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Association between pupillary light reflex and sensory behaviors in children with autism spectrum disorders

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ABSTRACT

Atypical pupillary light reflexes (PLR) has been observed in children with autism spectrum disorders (ASD), which suggests potential autonomic nervous system (ANS) dysfunction in ASD. ANS is also involved in modulating sensory processing and sensory dysfunction has been widely reported in children with ASD. However, the potential association between physiological measurements of PLR and behavioral observations (e.g. sensory behaviors) has not been examined extensively in literature. In this study, we investigated the potential correlation between PLR and frequently observed sensory behaviors in children with ASD. We found a significant association between PLR constriction amplitude and a set of sensory behaviors in the ASD group but not in typically developing children. Children with ASD who showed more atypical sensory behaviors also had smaller PLR constriction amplitudes. A smaller PLR constriction amplitude suggests lower parasympathetic modulation. This observation implies that some atypical sensory behaviors in children with ASD could be associated with decreased parasympathetic modulation.

1. Introduction

Autism spectrum disorders (ASDs) are complex developmental disorders with symptoms in social functioning, communication, and restricted or repetitive behaviors. Multiple atypical neurological and behavioral measures have been found in ASD. We recently discovered that children with ASD showed significantly different pupillary light reflex (PLR) than typically developing children (Fan, Miles, Takahashi, & Yao, 2009; Daluwatte et al., 2013). PLR measures the dynamic changes in pupil size induced by optical luminance changes. Children with ASD showed multiple atypical PLR parameters including longer latency, less constriction amplitude, and shorter constriction/redilation times. We also found a significant age effect in PLR latency in children with typical development that was not observed in children with ASD (Daluwatte et al., 2013).

The pupil size is controlled by two antagonist iris muscles, the sphincter and dilator, which produce pupil constriction and dilation, respectively. The sphincter is mainly innervated by the parasympathetic nervous system and the dilator innervated by the sympathetic system (Barbur, 2004). The sympathetic tract passes through the ciliary ganglion without synapsing and emerges as the long ciliary nerves entering the eye along the optic nerve. These postganglionic sympathetic nerves travel within the suprachorodial space to innervate the iris dilator muscle (Appenzeller, 1999). The preganglionic parasympathetic

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nerve branches off to the ciliary ganglion and emerges as several short ciliary nerves which innervate the iris sphincter muscle (Appenzeller, 1999). Due to such underlying control mechanisms from the autonomic nervous system (ANS), PLR provides a simple yet reliable clinical assessment of ANS dysfunction (Barbur, 2004; Bremner, 2009).

In addition to pupillary pathway, ANS dysfunction in cardiovascular system has also been reported in children with ASD (Bal et al., 2010; Ming, Julu, Brimacombe, Connor, & Daniels, 2005; Ming et al., 2011). In fact, ANS in general is involved in a multitude of physiological and behavioral activities beyond the pupillary and cardiovascular controls. For example, ANS is known to play a role in modulating the sensory processing (Kootz & Cohen, 1981; Saper, 2002; Vallbo, Hagbarth, Torebjork, & Wallin, 1979). Human senses can be divided into five traditional groups (vision, auditory, taste, smell, and touch) and various non-traditional senses such as temperature and pain. Sensory system is an essential part of the neurological system that transduces the physical world to our perception. There are four basic patterns in sensory processing: low registration, sensory seeking, sensory sensitivity, and sensation avoiding (Dunn, 1997). Abnormality in sensory processing has been frequently reported in children with ASD (Kientz & Dunn, 1997; Klintwall et al., 2011; Tomchek & Dunn, 2007). For example, children with ASD avoid auditory stimulation by withdrawal while seeking for proprioceptive and vestibular stimulation by repetitive behaviors such as rocking, spinning, or flapping their hands (Case-Smith & Bryan, 1999). While identifying atypical sensory behaviors in ASD, it is also important to understand its association with physiological measures to better understand the causes and effects of such atypical sensory behaviors in ASD.

Due to the widespread implication of ANS dysfunction in ASD, it is valuable to understand whether different ANS measures may be correlated with atypical sensory behaviors observed in ASD. Indeed, Woodard et al. (2012) recently reported an association between sensory processing and heart rate responses to a variety of sensory stimuli in children with ASD. We investigated in this study the potential association between PLR and atypical sensory behaviors observed in children with ASD. We hypothesize that some atypical sensory behaviors observed in children with ASD are associated with PLR parameters because both are regulated by the ANS.

2. Methods

2.1. Participants

Data on frequently observed atypical sensory behaviors in children with ASD were collected from a group of children who participated in a PLR study (Daluwatte et al., 2013). Children with ASD (referred to as the "ASD" group) were recruited from regional autism clinics and their diagnoses were evaluated and confirmed by the pediatrician and/or neuropsychologist. Children with typical development (referred to as the "TD" group) were recruited from the local community. All children in the TD group were screened for autism using the Social Communication Questionnaire Lifetime (Eaves, Wingert, Ho, & Mickelson, 2006) and scored below the clinical cutoff of 15.

The ASD group included 152 children from 5 to 19 years with an average age of 10.7 ± 3.4 years. Among the children with ASD, 86 were diagnosed with autism, 32 with Asperger syndrome and 34 with PDD-NOS. The TD group included 107 children from 6 to 17 years (10.9 ± 2.9 years). There were 135 boys (10.9 ± 3.5 years), 17 girls (9.8 ± 2.6 years) in the ASD group, and 79 boys (11.1 ± 3.1 years), 28 girls (10.6 ± 2.4 years) in the TD group. The ASD group was further divided between those who took some medication (stimulants, atypical antipsychotics, serotonin reuptake inhibitors, antihistamines, antiepileptics etc.) within 48 h before the PLR test and those with no medication use. In the "w/med" group, seventy children were exposed to one or more medications; whereas 82 were medication free (the "w/o med" group). No one in the TD group had taken medication. Sensory behavioral data were not available for 4 participants in the ASD group and one participant in the TD group.

This study was approved by the Institutional Review Board of the University of Missouri. All participants and their legal guardians provided written informed assent and consent prior to participating.

2.2. Instrument and procedure

2.2.1. PLR measurement

The binocular pupillography recording system used to measure PLR was described previously in detail (Daluwatte et al., 2013). The system used near-infrared cameras (GC660, Allied Vision Technologies, Stadtroda, Germany) to record pupil images at a speed of 115 frames-per-second (fps). PLR was stimulated using a 100 ms green light flash which was produced using 530 nm green LEDs. PLR was measured at four stimulation intensities in both light-adapted (LA) and dark-adapted (DA) conditions (LA 69.3 cd/m^2, LA 872.1 cd/m^2, LA 8721.1 cd/m^2 and DA 63.1 cd/m^2).

As explained in Daluwatte et al. (2013), a total of five PLR parameters were obtained: (1) resting pupil diameter; (2) PLR latency (time from stimulus to onset of constriction); (3) constriction time (time from onset of constriction to reach minimal diameter); (4) redilation time (time for the pupil to recover half of the constriction since minimal pupil diameter); (5) constriction amplitude (maximal relative change in pupil area during constriction). PLR parameters from both eyes during 8 repeated measurements were averaged to obtain the PLR parameters at each stimulus.

2.2.2. Sensory behaviors

A set of sensory behaviors (29 items) was selected from the Sensory Profile (the "Caregiver Questionnaire" from Pearson Education, Inc., San Antonio, TX) (Dunn, 1994, 1999; Kientz & Dunn, 1997). These items were chosen on the basis of being