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Early executive function differences in infants born moderate-to-late preterm

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ABSTRACT

Individuals who are born very preterm (< 32 weeks gestation) show differential development of prefrontal cortex structure, function, and dependent behaviors, including executive function (EF) skills, beginning during late infancy and extending into adulthood. Preschool-aged children born moderate-to-late preterm (PT; 32–36 weeks gestation) show smaller discrepancies in EF development, but it is unclear whether these differences first emerge during the early childhood years, when EF is rapidly developing, or if they arise from alterations in complex cognitive skills measurable in late infancy. In the current study, we examined whether differences in complex attention, memory, and inhibition skills (precursor skills to EF) are altered in healthy infants born moderate-to-late PT at 9-months corrected age. Infants born PT demonstrated poorer memory at test following habituation than their full-term peers. Furthermore, lower gestational age at birth was associated with poorer performance on five of the six early EF tasks. Results indicate that even in the context of low medical and environmental risk, performance on the Bayley within the normal range, and no group-level differences in processing speed, infants born moderate-to-late PT show subtle alterations in cognitive skills presumed to be dependent on prefrontal cortex by 9-months of age, likely setting the stage for long-term differences in EF development.

1. Introduction

Preterm (PT; < 37 weeks gestation) birth represents a major public health concern. While the long-term correlates of very PT birth (< 32 weeks) have been documented, interest has recently increased in monitoring outcomes of children born only moderate-to-late preterm (32–36 weeks gestation). Infants born moderate-to-late PT represent approximately 8% of all births in the United States (and 80% of all PT births; [1]. Although the risk of serious medical problems is low, short-term morbidity is still higher in comparison to full-term (FT) infants [2]. Emerging evidence suggests there are also long-term impacts of moderate-to-late prematurity; older children and adolescents born moderate-to-late PT are at higher risk for a diverse set of problematic outcomes, including poor school performance [3].

There is little information about the neurodevelopmental impacts of moderate-to-late PT birth on specific cognitive or socioemotional processes. In contrast, the impact of prematurity on higher-order cognitive abilities, including executive function (EF) skills such as attention flexibility, working memory, and inhibitory control, has been well-characterized in individuals born very PT. EF impairments in individuals born very PT are measurable by late infancy [4] and persist beyond early adolescence (e.g. [5]). A complementary neuroimaging literature indicates that EF differences associated with very PT birth are likely related to disruptions in prefrontal cortex structure and function (e.g. [6]).

Like children born very PT, preschool-aged children born within the moderate-to-late PT range also show poorer EF development than their FT peers [7–10]; similarly, older children born moderate-to-late PT show altered structural and functional prefrontal cortex development [11,12]. However, it is unclear if alterations in prefrontal-dependent behaviors first emerge during the early preschool period, when EF is rapidly developing and the demands of the environment are increasing, a pattern that would be consistent with 'growing into deficit', or if differential EF development begins even earlier in life. Neuroimaging research indicates that frontal lobe circuits that later support EF develop rapidly during the third trimester of gestation [13]; additionally, by term-equivalent age, moderate-to-late PT infants show widespread changes in structural brain development (e.g. [14]), suggesting

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differences in frontal lobe development and dependent behaviors may emerge quite early.

EF has traditionally been conceptualized as a later developing skill, but precursor skills to EF can be measured even before the preschool years [15]. Rudimentary EF abilities are clearly evident by the end of the first year of life, as infants become increasingly able to tolerate delays during the classic A not B task, representing advancing inhibition and working memory skills. Early individual differences in infant brain and behavioral measures of complex attention, memory, and inhibition skills are also predictive of later EF during childhood [15], demonstrating the predictive validity of these infant cognitive measures.

Interestingly, preliminary studies of complex cognitive skills in healthy PT infants has suggested that while low-risk PT infants initially may be faster at disengaging and shifting attention [16–18], this "benefit" in attentional processing disappears by 4–6 months of age. Similarly, healthy PT infants outperform FT infants on early measures of working memory and inhibitory control when tested at their corrected-age [19], but not when comparing groups based on chronological age. By 18 months, toddlers born moderate-to-late PT show poorer orienting and alerting than those born FT [20], suggesting early "benefits" in attentional processing may instead reflect an altered trajectory of development. Fully describing the developmental antecedents of atypical EF in at-risk infants, including children born moderate-to-late PT, is therefore critical to understand how and when disruptions emerge.

In the current study, we examined whether infants born moderate-to-late PT showed differential development of complex attention, memory, and inhibition skills presumed to be partially dependent on prefrontal cortex (referred to as "early EF" skills for brevity) within the first year of life. Given studies with very PT children that suggest that differences in complex cognitive skills are measurable by late infancy [4] and cascade over the course of development into later EF impairments [21], we predicted that infants born moderate-to-late PT would also show differential development of early EF skills by the end of the first year of life. Previous studies have documented that EF development in older children is sensitive to medical complications and sociodemographic risk factors that commonly co-occur with PT birth. As such, we recruited a low-medical and low-environmental risk (i.e. middle-to-upper socioeconomic status families) sample of moderate-to-late PT infants in order to minimize impacts of these potentially confounding factors.

2. Materials and methods

2.1. Participants

Nine-month-old infants were recruited based on gestational age from a database of families who endorsed interest in participating in child development research. Families in this database were recruited via birth records from local hospitals. The sample consisted of 71 infants born moderate-to-late preterm (PT; 30–36 weeks gestation) and 67 infants born full-term (FT; 37–42 weeks gestation). Infants were tested within ± 1 week of turning 9-months-old (9-months corrected-age for PT infants). Infants were predominantly Caucasian (90.6%), lived in college-educated (91.3%), two-parent families (99.3%), with median household incomes between $101,000–$125,000. Exclusion criteria included neurological insult or disease, intrauterine growth restriction, congenital heart disease, serious medical illness (e.g. organ transplant), and for FT children only, admission to a special care or intensive care nursery for > 24 h as a newborn. Hollingshead scores, reflecting overall familial socioeconomic status, did not differ for the two groups. See Table 1 for demographic characteristics of the sample.

Birth hospitalization records and newborn well-child check records were obtained for 97% of the sample to confirm gestational age and to document perinatal history; midwife records were obtained for the remaining 3% of infants who were planned home births. See Table 2 for perinatal characteristics of the sample.

Table 1
Sample demographic characteristics.

	Preterm (*n* = 71)	Full-term (*n* = 67)	
	n (%)	*n* (%)	*p*
Chronological age in months - *M* (*SD*)	10.30 (0.43)	9.14 (0.14)	0.00*
Corrected age in months - *M* (*SD*)	9.13 (0.15)		
Child's sex - # male	38 (53.5)	33 (49.3)	0.61
Child's ethnicity - # Caucasian	67 (94.4)	58 (86.6)	0.15
Maternal education			0.42
High school degree or GED	4 (5.6)	1 (1.5)	
Associate degree	3 (4.2)	4 (6.0)	
Bachelor's degree	28 (39.4)	25 (37.3)	
Graduate or professional degree	36 (50.7)	37 (55.2)	
Maternal work			0.08
Full-time work for pay	34 (47.9)	41 (61.2)	
Part-time work for pay	25 (35.2)	11 (16.4)	
Student	3 (4.2)	2 (3.0)	
Stay at home parent	9 (12.7)	13 (19.4)	
Annual household income			0.68
≤ $50,000	3 (4.3)	4 (6.3)	
$51,000–$100,000	17 (23.2)	9 (14.1)	
$101,000–$150,000	27 (39.1)	26 (40.6)	
≥ $151,000	23 (33.3)	25 (39.1)	
Marital status - # married	70 (98.6)	65 (97.0)	0.61
Hollingshead score – *M* (*SD*)	52.62 (7.74)	53.37 (9.57)	0.61

Notes. Five families (3 FT, 2 PT) declined to provide annual household income.
* $p < 0.05$.

2.2. General procedure

Infants completed a battery of behavioral and looking-time tasks designed to target early frontal lobe functions, selected from the adult and child neuropsychology literature. All infants also completed the Bayley-III Screening Test as a global developmental assessment of cognitive, motor, and language skills. The entire testing session lasted approximately 90 min. Parents of infants completed a questionnaire measure of their child's early attention skills (Infant Behavior Questionnaire, IBQ). Written informed consent was obtained from parents. Families received a small present (infant board book or infant T-shirt) as compensation. Study procedures were approved by the University of Minnesota's Institutional Review Board.

Additional methodological details of the infant "early EF" measures are included in the Supplemental methods. Each infant completed the tasks in a fixed order (reversal learning, A not B, problem solving, habituation, attention flexibility, processing speed/attention shifting, Bayley). The tasks were presented in a fixed order because we anticipated infants' energy and interest would decline across the session and could best be maintained by intermixing behavioral and eye-tracking tasks.

For eye-tracking tasks, infants were seated on their parent's lap, approximately 48 in. from the screen, in a darkened room. An opaque curtain separated the parent and infant from the experimenter. Computerized stimuli were presented via Macromedia Director MX 2004 on a 42 inch LCD monitor. Infant eye movements were recorded using a hidden digital video camera, located directly below the screen, with infrared night vision. Video feed of the infant was presented live to the experimenter, who was blind to what stimuli were presented to that infant, for preliminary online data coding and to enable repositioning of the camera. The experimenter used key presses to indicate whether the infant was looking at the center, left side, right side, or away from the screen. The live video feed was burned to DVD for final offline coding of eye movement data.

For behavioral tasks, infants were seated on their parent's lap so that they were able to reach stimuli presented on a 31.5 × 31.5 inch square white table. Infant behavior was recorded using a hidden digital video