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Neural measures of social attention across the first years of life: Characterizing typical development and markers of autism risk

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ABSTRACT

Few studies employing event-related potentials (ERPs) to examine infant perception/cognition have systematically characterized age-related changes over the first few years of life. Establishing a 'normative' template of development is important in its own right, and doing so may also better highlight points of divergence for high-risk populations of infants, such as those at elevated genetic risk for autism spectrum disorder (ASD). The present investigation explores the developmental progression of the P1, N290, P400 and Nc components for a large sample of young children between 6 and 36 months of age, addressing age-related changes in amplitude, sensitivity to familiar and unfamiliar stimuli and hemispheric lateralization. Two samples of infants are included: those at low- and high-risk for ASD. The four components of interest show differential patterns of change over time and hemispheric lateralization; however, infants at low- and high-risk for ASD do not show significant differences in patterns of neural response to faces. These results will provide a useful point of reference for future developmental cognitive neuroscience research targeting both typical development and vulnerable populations.

1. Introduction

The recording of the brain's electrical activity via the event-related potential (ERP) provides a window into infant perception and processing when other avenues of overt measurement are not yet available because of limited motor, communication and cognitive abilities. Infant and toddler studies using ERP often focus on a similar set of dependent and independent variables in order to answer questions about early perception and cognition. In exploring each component, analyses are often completed separately in order to address different aspects of the ERP response: amplitude (strength), latency (speed) and scalp topography (putative generators). Amplitude is thought to reflect the degree of synchronous firing of cortical pyramidal cells in response to a stimulus. Latency, which requires the identification of each individual component's peak, reflects the speed with which the maximal neural response is generated. Finally, topography provides a way of not only defining a component (e.g., the P300b is maximal over parietal scalp, whereas the P300a is maximal over frontal scalp)

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but also inferring underlying neural generators. These metrics have informed our current understanding of normative developmental changes in sensation and perception, as well as our emerging conceptualizations of developmental delay and disorder.

Several specific ERP components have become commonly used in the field of infant studies, and many of these components have now been explored by researchers in the field developmental psychopathology in the interest of delineating how and when typical and atypical development diverge early in life. In recent years, there has been a growing desire to find measures for very young children that are more sensitive to developmental difference than behavioral assays. In large part, this is due to the growing study of autism spectrum disorder (ASD), a developmental disorder that leads to impaired communication and social engagement, as well as a heightened presence of repetitive interests and behaviors. While ASD is thought to be primarily heritable, diagnostic measures relying on behavior are not reliably sensitive and specific for infants and toddlers in the first year or 18 months of life (e.g., Lord et al., 2012). As a result, there is a desire to 'bypass' behavior in the early identification of ASD; ERPs are candidate measures of brain development and response to stimuli. However, because children with ASD cannot predictably be identified in the first two years of life, the population of interest is infant siblings of children with ASD. These 'infant sibs' are of great interest for two reasons: first, roughly 20% of these infants will themselves go on to be diagnosed with ASD (Ozonoff et al., 2011a,b); and second, those who do not receive a formal diagnosis often exhibit sub-clinical features similar to those observed in ASD, conceptualized as the 'broader endophenotype' of ASD (Rogers, 2009; Elsabbagh and Johnson, 2010). Consequently, these high-risk infants can reveal much about the neural underpinnings of ASD.

If ERPs are to provide a useful window into whether and when development has gone awry, it is essential to understand the normative age progression of the neural response, as well as what other kinds of factors might affect the brain's reaction to stimuli. The effect of age on ERP response has been widely explored, largely in infant cross-sectional studies and in longitudinal investigations of school-age children (e.g., Taylor et al., 2004; Itier and Taylor, 2004) or very young infants (Webb et al., 2005). Because of the centrality of social stimuli in infant development, a number of studies have explored differential responses to familiar social stimuli (generally the mother's face) versus unfamiliar social stimuli (a stranger's face). Finally, because hemispheric lateralization is a critical normative process associated with increased specialization and efficiency of neural networks, topographic region (that is, right versus left hemisphere) is often explored as a metric of brain development. Though there are many ERP components that have been studied in infant and toddler development, four visual components consistently appear in investigations of young children and will be addressed here: the P1, N290, P400 and Nc. A review of each follows, with a focus on the role of age, familiarity and hemisphere. Finally, because one of the central questions for the current investigation is the degree to which these patterns of response might vary in children at risk for ASD, a review of the current literature in children with ASD (or with a family history of the disorder) will be presented. For the purposes of the current paper, we will focus our attention on variables that affect the amplitude of the neural response.

1.1. P1

The P1 is a positive-going deflection that is measured over occipital regions approximately 90–150 ms after a visual stimulus. It is predictably elicited by visual stimuli in general (as opposed to particular types of stimuli, like faces) and is therefore thought to reflect sensory experience rather than higher-order processing. In infants and young children, the P1 increases in amplitude with age (Kos-Pietro et al., 1997). However, sometime between ages 2 and 4, this pattern reverses, and the amplitude of the P1 decreases with increasing age (Kuefner et al., 2010; Kos-Pietro et al., 1997; Hileman et al., 2011; Itier and Taylor, 2004), which may reflect the natural developmental course of synaptic pruning. Despite these developmental changes, the P1 in infants does not appear to be sensitive to familiarity of the stimulus (De Haan and Nelson, 1997, 1999). Moreover, the P1 is generally observed bilaterally over posterior electrodes (Csibra et al., 2008; but see McCleery et al., 2009). Little research has explored whether very young children with or at risk for ASD show differences in the P1, but school-aged children with ASD show typical patterns of reduced P1 amplitude with age (Hileman et al., 2011). In sum, then, the P1 is a bilateral response evoked by visual stimuli (with minimal sensitivity to familiarity) that shows a non-linear pattern of growth with age and does not seem to be clearly affected in ASD.

1.2. N290/P400

The N290 and P400 are a pair of components that are thought to be functionally and topographically similar. Together, they are thought to be the infant precursor to the adult N170, a face-sensitive component (Scott et al., 2006; Csibra et al., 2008; De Haan et al., 2003). The N290 is a negative amplitude shift observed in infants that has repeatedly shown sensitivity to faces (Csibra et al., 2008; De Haan et al., 2003); however, age-related changes in the amplitude of the N290 are unclear. Initial reports indicated a lack of familiarity modulation in the N290 (De Haan and Nelson, 1997, 1999), but other studies have reported that the amplitude of the N290 is affected by familiarity of the stimulus (Scott et al., 2006; Key and Stone, 2012). Despite the gradual right-ward shift of face-sensitive neural activity captured by this cluster of components (De Haan et al., 2003), consistent hemispheric differences in the N290 have not been clearly documented in the literature (Luyster et al., 2011; McCleery et al., 2009; Webb et al., 2006). Previous investigations have not found consistent differences in the N290 in young children with or at risk for ASD. Across studies, there do not appear to be straightforward effects of ASD risk on the amplitude of the N290 to faces (Key and Stone, 2012), though there may be slight differences in the lateralization of the component (Luyster et al., 2011; McCleery