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Low-contrast response deficits and increased neural noise in children with autism spectrum disorder

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ABSTRACT

A battery of short-duration neurophysiological tests were designed and implemented using visual evoked potentials (VEPs) to examine specific neural mechanisms in children with and without autism spectrum disorder (ASD). Contrast-sweep conditions (bright or dark isolated-checks) were used to elicit steady-state VEPs to examine the integrity of ON/OFF pathways. Children with ASD displayed deficits in low-contrast responses at the stimulus frequency of 12.5 Hz, notably under conditions that emphasized activity in the magnocellular pathway. Signal-to-noise ratios were weaker in the ASD group, particularly for the OFF pathway. There were no group differences in the amplitude of responses. In addition, the ASD group displayed significantly higher levels of neural noise than controls. For the response at the stimulus frequency, the ASD group produced a relatively constant level of noise across the contrast range tested, with higher levels than controls at low contrasts and approximately equal levels of noise at moderate to high contrasts.

1. Introduction

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental disorder that is often diagnosed during early childhood and is characterized by impairments in social communication, reciprocal social interaction, and repetitive or restricted behaviors and interests (American Psychiatric Association, 2013). Sensory symptoms have also been described as a hallmark of the disorder through both empirical and anecdotal accounts (Grandin & Scariano, 1986; Kern et al. 2006; O'Neill & Jones, 1997). Given the high prevalence of hyper- and hypo-sensitivities (Leekam, Nieto, Libby, Wing & Gould, 2007), sensory symptoms have been incorporated into the DSM-5 criteria for ASD (American Psychiatric Association, 2013). Electrophysiological studies of the visual system in individuals with ASD have revealed abnormalities Q3 in both low-level (Vandenbroucke, Scholte, van Engeland, Lamme, & Kemner, 2008) as well as higher-level visual pathways (McPartland, Coffman, & Pelphrey, 2011). Although there is evidence to suggest that an underlying basic sensory problem may have a direct impact on the signs and symptoms of ASD, many studies focus on later visual processes that are known to be associated with high-level perception (e.g., social-cognitive deficits), and fewer studies examine low-level sensory processing. In order to better understand the altered perceptual functioning found in many individuals with ASD, the early stages of sensory processing, including neural responses to basic non-social stimuli must be examined further (McPartland et al., 2011; Simmons et al., 2009).

Recording visual evoked potentials (VEPs) are a noninvasive means to examine the integrity of specific brain mechanisms that may underlie the disorder. Through an analysis of real-time brain activity, reflected in the electroencephalogram (EEG), with a temporal resolution on the order of milliseconds, information about summed excitatory and inhibitory postsynaptic potentials can be gathered quickly (Zemon, Kaplan & Ratliff, 1980, 1986). In the current study, contrast response functions were obtained to examine several aspects of early-stage visual processing in children with and without ASD. Specifically, low-contrast bright and dark isolated-check stimuli were presented to selectively tap ON and OFF cells in the magnocellular pathway (Zemon & Gordon, 2006). The magnocellular pathway is made up of the two ventral layers of neurons in the dorsal lateral geniculate nucleus of the thalamus (dLGN) and plays a critical role in the perception of form, movement, depth and brightness (Kaplan, 2004). The cortical recipients of magnocellular input signals are responsive to low

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contrast stimuli and exhibit low spatial resolution and high temporal resolution (Lee, Pokorny, Smith, Martin & Valberg, 1990; Tootell, Hamilton, & Switkes, 1988; Tootell, Silverman, Hamilton, Switkes & De Valois, 1988).

ON and OFF pathways constitute distinct parallel subsystems that transmit positive- and negative-contrast information to the visual cortex, and the resulting cortical activation forms the basis of brightness and darkness perception (Schiller, 1982; Zemon, Gordon & Welch, 1988). When light hits the central field, ON cells are excited, and when light hits the surrounding field, OFF cells are excited (Schiller, Sandell & Maunsell, 1986). Therefore, light objects on dark backgrounds are detected via ON cells and dark objects on light backgrounds are detected via OFF cells. Isolated-check VEPs use these principles to assess select neural pathways in the visual system by examining central vision through the display of a single contrast-polarity stimulus pattern. Furthermore, given that ON and OFF cells are considered distinct components of the visual system, sensory information is likely processed in a differential manner (De Valois, 1977; Magnussen & Glad, 1975; Zemon et al. 1988). In order to emphasize magnocellular pathway contributions, stimuli are varied in the low-contrast region at moderate to high temporal frequencies (Zemon & Gordon, 2006).

Previous studies have used bright and dark isolated-check stimuli to examine developmental effects on responses to temporally-modulated spatial patterns. Findings indicate that maturational changes occur in both magnitude and phase of response frequency components throughout the lifespan; the developmental time course within ON and OFF pathways appears to be similar (Zemon et al. 1995). Findings in typically developing children indicate that response amplitude decreases with age above the age of six (Dustman & Beck, 1966, 1969; Shaw & Cant, 1981); this finding holds under both bright and dark-check conditions (Zemon et al., 1995). In addition, the dark-check condition produces larger responses than does the bright-check condition in young infants (Hartmann, Hitchcox, & Zemon, 1992), similar to that found in adults. According to Zemon et al. (1995), these findings may be attributed to changes in cortical circuitry. Specifically, the decrease in amplitude is thought to reflect the loss of excitatory synaptic activity that occurs with increasing age (Fosse, Heggelund, & Fonnum, 1989; Rakic, Bourgeois, Eckenhoff, Zecevic, & Goldman-Rakic 1986; Zemon et al., 1995).

While bright and dark isolated-check conditions have not yet been applied to the study of early-stage visual processing in ASD, several studies have attempted to examine the integrity of the magnocellular pathway in individuals with ASD, high-risk infants, and in the broader autism phenotype. A recent study by Greenaway, Davis, and Plaisted-Grant (2013) found significantly higher contrast discrimination thresholds on the steady-pedestal condition of the Pokorny and Smith task (Pokorny & Smith, 1997) in a sample of high-functioning children with ASD. The steady-pedestal condition is thought to reflect magnocellular activity, while the pulsed-pedestal condition is thought to reflect parvocellular activity. The cortical recipients of parvocellular input signals are responsive to high contrast stimuli and exhibit high spatial resolution (Lee et al., 1990; Tootell, Hamilton et al., 1988; Tootell, Silverman et al., 1988). No group differences were found in response to the pulsed-pedestal condition, thus indicating selective magnocellular impairment in children with ASD. McCleary, Allman, Carver and Dobkins (2007) applied luminance contrast sensitivity methods to a sample of infant siblings of children with ASD. This high-risk sample displayed thresholds that were almost double (i.e., lower sensitivities) those of controls in a condition emphasizing the magnocellular pathway, while there were no group differences in a condition emphasizing the parvocellular pathway. Sutherland and Crewther (2010) used electrophysiological and psychophysical measures to examine the visual system in typically developing adults with high vs. low scores on the Autism Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001). Higher scores reflect a greater number of ASD symptoms, thus capturing the broader autism phenotype. Results indicated that high scorers displayed weaker initial cortical responses at low contrasts and poorer performance on Navon figures that assess the ability to distinguish global aspects of figures. Overall, the authors argued that results may reflect deficits in global visual perception in individuals with ASD.

In comparison, Bertone, Mottron, Jelenic, and Faubert (2005) examined orientation discrimination using a flicker contrast sensitivity task. Results indicated better orientation discrimination for first-order, luminance-defined gratings and decreased orientation discrimination for second-order, texture-defined gratings in ASD participants. The authors attributed the dichotomy of enhanced and diminished processing of visual-spatial information to abnormal connectivity and enhanced lateral inhibition, not magnocellular or parvocellular function. Koh, Milne, and Dobkins (2010) also reported no difference in response to a luminance-defined contrast sensitivity task. Fujita, Yamasaki, Kamio, Hirose, and Tobimatsu (2011) identified subcortical deficits through an examination of the magnocellular and parvocellular pathways in adolescents and adults with ASD using 128-channel high-density EEG recording. An analysis of peaks and troughs in the VEP waveforms indicated longer N1 (100 ms) latencies in the ASD group with chromatic, but not achromatic stimulation. Results were indicative of impaired parvocellular and intact magnocellular functioning in ASD. While conflicting results have been reported, stimulus parameters significantly impact which pathways are being targeted.

Neumann et al. (2010) evaluated both early- and late-stage visual processing in 10 high functioning adolescents and adults with ASD using an adapted version of the Embedded Figures Task (Mottron, Burack, Iarocci, Belleville, and Enns, 2003). The task required participants to determine whether the letter "S" or "H" was embedded or isolated in a pattern stimulus. Results indicated no differences between ASD and control participants in behavioral performance (accuracy and reaction time). At early stages of processing (100–150 ms), differences were found in magnetoencephalographic (MEG) responses for the embedded condition, but not for the isolated condition. At later time intervals (350–400 ms), amplitude differences were found between groups for all conditions. In addition, an analysis of source localization showed peaks in brain activity in the primary visual cortex of ASD participants for all conditions and time windows, while brain activity in the control participants peaked in other cortical areas. The authors argued that the enhanced activation seen in V1 of ASD participants provides support for the Enhanced Perceptual Functioning theory (Mottron, Dawson, Soulieres, Hubert, and Burack 2006). The differences seen in early time domains may be indicative of reduced processing when the context is irrelevant. Furthermore, differences in the location of responses are said to reflect bottom-up processing in ASD participants (Neumann et al., 2010).

Baruth, Casanova, Sears, and Sokhadez (2010) examined early-stage visual processing in high functioning children and adolescents with ASD (ages 9–20) using event-related potentials (ERPs) to an oddball visual illusory task. Results indicate that P50 amplitudes in parieto-occipital regions of interest were significantly more positive in the ASD group in response to non-target stimuli, while P50 latencies were significantly reduced. In general, the ASD group displayed abnormally large responses to task irrelevant stimuli, particularly in parieto-occipital and frontal regions of interest. Behavioral results indicated no group differences in reaction time; however, ASD participants displayed difficulty with stimulus discrimination and had a greater number of motor response errors. The authors argue that weak inhibitory

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