Developmental Cognitive Neuroscience xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: www.elsevier.com/locate/dcn

Developmental sequelae and neurophysiologic substrates of sensory seeking in infant siblings of children with autism spectrum disorder

Cara R. Damiano-Goodwin[a,1], Tiffany G. Woynaroski[b,c,1], David M. Simon[d,e], Lisa V. Ibañez[f], Michael Murias[g], Anne Kirby[h], Cassandra R. Newsom[c,i], Mark T. Wallace[b,c,e,j,k], Wendy L. Stone[f], Carissa J. Cascio[c,e,k,*]

[a] Duke Center for Autism and Brain Development, Duke University, Durham, NC, USA
[b] Department of Hearing and Speech Sciences, Vanderbilt University Medical Center, Nashville, TN, USA
[c] Vanderbilt Kennedy Center, Vanderbilt University Medical Center, Nashville, TN, USA
[d] Neuroscience Graduate Program, Vanderbilt University Medical Center, Vanderbilt University, Nashville, TN, USA
[e] Vanderbilt Brain Institute, Vanderbilt University Medical Center, Vanderbilt University, Nashville, TN, USA
[f] Department of Psychology, University of Washington, Seattle, WA, USA
[g] Duke Institute for Brain Sciences, Duke University, Durham, NC, USA
[h] Department of Occupational Therapy, University of Utah, Salt Lake City, UT, USA
[i] Department of Pediatrics, Vanderbilt University Medical Center, Nashville, TN, USA
[j] Department of Psychological Sciences, Vanderbilt University, Nashville, TN, USA
[k] Department of Psychiatry and Behavioral Sciences, Vanderbilt University Medical Center, Nashville, TN, USA

ARTICLE INFO

Keywords:
Sensory
Autism
Infant siblings
Longitudinal
Frontal asymmetry
EEG

ABSTRACT

It has been proposed that early differences in sensory responsiveness arise from atypical neural function and produce cascading effects on development across domains. This longitudinal study prospectively followed infants at heightened risk for autism spectrum disorder (ASD) based on their status as younger siblings of children diagnosed with ASD (Sibs-ASD) and infants at relatively lower risk for ASD (siblings of typically developing children; Sibs-TD) to examine the developmental sequelae and possible neurophysiological substrates of a specific sensory response pattern: unusually intense interest in nonsocial sensory stimuli or "sensory seeking." At 18 months, sensory seeking and social orienting were measured with the Sensory Processing Assessment, and a potential neural signature for sensory seeking (i.e., frontal alpha asymmetry) was measured via resting state electroencephalography. At 36 months, infants' social symptomatology was assessed in a comprehensive diagnostic evaluation. Sibs-ASD showed elevated sensory seeking relative to Sibs-TD, and increased sensory seeking was concurrently associated with reduced social orienting across groups and resting frontal asymmetry in Sibs-ASD. Sensory seeking also predicted later social symptomatology. Findings suggest that sensory seeking may produce cascading effects on social development in infants at risk for ASD and that atypical frontal asymmetry may underlie this atypical pattern of sensory responsiveness.

1. Introduction

Autism spectrum disorder (ASD) is characterized by social and communication deficits accompanied by a pattern of repetitive behaviors, restricted interests, and unusual responses to sensory stimuli. Atypical sensory responsiveness has been observed or reported in many individuals with ASD from infancy to adulthood (Baranek et al., 2006; Crane et al., 2009; Dawson and Watling, 2000). Previous research indicates that atypical sensory responsiveness emerges early in life (i.e., as early as 2–6 months of age; Bryson et al., 2007; Dawson et al., 2000), possibly *before* some of the social and communicative impairments typically associated with ASD (Baranek, 1999a,b; Dawson et al., 2000; Mulligan and White, 2012). This evidence is consistent with the developmental primacy of basic sensory neural pathways, many of which are in place prenatally (Anderson and Thomason, 2013). Recent work also suggests that sensory responsiveness is related to other core symptoms of ASD (Foss-Feig et al., 2012; Gabriels et al., 2008; Kern et al., 2007; Stevenson et al., 2015). Together, this evidence suggests that atypical sensory behaviors may serve as early markers of ASD risk. Furthermore, since the early sensory environment likely influences the

* Corresponding author at: 1601 23rd Ave., S, Suite 3057, Nashville, TN 37232, USA.
E-mail address: carissa.cascio@vanderbilt.edu (C.J. Cascio).
[1] Damiano-Goodwin and Woynaroski made equal contributions to this work.

http://dx.doi.org/10.1016/j.dcn.2017.08.005
Received 9 August 2016; Received in revised form 6 July 2017; Accepted 9 August 2017

development of social and communicative skills associated with ASD, a better understanding of the cascading effects of basic sensory disturbances may elucidate the developmental trajectory of later-developing social and communication deficits in ASD. However, to better understand this process, prospective longitudinal studies are needed to examine the predictive value of sensory behaviors on social and communicative development (Cascio et al., 2016).

Given the early development of atypical sensory responsiveness, it is possible that behavioral response patterns to sensory stimuli may serve as an early biomarker or endophenotype of ASD. An endophenotype is a heritable intermediate phenotype that is expressed in both affected and non-affected family members. The identification of endophenotypes provides clues into the biological underpinnings of a disorder (Gottesman and Gould, 2003), and may ultimately help to discriminate between inherited behavioral features of the disorder and features that are secondary or epiphenomenal. Infant siblings of individuals with ASD are an ideal population in which to study candidate endophenotypes. This line of research compares infant siblings of children diagnosed with ASD (Sibs-ASD) to infant siblings of typically developing children (Sibs-TD), in order to better understand the characteristics associated with a genetic risk for ASD. Sibs-ASD are at heightened risk for ASD and, even when they are not later diagnosed with ASD, often show subclinical symptoms associated with the disorder (Georgiades et al., 2013; Messinger et al., 2013; Ozonoff et al., 2014; Stone et al., 2007). Despite some preliminary studies suggesting that atypical sensory responsiveness may be an early characteristic of the broader ASD phenotype (Brian et al., 2008; Loh et al., 2007; Ozonoff et al., 2008), the developmental trajectory of atypical sensory responsiveness in Sibs-ASD and the neural mechanisms driving these atypicalities remain poorly understood.

Previous research suggests that atypical sensory responsiveness in ASD can be characterized as three separate empirically-derived constructs: hyper-responsivity, hypo-responsivity, and sensory seeking (Ben-Sasson et al., 2008; Boyd et al., 2010). Most previous research has focused on hypo- or hyper-responsivity (i.e., reduced or exaggerated behavioral responses to sensory stimuli, respectively) in ASD. There is little research focusing specifically on sensory seeking (Ben-Sasson et al., 2009), defined here as behaviors with the goal of enhancing or prolonging a nonsocial sensory experience (e.g., visual examination, repetitive touching, banging, or licking an object). In understanding the developmental trajectory of ASD symptoms, sensory seeking is particularly of interest because these behaviors are likely to divert attention away from social learning opportunities. In addition, though sensory seeking may be directed towards other individuals (e.g., hair stroking), the odd nature of these behaviors may actually obstruct the development of typical social relationships. Supporting this, sensory seeking has been linked to increased severity of concurrent social and communication deficits in children with ASD (Hilton et al., 2007; Liss et al., 2006; Watson et al., 2011).

The extent to which early sensory seeking behaviors and early sensory experiences more broadly relate to later ASD symptomatology remains unclear, however. In addition, because sensory atypicalities are present so early in infancy and emerge before many of the social and communicative impairments associated with ASD, the neural networks that support these atypical sensory behaviors may also be critically involved in the emergence of the core diagnostic features of ASD. Yet, very little is currently known about the neural correlates of sensory responsiveness in typically developing infants, and virtually nothing is known about these processes in Sibs-ASD. To address these questions, the present study examines sensory seeking behaviors in Sibs-ASD and the neural mechanisms that may be driving these behaviors. The present study also investigates the extent to which sensory seeking behaviors might be related to later ASD symptomatology, and thus their potential utility as early markers or endophenotypes for ASD.

As a potential neural basis for sensory seeking in infants at risk for ASD, the current study measured asymmetry in resting state alpha band oscillations (approximately 6–9 Hz in infants) at frontal electrode sites using EEG. Frontal asymmetry as measured by resting state EEG (i.e., the relative difference in power between hemispheres in the alpha band) is a reliable and stable measure that has been used to index risk for psychopathology across the lifespan (Coan and Allen, 2004). Frontal asymmetry is believed to reflect individual differences in the lateralization of brain activity which may be attributable to differences in thalamic inhibition of cortical processing across hemispheres (Jensen and Mazaheri, 2010). It is partly heritable (Anokhin et al., 2006) and has been studied as a potential endophenotype in other clinical conditions, such as depression (Allen and Cohen, 2010). Frontal asymmetry may also serve as a marker of cortical development, as hemispheric differences in alpha power tend to change over the course of the first two years of life, and may contribute to changes in exploratory behavior over this developmental period (Fox et al., 1994; Fox et al., 2001).

Patterns of resting frontal asymmetry may be particularly useful for understanding sensory seeking in Sibs-ASD, as frontal asymmetry has already been correlated with ASD symptomatology. More specifically, more severe ASD symptoms and social inhibition have been observed in children with ASD with relatively greater right frontal asymmetry (Burnette et al., 2011; Sutton et al., 2005), whereas fewer parent-reported social deficits have been observed in children with relatively greater left frontal asymmetry. Most relevant to the present study, by the age of 18 months Sibs-ASD on average demonstrate relatively greater right frontal asymmetry, whereas Sibs-TD on average display relatively greater left frontal asymmetry (Gabard-Durnam et al., 2015).

Frontal asymmetry has also been associated with sensory responsiveness in Sibs-ASD. Specifically, the atypical pattern of greater right frontal asymmetry has already been observed to co-occur with higher sensory hyporesponsivity in this high risk group (Simon et al., under review). This finding is of interest because hyporesponsivity has been theoretically and empirically linked to sensory seeking. Dunn's (1997) Model of Sensory Processing postulates that sensory seeking and hyporesponsivity are both associated with a high neurological threshold, but represent different behavioral response patterns (i.e., active versus passive). Consistent with this theoretical framework, past studies have demonstrated behavioral associations between hyporesponsivity and sensory seeking in children diagnosed with ASD (Ausderau et al., 2014; Dunn, 1997; Freuler et al., 2012). Together, these results suggest that frontal asymmetry may reflect differences in neural organization and processing that relate to sensory atypicalities in a population at risk for ASD.

The specific aims of the present study are as follows: (a) to determine whether high-risk Sibs-ASD differ from low-risk Sibs-TD in sensory seeking behaviors at 18 months, (b) to evaluate whether resting frontal asymmetry may reflect a potential neural mechanism underlying sensory seeking differences, and (c) to examine whether early sensory seeking is related to concurrent social orienting and later social deficits associated with ASD at 36 months. We hypothesized that increased sensory seeking at 18 months diverts attention from important social cues and thus reduces social orienting, which ultimately has cascading effects on social development and results in more social deficits at 36 months. We also anticipated that Sibs-ASD would exhibit more atypical frontal asymmetry patterns (i.e., greater right frontal asymmetry) as previously observed in Sibs-ASD at 18 months (Gabard-Durnam et al., 2015). Further, we predicted that right frontal asymmetry would serve as a potential neural correlate of increased sensory seeking, as right frontal asymmetry has been linked with ASD symptomatology in children who are diagnosed with or at risk for ASD (Burnette et al., 2011; Simon et al., 2017; Sutton et al., 2005).

2. Materials and methods

2.1. Overview of study design

To test our hypotheses, we drew upon data from a multisite,