



Early enhanced processing and delayed habituation to deviance sounds in autism spectrum disorder

Caitlin M. Hudac^{a,*}, Trent D. DesChamps^a, Anne B. Arnett^a, Brianna E. Cairney^a, Ruqian Ma^a, Sara Jane Webb^{a,b,1}, Raphael A. Bernier^{a,1}

^a Department of Psychiatry and Behavioral Sciences, University of Washington, CHDD Box 357920, Seattle, WA 98195, USA

^b Center for Child Health, Behavior, and Disabilities, Seattle Children's Research Institute, 2001 8th Ave #400, Seattle, WA 98121, USA

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ABSTRACT

Children with autism spectrum disorder (ASD) exhibit difficulties processing and encoding sensory information in daily life. Cognitive response to environmental change in control individuals is naturally dynamic, meaning it habituates or reduces over time as one becomes accustomed to the deviance. The origin of atypical response to deviance in ASD may relate to differences in this dynamic habituation. The current study of 133 children and young adults with and without ASD examined classic electrophysiological responses (MMN and P3a), as well as temporal patterns of habituation (i.e., N1 and P3a change over time) in response to a passive auditory oddball task. Individuals with ASD showed an overall heightened sensitivity to change as exhibited by greater P3a amplitude to novel sounds. Moreover, youth with ASD showed dynamic ERP differences, including slower attenuation of the N1 response to infrequent tones and the P3a response to novel sounds. Dynamic ERP responses were related to parent ratings of auditory sensory-seeking behaviors, but not general cognition. As the first large-scale study to characterize temporal dynamics of auditory ERPs in ASD, our results provide compelling evidence that heightened response to auditory deviance in ASD is largely driven by early sensitivity and prolonged processing of auditory deviance.

1. Introduction

Detection of change in the environment is a fundamental element of human perception. Pre-attentive neural encoding of change mediates the automatic evaluation of incoming information and reflexively triggers attention to important information in the environment (Schröger, 1997). As such, disruption to mechanisms responsible for low-level processing of change may negatively affect attention orienting and environmental adaptation. Evidence suggests that these key elements of sensation and perception are disrupted among individuals with autism spectrum disorder (ASD), a neurodevelopmental disorder characterized by social communication impairments and restricted and repetitive behaviors and interests, and may contribute to common sensory-related features of the disorder (e.g., hypersensitivity, hyposensitivity, sensory-seeking behaviors) (Lane, Young, Baker, & Angley, 2010). Although auditory hypersensitivity is one of the most commonly reported sensory processing impairments in ASD (Gomes, Rotta, Pedroso, Sleifer, & Danesi, 2004; Tomchek & Dunn, 2007), there is evidence that it co-occurs with increased sensory seeking (Liss,

Saulnier, Fein, & Kinsbourne, 2006).

Atypical electrophysiological responses to stimulus change at early stages of sensory information processing have been reported in ASD and associated with behavioral symptoms, such as sensory and attention problems (Cui, Wang, Liu, & Zhang, 2016; Keehn, Mueller, & Townsend, 2013; Orekhova & Stroganova, 2014). The auditory oddball task (Polich, 2007) is commonly used to assess initial detection and discrimination of an infrequent (deviant) auditory tone relative to a frequent tone by measuring an electrophysiological difference component known as the mismatch negativity (MMN) (Näätänen, Paavilainen, Rinne, & Alho, 2007). The MMN is measured and computed as the difference between electrophysiological responses to frequent and deviant stimuli across frontocentral electrodes approximately 100–200 ms post-stimulus onset, overlapping and in part driven by the N1 sub-component (Jääskeläinen et al., 2004). If a stimulus is sufficiently deviant, such as an unexpected novel stimulus, the MMN is followed by a P3, a frontocentral positive-going ERP component occurring approximately 250–350 ms post stimulus that represents early attention orienting (Friedman, Cycowicz, & Gaeta, 2001; Polich, 2007).

* Corresponding author.

E-mail address: chudac@u.washington.edu (C.M. Hudac).

¹ Authors equally contributed as senior author.

Over the past three decades, studies of children and adults with ASD have reported atypical MMN/N1 and P3/P3a/P3b responses to the auditory oddball task (Cléry et al., 2013; Čeponienė et al., 2003; Ferri, et al., 2003a; Gomot et al., 2011; Gomot, Giard, Adrien, Barthélémy, & Bruneau, 2002; Jansson-Verkasalo et al., 2003; Kemner, van der Gaag, Verbaten, & van Engeland, 1999; Kemner, Verbaten, Cuperus, Camfferman, & van Engeland, 1995; Korpilahti et al., 2007; Kujala et al., 2007; Kujala, Lepistö, Nieminen-von Wendt, Näätänen, & Näätänen, 2005; Lepistö, Nieminen-von Wendt, Wendt, Näätänen, & Kujala, 2007; Lepistö et al., 2006; Yu et al., 2015). However, discrepant findings in the literature regarding the timing and magnitude of these responses in ASD have led to different conclusions about how stages of neural processing diverge from typical development and how dysfunctional auditory deviance detection relates to behavioral impairments. All three potential patterns of results have been identified: (1) ASD group differences suggesting a reduced or hyposensitive ASD response (i.e., smaller amplitudes, slower latencies) for the MMN (M. A. Dunn, Gomes, & Gravel, 2008; Jansson-Verkasalo et al., 2003; Kujala et al., 2005, 2007; Lepistö et al., 2006; Seri, Cerquiglioni, Pisani, & Curatolo, 1999) and P3/P3a/P3b (Courchesne, Kilman, Galambos, & Lincoln, 1984; Čeponienė et al., 2003; Ferri, et al., 2003b; Kemner et al., 1995; Lepistö et al., 2006, 2007, 2005); (2) ASD group differences suggesting enhanced or hypersensitive response (i.e., larger amplitudes, faster latencies) for the MMN (Ferri, et al., 2003b; Korpilahti et al., 2007; Lepistö et al., 2006) and P3/P3a/P3b (Ferri, et al., 2003b; Gomot et al., 2002, 2011; Kujala et al., 2007; Lepistö, Nieminen-von Wendt, von Wendt, Näätänen, & Kujala, 2007); and (3) no group difference between ASD and controls, suggesting intact auditory processing (Dunn et al., 2008; Kemner et al., 1995). These distinct patterns of results in ASD may reflect methodological decisions, including stimulus types (i.e., kind of deviance) and task demands (i.e., passive or active task), but may also be driven by individual differences (e.g., cognitive abilities, development/maturation).

Critically, an additional gap in the existing research on auditory deviance detection in ASD is the contribution of dynamic processing across time, specifically habituation or sensitization of neural responses over the course of the experiment. Discrepancies in the literature may be explained by atypicalities in this dynamic pattern, with group differences potentially amplified, attenuated, or washed out entirely depending on the length of the experimental procedure, the type of deviant stimuli, and the number of ERP trials. Thus, the current study aims to expand on existing research by characterizing the temporal dynamics of electrophysiological response to two types of auditory deviance in ASD. The detection of environmental change requires complex integration of stimulus perception and encoding within memory and cognitive systems (Johnson, Spencer, Luck, & Schöner, 2009) and this process evolves over the course of an experiment (Rockstroh et al., 2011). Evidence of slower neural activation in ASD (Kleinhans, Johnson, & Richards, 2009; Kleinhans, Richards, Greenson, Dawson, & Aylward, 2015) suggests important differences may be tethered to dynamic patterns rather than an overall capacity for deviance detection. For instance, infants at risk for developing ASD exhibited a lack of habituation (i.e., they did not show decrement of the signal) during an auditory oddball task (Guiraud et al., 2011), consistent with accounts of atypical sensory processing. Work with school-age children with ASD similarly demonstrated a lack of habituation (Hudac et al., 2015) or atypically delayed responses due to sensitization (i.e., increase of signal) (Hudac et al., 2017) in social perception tasks.

In this study, we aimed to clarify the dynamic nature of auditory deviance detection in a large, carefully characterized sample of youth with ASD ($n = 102$) and without ($n = 31$) using a passive, auditory oddball task during EEG acquisition. We targeted the temporally dynamic aspect of discrimination between repeatedly presented “frequent” tones and (a) rare “infrequent” tones (*frequency deviance*) or (b) unique, non-repeated “novel” sounds (*novelty deviance*) by measuring change in ERP response to these deviant sounds over time. To this end,

Table 1

Participant characterization. Participants included typically developing children (Control) and individuals with autism spectrum disorders (ASD). Abbreviations: SD, standard deviation; VIQ, verbal intelligence quotient; NVIQ, nonverbal intelligence quotient; ADOS-2, Autism Diagnostic Observation Schedule 2nd Edition; SA CSS, social affective calibrated severity score; RRB CSS, restricted and repetitive behavior calibrated severity score.

	Control		ASD		Differences
	Mean (SD)	Range	Mean (SD)	Range	<i>p</i> value
N	31		102		
Female: Male	10:21		20:82		.22
Age (Years)	13.27 (2.34)	9–17	12.29 (3.56)	4–23	.15
VIQ	115.06 (13.91)	94–139	81.3 (30.58)	15–148	< .0001
NVIQ	115.71 (16.39)	90–159	82.26 (30.08)	19–154	< .0001
Data retained (%)	82.9 (11)	47–97	68.81 (19.9)	17–99	< .0001
Deviant conditions (%)	82.28 (11.64)	42–96	68.8 (20.38)	15–99	< .0001
ADOS-2 Overall			14.78 (5.08)	6–26	
SA CSS			7.72 (2.05)	3–17	
RRB CSS			7.38 (2.43)	0–10	
Sensory problems					
Hyper-reactive			2.81 (1.01)		
Distractibility			2.57 (0.93)		
Hypo-reactive			3 (0.92)		
Sensory seeking			2.3 (1.28)		

we examined polynomial (i.e., linear, quadratic) effects of time on the N1 (frequency deviance) and P3a (novelty deviance) over the course of the experiment, as these ERP components are primary contributors to the averaged MMN and P3a signals. We anticipated atypical dynamic patterns in ASD would indicate a lack of habituation (Guiraud et al., 2011; Hudac et al., 2015). Lastly, considering known associations between behaviors and sensory sensitivities (Boyd et al., 2010; Boyd, McBee, Holtzclaw, Baranek, & Bodfish, 2009), we examined how individual ERP patterns were associated with sensory-related behaviors in ASD.

2. Material and methods

2.1. Participants

142 children and young adults age 4–23 years with ASD ($N = 108$; 22 female) and typically developing control children ($N = 34$; 11 female) were enrolled in this study and completed the EEG session. The final sample of 133 individuals comprises individuals who provided clean EEG data and characterization details are provided in Table 1. Parents gave written consent and participants provided written consent or written assent as chronological- and mental-age appropriate. The local ethical review board approved all research procedures.

All participants received a standard battery of cognitive and behavioral assessments including the Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999) or the Differential Ability Scales-Second edition (Elliott, 2007), dependent on participant’s age. ASD diagnoses based on DSM-5 criteria were confirmed by expert clinician judgment following gold-standard assessment that included the Autism Diagnostic Interview-Revised (ADI-R) (Lord, Rutter, & Goode, 1989), the Autism Diagnostic Observation Schedule-2 (ADOS-2) (Lord, Rutter, &

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