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Functional neural bases of numerosity judgments in healthy adults born preterm

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ABSTRACT

High rates of mathematics learning disabilities among individuals born preterm (< 37 weeks GA) have spurred calls for a greater understanding of the nature of these weaknesses and their neural underpinnings. Groups of healthy, high functioning young adults born preterm and full term (n = 20) completed a symbolic and non-symbolic magnitude comparison task while undergoing functional MRI scanning. Collectively, participants showed activation in superior and inferior frontal and parietal regions previously linked to numeric processing when comparing non-symbolic magnitude arrays separated by small numeric distances. Simultaneous deactivation of the default mode network also was evident during these trials. Individuals born preterm showed increased signal change relative to their full term peers in right inferior frontal and parietal regions when comparing the non-symbolic magnitude arrays. Elevated signal change during non-symbolic task blocks was associated with poorer performance on a calculation task administered outside of the scanner. These findings indicate that healthy, high-functioning adults born preterm may recruit fronto-parietal networks more extensively when processing non-symbolic magnitudes, suggesting that approximate number system training may be an inroad for early intervention to prevent mathematics difficulties in this population.

1. Introduction

As many as 11% of births worldwide are preterm (< 37 weeks GA; Blencowe et al., 2012). The adverse clinical experiences associated with preterm birth place these children at increased risk for cognitive and academic difficulties across the lifespan (Aylward, 2005). Although cognitive impairments are most prevalent amongst those born at the lowest gestational ages (i.e., < 33 weeks GA), recent studies indicate that rates of special education placement, learning disabilities and cognitive delay are increased even amongst children born moderately (32–34 weeks GA) or late preterm (34–36 weeks GA) relative to the general population (Baron, Erickson, Ahronovich, Baker, & Litman, 2011; de Jong, Verhoeven, & van Baar, 2012; Nepomnyaschy, Hegyi, Ostfeld, & Reichman, 2012). Difficulties in mathematics are especially common, with over 50% of children born very preterm experiencing delays in basic numeric skill acquisition (Litt, Taylor, Klein, & Hack, 2005; Pritchard et al., 2009; Taylor, Espy, & Anderson, 2009; Taylor, Klein, et al., 2011). Nevertheless, a substantial proportion of the population with preterm birth go on to show typical schooling trajectories and high levels of adaptive behavior as adults, highlighting the potential for resilience even in the face of adverse perinatal experiences (Clark et al., 2013; Saigal, 2014). There is a critical need to identify the factors that contribute to this resilience, as they represent potentially fruitful targets for intervention.

Disruptions to brain development likely play a key role in accounting for elevated rates of cognitive and behavioral morbidity among individuals born preterm (Clark et al., 2013; Rogers et al., 2012; Woodward, Clark, Bora, & Inder, 2012). Structural MRI studies show alterations in white matter development, including reduced fractional anisotropy and increased radial diffusivity in central white matter tracts in the brains of children and adolescents born preterm (Counsell et al., 2003; Duerden, Card, Lax, Donner, & Taylor, 2013). In addition to reduced total cerebral volume, disproportionate reductions in the volumes of the hippocampus, thalamus, parietal and frontal cortical regions are prevalent, with these volumetric losses persisting into adulthood (Nosarti et al., 2014; Peterson et al., 2000; Taylor, Filipek, et al., 2011). Again, the relation of reduced gestational age to these neural abnormalities appears to follow a dose-response curve, with those born moderately or late preterm showing more subtle disruptions to neural connectivity and morphology than those born very preterm

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(Kelly et al., 2016; van Soelen et al., 2010). Concerning mathematical cognition, one of the earliest studies using MRI with adolescents born preterm reported a decrease in gray matter volume in the intraparietal sulcus (IPS), a region of the brain that has been linked repeatedly to numeric processing (Isaacs, Edmonds, Lucas, & Gadian, 2001). Reductions in IPS volume correlated with lower performance on a calculation task, suggesting that aberrant neural development may explain disproportionately high rates of mathematics learning difficulties in this population.

Fewer studies have focused on the functional neural bases of cognitive performance in individuals born preterm. The limited existing evidence suggests that adults born preterm draw on distinct neural networks from those typically activated during cognitive tasks. Kalpakidou et al. (2014), for instance, reported that blood oxygen level dependent (BOLD) activity during a functional MRI (fMRI)-based verbal fluency task was higher in adults born preterm relative to full term controls across an array of neural regions including the caudate nucleus, thalamus, insula, superior temporal gyrus, and right precentral and postcentral gyri. These neural differences were present despite similar levels of behavioral performance between the groups. In another study, preterm-born adults showed increased BOLD activation in the middle temporal gyrus, posterior cingulate and precuneus during a sustained attention task, as well as reduced activity in the cerebellum and supramarginal gyrus during a response inhibition task (Lawrence et al., 2009). Daamen et al. (2015) found that adults born extremely preterm showed increased suppression of the default mode network (DMN) relative to controls while performing a working memory task and suggested that this indicated increased utilization of neural resources in the face of cognitive load. There is also evidence for neural compensation among adults born preterm: although they showed reduced hippocampal volumes relative to full term adults, they were characterized by increased parahippocampal volumes and increased BOLD signal in the parahippocampal cortex during a memory task (Lawrence et al., 2010). Overall, these studies hint that preterm birth may presage alterations in the organization of functional neural networks that support effective cognitive performance.

To our knowledge, very few studies have examined mathematical processing in individuals born preterm using fMRI, despite growing calls to understand the nature of the mathematics difficulties in this population (Simms et al., 2013; Taylor et al., 2009). An exception is the Bavarian Longitudinal Study, which found that the relation of childhood mathematics achievement to functional connectivity within fronto-parietal neural networks was different for adults born preterm relative to those born full term (Bauml et al., 2016). Specifically, higher mathematics performance in childhood correlated with higher functional connectivity in the left lateral occipital/middle temporal cortex and right angular gyrus in adults born preterm, whereas the reverse was true in the full term group. Higher mathematics scores also predicted reduced functional connectivity in the superior frontal gyrus in the preterm group, whereas the reverse was true for the full term group. Thus, there may be differences in the networks underscoring mathematics capabilities in adults born preterm and full term.

Recent behavioral studies have reported that young children born preterm are slower and less accurate when discriminating between non-symbolic magnitude arrays (i.e., at numerosity judgments; Guarini et al., 2014), an ability linked to higher levels of mathematics performance in typically developing samples (Halberda, Ly, Wilmer, Naiman, & Germine, 2012; Libertus, Feigenson, & Halberda, 2013; Libertus, Odic, & Halberda, 2013). Importantly, numeric processing involves not only recognizing differences in non-symbolic magnitudes, such as different numbers of dots, but also mapping these magnitudes to culturally specific numeric symbols, such as the number '5' (Geary, 2006; Piazza, Pinel, Le Bihan, & Dehaene, 2007). It is not clear from existing research whether individuals born preterm are prone to difficulties in either or both of these domain-specific numeric processes or whether they may be able to overcome difficulties in basic numeric processing by drawing on alternative neural networks.

To address this question, we examined the functional neural bases of non-symbolic and symbolic magnitude processing in healthy, high-functioning young adults born preterm. Specifically, we aimed to determine whether there were differences in the BOLD response patterns of the preterm vs. full term groups when comparing non-symbolic and symbolic magnitudes with small and large ratio differences. Consistent with Weber's law, the difficulty associated with differentiating two magnitudes increases as the numeric distance between the values decreases (Brannon, 2006; Libertus & Brannon, 2009). Thus, cognitive load should be higher when the ratio between magnitudes is larger (e.g., 8 vs. 10, a ratio of 0.8 as opposed to 5 vs. 10, a ratio of 0.5). We hypothesized that there would be differences in the neural regions associated with numeric processing in the two study groups and that these differences would be most pronounced for more difficult numeric comparisons, i.e., those with a smaller distance between them and a larger Weber ratio. Based on the limited existing fMRI data on numeric processing in adults born preterm (Bauml et al., 2016), we expected group differences in BOLD response patterns to be particularly pronounced in fronto-parietal regions linked to magnitude processing. Given Daamen et al.'s (2015) evidence for increased suppression of the DMN amongst adults born preterm when they performed a working memory task, we also anticipated that the preterm group would show greater deactivation of DMN regions relative to the full term group when making judgments of relative magnitude.

2. Material and methods

2.1. Participants

All procedures were approved by the University of Arizona Institutional Review Board and participants provided written, informed consent to study participation. Participants also provided written authorization to request their hospital birth records to verify their gestational age and birth weight and were asked to verify this information with their parents. Eleven students born preterm (< 37 weeks gestation) and 12 students born full term were recruited via an undergrad participant pool, fliers and class announcements at the University of Arizona. One student was excluded due to excessive motion in the scanner and two because birth information could not be verified, leaving 10 participants in each group. Descriptive characteristics for these participant groups are described in Table 1.

2.2. Procedure

Participants completed a laboratory screening visit during which they filled in a questionnaire regarding background information and health and were administered cognitive measures in a fixed order. Participants who reported no contraindications to MRI and no history of head trauma or neurological conditions were invited for a second visit to the MRI suite to complete the fMRI task. Participants received class credit or $50 compensation following study completion.

Table 1
Descriptive characteristics of preterm and full term groups.

	Preterm	Full term	*p*
M (SD) Gestational age	32.30 (2.94)	40.05 (0.85)	< 0.001
M (SD) Birthweight	3.87 (0.81)	7.83 (1.22)	< 0.001
M (SD) Age	19.52 (1.05)	20.61 (1.73)	0.20
n (%) Male	3 (30)	5 (50)	0.36
n (%) White, non-Hispanic	7 (70)	5 (50)	
n (%) White, Hispanic	3 (30)	5 (50)	0.36
M (SD) IQ[a]	106.11 (12.13)	103.89 (13.03)	0.71

[a] Assessed using the Kauffmann Brief Intelligence Test (Kaufman & Kaufman, 2004).