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Effects of multisensory stimuli on inhibitory control in adolescent ADHD: It is the content of information that matters

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ABSTRACT

Even though deficits in inhibitory control and conflict monitoring are well-known in ADHD, factors that further modulate these functions remain to be elucidated. One factor that may be of considerable importance is how inhibitory control is modulated by multisensory information processing. We examined the influence of concurrent auditory conflicting or redundant information on visually triggered response inhibition processes in adolescent ADHD patients and healthy controls. We combined high-density event-related potential (ERP) recordings with source localization to delineate the functional neuroanatomical basis of the involved neurophysiological processes. In comparison to controls, response inhibition (RI) processes in ADHD were compromised in conflicting conditions, but showed no differences to controls when redundant or no concurrent auditory information was presented. These effects were reflected by modulations at the response selection stage (P3 ERP) in the medial frontal gyrus (BA32), but not at the attentional selection (P1, N1 ERPs) or resource allocation level (P2 ERP). Conflicting information during RI exerts its influences in adolescent ADHD via response selection mechanisms, but not via attentional selection. It is not the mere presence of concurrent information, but the presence of conflicting information during RI that may destabilize goal shielding processes in medial frontal cortical regions, by means of increasing the automaticity of response tendencies. The occurring RI deficits might relate to the increased impulsivity in adolescent ADHD and a corresponding vulnerability to react to an increased automaticity of pre-potent response tendencies. ADHD patients show a bias to a specific *content* of information which can modulate inhibitory control.

1. Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is one of the most prevalent neurodevelopmental disorders (Polanczyk et al., 2007). The diagnose of ADHD and the corresponding subtypes (inattentive, the hyperactive/impulsive or the combined ADHD subtype) is based on the expression of the three core symptoms inattention, hyperactivity and impulsivity (Ahmadi et al., 2014; Barkley, 1997; Randall et al., 2009). Besides these three core symptoms, deficits in executive functions, conflict monitoring and especially in inhibitory control are increasingly focused upon in current ADHD research (Albrecht et al., 2013; Bluschke et al., 2016b; Booth et al., 2005; Hart et al., 2013; Rubia et al., 2005; Wright et al., 2014). The deficits in inhibitory control are particularly important to consider because inhibitory deficits have been shown to be a major factor for the educational outcomes of adolescent ADHD (Berlin et al., 2003; Loe and Feldman, 2007). While the necessity to consider inhibitory deficits in adolescent ADHD is without question (Aron and Poldrack, 2005; Hart et al., 2014), it is unknown what factors, or boundary conditions modulate response inhibition processes in adolescent ADHD on a behavioral and neurofunctional level. This question is of major relevance for patients with adolescent ADHD, because employment opportunities are dependent on educational success. The exact identification of the nature of inhibitory deficits in adolescent ADHD may grant a possibility to create environmental settings, in which adolescents with ADHD are less prone to exhibit ADHD-specific behavioral problems and might thus help to improve educational outcome and opportunities in their future lives. On a neurofunctional level, the brain has been shown to undergo immense developmental processes during ongoing brain maturation between childhood and adolescence (Sowell et al., 2001, 2003) and especially response inhibition functions are assumed to not fully mature until early adolescence (for review: Luna and Sweeney, 2004). In line with this observation, response inhibition deficits have been shown to be more pronounced in children than in adolescents with ADHD (Tillman et al., 2008). This suggests that

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examining children with ADHD might be challenging, as inhibitory deficits might be too pronounced to allow a reliable examination of response inhibition processes. This particularly relates to the examination of neurofunctional correlates of the modulation of response inhibition processes. Children with ADHD might be overstrained by the necessary number of trials, which would have to be presented in order to examine modulatory aspects of response inhibition with a sufficiently big signal-to-noise-ratio for the analysis of neurofunctional data. Concerning adults, response inhibition processes are not assumed to develop much further between adolescence and adulthood (Luna and Sweeney, 2004; Williams et al., 1999). Furthermore, the importance of educational settings for achievements in future life is continuously reduced in adulthood. Therefore, the examination of response inhibition processes seems particularly relevant in adolescent ADHD.

One factor that may be of considerable importance in the context of adolescent ADHD is how inhibitory control is modulated by multisensory information processing. In healthy controls it was shown that redundant auditory (concurrent) information facilitates response inhibition performance (Chmielewski et al., 2015), while conflicting auditory (concurrent) information compromises response inhibition performance (Chmielewski et al., 2015). The improvement of inhibitory control by means of presenting a redundant auditory NoGo stimulus alongside the primary visual NoGo information relates to a corresponding decrease in the automaticity of response tendencies, which is be beneficial for inhibitory control (Chmielewski et al., 2015, 2016). Opposed to that, presenting a conflicting auditory Go stimulus alongside the primary visual NoGo information increases the automaticity of response tendencies and thus aggravates inhibitory control in healthy controls (Chmielewski et al., 2015, 2016). In comparison to healthy controls, ADHD patients exhibit increased impulsivity (Bari and Robbins, 2013; Barkley, 1997; Douglas, 1999; Durston et al., 2009) and a predisposition to engage in automatic behavior (Clark et al., 2000). It is therefore possible that inhibitory control in adolescent ADHD patients might be more affected whenever the automaticity of response tendencies is increased (Dippel et al., 2015; Stock et al., 2015), i.e. when conflicting auditory Go information is presented alongside the primary visual NoGo information. Alternatively, a similar pattern of results might occur because conflict monitoring processes are dysfunctional in adolescent ADHD (Albrecht et al., 2008; Bluschke et al., 2016a; McLoughlin et al., 2009). More specifically, as overcoming conflicts is a prerequisite to successfully inhibit inappropriate responses in the conflicting NoGo condition in this paradigm, overstrained conflict monitoring functions might potentiate already existing deficits in response inhibition. If such response inhibition deficits (due to increased automaticity or due to deficient conflict monitoring processes) were only revealed in the conflicting condition in adolescent ADHD, this would suggest that the mere presence of additional sensory input does not necessarily compromise cognitive performance in adolescent ADHD. Rather, deficits in cognitive control and response inhibition strongly depend on the *content* of additional information that needs to be integrated. Importantly, this would suggest that there is an ADHD-inherent bias to a specific *content* of information, which modulates inhibitory control.

However, another pattern of results is also possible: Since ADHD patients show an increased vulnerability to distracting information (Mullane et al., 2009; Pelham et al., 2011), response inhibition processes in adolescent ADHD may be particularly vulnerable to effects of multisensory information. When only considering the increased distractibility, or the predisposition to allocate residual attentional capacity to irrelevant distractors in adolescent ADHD (Chen and Cave, 2016), response inhibition performance in adolescent ADHD should be compromised whenever additional information is presented, irrespective of the content of the information.

To examine what cognitive-neurophysiological subprocesses during the process of response inhibition are differentially modulated by the content of concurrent information in adolescent ADHD, we use a system neurophysiological approach using high-density EEG recordings and source localization techniques:

If response inhibition processes in adolescent ADHD are compromised by concurrent information due to an increased distractibility (i.e. irrespective of the content of information), we expect this to be reflected in the N1 and P1 amplitude likely reflecting perceptual gating and bottom-up attentional selection unrelated to stimulus content (Herrmann and Knight, 2001). The neural sources of visual P1 and N1 modulations should then be detected in extrastriate cortical areas (Di Russo et al., 2002; Gomez Gonzalez et al., 1994; Heinze et al., 1994; Herrmann and Knight, 2001). Alternatively, the effects might also be reflected in resource allocation processes (indicated by modulations in the P2 amplitude), which are deployed to process sensory input (Geisler and Murphy, 2000; Sugimoto and Katayama, 2013). If differences in resource allocation processes would contribute to potential response inhibition deficits, this will be associated with modulations in activity in parieto-occipital regions (Freunberger et al., 2007).

If response inhibition deficits in adolescent ADHD would, however, only occur in the context of a specific content of multisensory information (due to an increased automaticity of response tendencies or due to conflict monitoring deficits in adolescent ADHD), we would expect this to reflected in the response selection stage. Such alterations in the response selection stage should relate to generation of response conflicts (Botvinick et al., 2001) and a corresponding engagement in goal-shielding processes at the response selection level, which are deployed to protect task goals (i.e. to successfully inhibit when responses would be inappropriate) from interference (Beste et al., 2017; Dreisbach and Haider, 2009; Gohil et al., 2017; Goschke and Bolte, 2014; Gruber and Goschke, 2004; Hofmann et al., 2012). During response inhibition it has repeatedly been shown that a frontal-midline NoGo-N2 event-related potential (ERP) component reflects pre-motor processes like conflict monitoring or updating of the response program, while a NoGo-P3 ERP-component reflects evaluative processing of the successful outcome of the inhibition or the inhibition process itself (Beste et al., 2010, 2011; Huster et al., 2013). These ERPs (NoGo-N2 and P3) at the response selection stage have already been shown to be reflected in alterations in the superior frontal gyrus (SFG), the supplementary motor area (SMA) and especially in the medial frontal gyrus (MFG) (Beste et al., 2010, 2011; Huster et al., 2013). More important, for the modulation of response inhibition processes by means of concurrent information, as intended in this study, especially the involvement of medial frontal areas has also been observed (Chmielewski et al., 2015, 2016). This suggests that a potential modulation-related aggravation of response inhibition performance in adolescent ADHD should either be reflected in decreases in the NoGo-N2 or NoGo-P3 component and hence in a corresponding decreased activation in medial frontal structures during the response selection stage. This is particularly probable, because medial frontal and basal ganglia structures show changes in ADHD (Bos et al., 2017; Brieber et al., 2007; Hoogman et al., 2017) that are related to changes in GABA, glutamate and dopamine concentrations in this region, which also play a major role in inhibitory control (Ende et al., 2015; Umemoto et al., 2014; Villemonteix et al., 2015).

Taken together, we hypothesize two possible outcomes for the adolescent ADHD group. If there is an increased vulnerability to react to highly automatized response tendencies, or if, alternatively, deficits in processing conflicting information contribute to response inhibition deficits in the adolescent ADHD group, we expect response inhibition deficits to occur in response inhibition performance under conflicting information. This should be reflected in a decreased activation in the MFC and in alterations at the response selection level. More specifically, the vulnerability to react to highly automatized response tendencies should be reflected in a decreased P3 amplitude, while deficits in conflict monitoring processes should be reflected in a decreased N2 amplitude. If, however, the increased distractibility in adolescent ADHD is underlying for response inhibition deficits in adolescent