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Neural and behavioral suppression of interfering flankers by children with and without autism spectrum disorder

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ABSTRACT

Electrophysiological responses, accuracy and reaction time were recorded while 7–11-year-olds with typical development (TYP; *N*=30) and autism spectrum disorder (ASD; *N*=19) inhibited conflicting information. Relative to the TYP group, children with ASD had larger decrements in accuracy for incongruent trials and were slower. In terms of neural responses, N2 mean amplitude was greater overall for children with ASD relative to TYP children. N2 neural responses related to a behavioral measure of inhibition and cognitive flexibility for TYP children, whereas it related to suppression of interfering information and maintenance of accurate responding for the children with ASD. Results suggest children with ASD recruit more neural resources and perform worse when inhibiting conflicting information relative to TYP peers.

1. Introduction

Executive function (EF) – the ability to manage complex or conflicting information in the service of a goal – is particularly important to development because EF is related to better academic performance, social skills, lower rates of aggression and disruptive behavior, and better outcomes in adulthood (see Diamond, 2013 for review). By mid-childhood, EF is comprised of inhibition, set-shifting and working memory sub domains (Lehto et al., 2003). Though EF impairment is not a core symptom of the disorder, EF deficits are frequently observed in children with autism spectrum disorder (ASD; Hill, 2004; Kenworthy et al., 2008; Pennington and Ozonoff, 1996) – a common neurodevelopmental disorder that is characterized by reduced social communication skills and the presence of restricted and repetitive behaviors. In particular, set shifting is extremely disrupted in ASD and inhibitory impairments are also present relative to comparison groups (Willcutt, 2008). Inhibition may be further divided into interference control (i.e., suppression of distracting stimuli) and response inhibition (i.e., suppression of dominant responses) (Nigg, 2000). Children with ASD have more difficulty with interference control and less pronounced difficulties with response inhibition relative to comparison groups (Geurts et al., 2004; Willcutt et al., 2008).

In the present study, we employed a common measure of interference control, the flanker task (Eriksen and Eriksen, 1974), that involves a central target stimulus flanked by stimuli of the same (congruent) or opposite (incongruent) orientation to examine the neural and behavioral responses of children with ASD and typical development. We used event related potentials (ERP) to examine neural responses that precede behavioral responses on the task. ERP offers a unique perspective because it measures aspects of EF that are difficult to capture behaviorally such as the neural activity underlying correct response inhibition and self-monitoring. We examined three ERP components – the P100, N2, and P3 – during the flanker portion of the developmentally appropriate Child Attention Network (ANT) task (Rueda et al., 2004). Each component represents a different aspect of attention and EF skills.

The P100 is an exogenous sensory component that is evoked through passive viewing of sensory information and is known to be modulated by spatial visual attention (Hillyard et al., 1998; Luck et al., 2011 for review). Directed attention to the location of the target generates greater P100 amplitudes. Enhanced P100 amplitudes correlate with better reaction times and target detection across tasks (Hillyard et al., 1998; Eimer et al., 2003). We examined the P100 to determine whether low level attention and sensory processing were similar between the groups.

The N2 component in the Child ANT task is thought to reflect executive attention and monitoring conflicting information between

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the target and flankers. N2 amplitudes decrease with development and maturation of the network of neural structures (e.g., the anterior cingulate) underlying it (Buss et al., 2011; Espinet et al., 2012; Giedd et al., 1999; Henderson, 2010; Johnstone et al., 2005; Jonkman, 2006; Lamm et al., 2006; Lewis et al., 2006; Lewis and Stieben, 2004). Incongruent flankers represent greater conflict, and relatively larger N2 amplitudes are observed in the incongruent condition (Van Veen and Carter, 2002). Developmentally, the effects of incongruent flankers on the N2 appear to emerge later than the effects of other EF tasks (e.g., the go-nogo), with differences between flanker conditions being more apparent in the N2s of older adolescents and adults but not young children (Checa and Rueda, 2011; Ladouceur et al., 2007; Rueda et al., 2004). However, the N2 effect has been detected as early as age 6 (Buss et al., 2011). Controlling for age, children with relatively larger differences in amplitude for incongruent relative to congruent flanker conditions have greater behavioral difficulty with incongruent trials and less effortful control by parent report (Buss et al., 2011). Furthermore, a generalized increase in absolute N2 amplitude (across conditions) is interpreted as “less efficient” processing (Dennis and Chen, 2009).

The P3, which is represented over central parietal leads, is comprised of two subcomponents, the P3a and P3b. The P3a is generated in the frontal lobe and is functionally associated with focal attention. Two main attention networks are activated during the P3a component, the ventral frontoparietal network (VFP), which has been postulated to be engaged in the detection of rare events and thus is modulated by stimulus frequency (Corbetta and Shulman, 2002), and the dorsolateral frontoparietal network (DLFP), which is involved in voluntary shifts of spatial visual attention and top down processing of stimuli (Bledowski et al., 2004; Donner et al., 2002; Goebel et al., 1998; Wojciulik and Kanwisher, 1999). The P3b subcomponent is thought to be associated with memory and event categorization and is generated in the temporal lobe via “target detection” (Baudena et al., 1995; Bledowski et al., 2004; Halgren et al., 1995; Linden et al., 2005; Puce et al., 1989) and “retrieval” or “mental tracking” of the target stimulus compared to memory templates necessary for target detection and memory updating (Jiang et al., 2000; Lepage et al., 2000, see Friedman et al., 2000 for review). Together, these components are hypothesized to represent inhibition of irrelevant information that is not directly involved in stimulus evaluation, in order to “amplify” the target signal for enhanced stimulus classification and memory consolidation. The P3 is altered by the frequency of a stimulus, habituation to a stimulus, and the familiarity or novelty of a stimulus (Luck et al., 2011) – all of which were held constant across the flanker conditions in this study; thus any amplitude differences should be a result of the variation between congruent and incongruent flanker conditions. Developmentally, P3 amplitude increases with age in the context of non-flanker tasks (see Luck et al., 2011 for review) and is viewed as a marker of increased inhibitory responding (Hämmerer et al., 2010). Although the P3 is present in this age range over parietal leads during inhibitory tasks requiring response inhibition, a protracted developmental course involving increased amplitude and scalp distribution is observed starting between age 7–10 and continuing to adulthood (Brydges et al., 2014; Jonkman, 2006). In the flanker task, the P3 is present in 7–14 year olds with larger parietal amplitudes for incongruent trials relative to congruent trials, and it is thought to reflect allocation of effort (Johnstone and Galletta, 2013).

1.1. The flanker task in ASD

Behavioral performance on flanker tasks is impaired in adults, adolescents and children with ASD relative to comparison groups without ASD (Adams and Jarrold, 2012; Christ et al., 2011; Dichter and Belger, 2008; Geurtset al., 2008, but see Sanderson and Allen, 2013). Individuals with ASD have slower reaction times and worse accuracy for the incongruent condition relative to comparison groups, and these effects were apparent even when the task was manipulated in ways that make it easier for youth without autism (Adams and Jarrold, 2012). Although EF is a frequent focus of research, there is little information about the neural profile of children with ASD during EF tasks. ERP provides a window into potential differences in neural processes that underlie behavioral responses on the flanker EF task.

To date, there have been three investigations of electrophysiological responses of children and adolescents with ASD during a flanker task with inconsistent findings. Tye and colleagues (2014) utilized a continuous performance cued-nogo task in which the central target (a letter) was flanked by letters. In this task, the N2, P3 and Contingent Negative Variation (CNV) components were analyzed, and, relative to children aged 8–13 years with ADHD and typical development, children with ASD had reduced absolute N2 amplitudes and increased CNV components, but, in contrast to previous reports (Adams and Jarrold, 2012; Christ et al., 2011; Dichter and Belger, 2008; Geurts et al., 2008), did not differ in behavioral performance during the task. ERP data suggest that children with ASD may have *more* efficient conflict monitoring during this task as seen by the reduction in N2 amplitudes (Dennis and Chen, 2009; Buss et al., 2011), which might explain the lack of performance deficits. However, analyses focused on the continuous performance aspect of the task and behavioral inhibition during Nogo trials rather than the flanker manipulation making it a less direct measure of interference suppression. Furthermore, the N2 amplitude was measured over a large window, 170–400 ms, using peak amplitude rather than mean amplitude, making the N2 susceptible to differences in the number of usable trials per group and condition, which were not controlled in this study. Using a more traditional flanker task, Samyn et al. (2014) found no differences in ERP response at the N2 or P3 component or behavioral performance (i.e., reaction time or number of errors) by 10–15-year-olds with ASD relative to an age-matched group without ASD, suggesting either no differences in interference control at the behavioral or neural level for 10–15-year-olds with ASD or poor sensitivity to EF differences. Finally, Larson et al. (2012) specifically examined the effects of congruent and incongruent flankers in the context of the previous trial condition and conflict adaptation. They found 9–17-year-olds with ASD made more errors and the effect of incongruent trials on accuracy was larger for children with ASD than the age-matched comparison group. In terms of N2, the group with ASD had less evidence of conflict adaptation from trial to trial, whereas the comparison group exhibited the expected pattern of conflict adaptation. Larson and colleagues included a relatively large sample size but a wide age range, which may have obscured differences between groups as the comparison group began to produce more consistent and predictable neural responses to the flanker task. As well, experimental design and analyses focused on conflict adaptation rather than interference control.

The current study addresses these inconsistent findings and the limited research focused specifically on the neural underpinnings of interference control in children with ASD by including a narrower age range and focusing exclusively on the flanker condition of a developmentally appropriate task designed to elicit ERP responses in young school-aged children. We selected this age range because there is evidence that neural markers related to processing conflict during the flanker task (i.e., N2, P3) are present for typically developing children (e.g., Buss et al., 2011; Jonkman, 2006), it is a rapid period of behavioral and neural development for the structures underlying the flanker task (Fjell et al., 2012), and evaluating whether responses of children with ASD diverge early in this period of development provides an opportunity for earlier intervention related to EF for children with ASD. In addition, we sought to build on previous work by examining the relations between the neural responses during this interference control task and behavioral performance across a battery of direct EF assessments rather than parent report measures. This provides the opportunity to examine whether the processes measured by ERPs reflect the same aspects of EF in ASD.