar et al. cues only differed in colour. As the P1 is known to be affected by variations in perceptual attributes of the visual stimulus, such as size (Woodman, 2010), we believe that this early informative – alerting cue difference at the P1 stage in our data may be the result of enhanced early perceptual processing of informative cues. However importantly, groups did not differ for this effect, in contrast to the later informative-positivity.

Importantly, groups differed only when the cue carried advance information and not in the case of alerting cues. As mentioned, cue-informativeness was not manipulated in previous ADHD studies, hampering interpretation of the observed altered preparatory processing in ADHD. This is key, as cues can contain advance information about the upcoming task, but also have general alerting properties (Albrecht et al., 2013; Banaschewski, Yordanova, Kolev, & Heinrich, 2008; Valko et al., 2009). The current findings therefore significantly add to our understanding of altered preparatory processing in ADHD, as they suggest impairments in processing the information conveyed by the cue rather than in general alerting.

In the current data set, we found some tentative evidence that early cue-information processing differences may precede later abnormalities reflected in potentially altered lateralisation of the switch-positivity in ADHD. The trend to difference in lateralisation

tentatively suggests altered activation of underlying brain areas. Based on combined ERP-fMRI findings, the switch-positivity appears to originate from the posterior parietal cortex (PPC) which comprises areas such as precuneus and superior parietal lobule (Jamadar et al., 2010a). Interestingly, models of PPC implicate this brain region to play key roles in attention allocation, as well as maintaining a preparatory state (Corbetta & Shulman, 2002; Malhotra, Coulthard, & Husain, 2009; Mulckhuyse, Engelmann, Schutter, & Roelofs, 2017). Crucially, the PPC has been identified as displaying altered activation patterns as well as structural (cortical thinning) lateralisation abnormalities in ADHD (Bush, 2010; Makris et al., 2006; Shaw et al., 2007; Vaidya, 2008). This chimes well with our current findings of a trend toward altered lateralisation of the switch-positivity component in ADHD, and the lateralisation deficit literature on ADHD in general (Frodl & Skokauskas, 2012; Hale et al., 2009; Valera et al., 2007). However, as altered lateralisation in ADHD was not an a-priori hypothesis in our study and the results were only marginally significant, this finding definitely warrants further examination and replication.

Taken together, the cue-related ERP findings point to altered proactive control in our sample of adults with ADHD. The fact that only negligible differences were found at the performance level, suggests neurophysiological measures to be more sensitive to these fine-grained differences in cognitive processes. The results suggest that proactive deviances in adults with ADHD might be already present during early anticipatory stages of cue processing (i.e., reduced use of information conveyed by the cue and reduced activation of general task goals), which may affect later stages of cue processing (i.e., deviant preparatory activation of task-specific rules).

### **Target-locked switch-negativity**

We did not observe group differences in the switch-negativity. The absence of differences in ERP indices related to the processing of targets may be surprising given previous findings (Bitter, 2011; Grane et al., 2016; Michelini et al., 2017). On the face of it, this appears to be a conflicting finding not only with respect to previous research but also regarding our current results suggesting potential difficulties in proactive cognitive control related to ADHD.

However, we believe that the specific experimental design of the current paradigm may have precluded group effects during processing of targets. The fact that the task rules remained on the screen from cue onset until a response was executed may be especially relevant in this regard. This, on the one hand, ensured that the task was easy enough to perform for both groups, but on the other hand, it probably resulted in the absence of group differences in target related ERPs. This is because our participants did not necessarily need to use the advance information provided by the cue at the initial stages in the cue-target interval since the information remained visible the entire time. Consequently, our findings indicating alterations in proactive control during the cue phase followed by unaffected target processing are not necessarily inconsistent.

Another observation needs discussion as well. Our data showed that the switch-negativity was only apparent for informative cues and not in the alerting or no-cue condition. This seems at odds with the assumption that the switch-negativity reflects reactive control processes, as one would expect most reactive control processes to take place in conditions that provide the least opportunity to apply proactive control, hence in the alerting and no-cue condition. Interestingly, a similar observation was made in previous research in which the switch-negativity was only visible for informative cues and not for uninformative cues (e.g., Jamadar, et al., 2010a,b; Karayanidis, Coltheart, Michie, & Murphy, 2003; Nicholson, Karayanidis, Poboka, Heathcote, & Michie, 2005; Kieffaber & Hetrick, 2005; Miniussi, Marzi, & Nobre, 2005; Poulsen, Luu, Davey, & Tucker, 2005). Future studies are needed to address this issue, but the observation that the switch-related modulation in brain activity at the target level only takes place in a condition that allows advance preparation, suggests that it may be the result of late proactive control processes that cannot be initiated until stimulus onset (Jamadar, Michie, & Karayanidis, 2010; Jamadar, Hughes, Fulham, Michie, & Karayanidis, 2010; Karayanidis et al., 2010a; Jamadar, Michie, & Karayanidis, 2010). However, this is speculation and further research on the functional significance of the switch-negativity is strongly warranted. Despite this, our current findings show that while adults with ADHD did not differ from controls for switch-related activity at the target-level, they did exhibit alterations in the usage of informative cues to prepare for an upcoming task.

## **Future perspectives and clinical implications**

First of all, due to the ingrained heterogeneity of ADHD, this finding needs to be replicated in other independent ADHD samples, and also with other tasks to show specificity of the findings. Future research should invest in trying to address the question of what in particular could mediate these alterations in proactive control processes in ADHD. One possibility is that individuals with ADHD suffer from a general inability to effectively make use of advance information, which could be related to deficient functioning of the fronto-parietal cognitive control network (Cortese et al., 2012). On the other hand, it could be that individuals with ADHD do not effectively apply proactive control due to difficulties in applying the necessary effort. This idea is in line with the account that individuals with ADHD have difficulty mobilising energetic resources (Johnson, Wiersema, & Kuntsi, 2009; Sonuga-Barke, Wiersema, van der Meere, & Roeyers, 2010; Wiersema, van der Meere, Roeyers, Van Coster, & Baeyens, 2006). Notably, proactive control, i.e., actively maintaining goal-relevant information across delay periods, is more effortful and hence engages more cognitive-energetic resources than reactive control, which can be seen as a last minute or “on the spot” mode of control (Braver, 2012). Alternatively, in terms of motivational accounts, the current findings might be explained by altered motivation to recruit sufficient levels of proactive control (Johnson et al., 2009; Sonuga-Barke et al., 2010). Further research into the dual model of cognitive control; differentiating proactive and reactive control (e.g., Pani et al., 2013) may help to better define ADHD-related neuropsychological profiles and therefore aid in devising new and/or optimising existing clinical intervention strategies.

## **Conclusions**

In the current EEG experiment, we investigated cognitive control processes in adults with ADHD from the perspective of Braver’s (2012) dual model of cognitive control. At the performance level, only a trend to generally slower responding was found in the ADHD group. The ERP findings however suggest preparatory proactive rather than reactive cognitive control difficulties in adults with ADHD, evidenced by reduced usage of cue information and potentially deviant preparatory switch-related activity.

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