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Early developmental trajectories of preterm infants

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A B S T R A C T

Background and objectives: Preterm infants are at risk for neuro-developmental impairments and atypical developmental trajectories. The aims of this study were to delineate early developmental trajectories of preterm and full-term infants.
Methods: The cognitive, language, and motor development of 149 infants – 19 extremely preterm (EPT), 34 very preterm (VPT), 57 moderately preterm (MPT), and 39 full-term (FT) – was evaluated using Mullen Scales at 1, 4, 8, 12, and 18 months. Mixed models were applied to examine group differences. Gender, maternal education, and neurobehavior were included as predictors of developmental trajectories.
Results: The EPT and VPT infants achieved significantly lower scores than the FT infants in all domains, with a significantly increasing gap over time. The MPT infants' trajectories were more favorable than those of the EPT and VPT infants yet lower than the FT infants on the Visual Reception, Gross, and Fine Motor subscales. Male gender and lower maternal education were associated with lower scores that declined over time. Abnormal neonatal neurobehavior was associated lower Mullen scores and with less stability in scores over time.
Conclusions: The EPT and VPT infants were found to have disadvantages across all domains. The MPT infants revealed more favorable developmental trajectories yet displayed vulnerability compared to the FT infants. Gender, maternal education, and neonatal neurobehavior are important in predicting the developmental outcomes of preterm infants.

1. Introduction

Preterm birth, which is defined as a birth that takes places before the completion of 37 weeks of pregnancy, occurs in 12–13% of live births in the USA and in 5–9% of live births in other developed countries. It is the leading cause of perinatal morbidity and mortality in developed countries (Beck et al., 2010; Goldenberg, Culhane, Iams, & Romero, 2008). The biological vulnerability conferred by preterm birth, which is potentially amplified by environmental disadvantage, profoundly affects development and has consequences that extend across the lifespan (Aylward, 2005; Johnson & Marlow, 2014; Moster, Lie, & Markestad, 2008). As the long-lasting effects of preterm birth on health, well-being, school performance, and participation are significant and costly, it is important to study the precursors of these difficulties and thus facilitate their early identification and intervention.

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In their comprehensive review of the developmental pathways that follow preterm birth, Sansavini, Guarini, and Caselli, 2011 describe the etiology underlying the adverse developmental outcomes of preterm infants as having a “complex interaction between biological and socio-environmental constraints associated to preterm birth which occurs in a critical period of rapid development of the neural system and thus leads to an atypical development” (p 102). Typical fetal development occurs under specific sensory conditions that facilitate neurological development and maturation. Premature birth interrupts these physiological processes, with the neonatal intensive care unit (NICU) environment imposing artificial conditions on the developing premature infant. In the NICU, a premature newborn is both under- and over-stimulated and may also experience elevated stress due to having to undergo an average of 10 painful procedures per day. These sub-optimal conditions during a critical period of brain development may result in atypical developmental trajectories (Als et al., 2004; Carbajal et al., 2008; Sansavini et al., 2011).

In severe cases, preterm birth is associated with neurological injury (e.g., periventricular leukomalacia, intraventricular hemorrhage, and hydrocephalus) that results in neuro-sensory, motor, and severe cognitive disabilities (Volpe, 2009). However, even in the absence of identifiable severe neurological damage, evidence of atypical brain development and alterations to brain structure and organization exists (Aylward, 2005). As a result, even though preterm children do not frequently exhibit severe damages, many children with a wide range of gestational ages can present with low-severity impairments (Aylward, 2005; Sansavini et al., 2011).

In their review, Sansavini, et al. (2011) further describe changes in the literature exploring prematurity outcomes; these changes include a shift from studying high-severity, low-prevalence neuro-motor and sensory disabilities to exploring low-severity, high-prevalence cognitive deficiencies. Cognitive abilities, including measures such as developmental and IQ tests, are now common broad measures of prematurity outcomes (Aarnoudse-Moens, Weisglas-Kuperus, Van Goudoever, & Oosterlaan, 2009; Arpino et al., 2010; Saigal & Doyle, 2008). A meta-analysis that examines IQ differences between preterm and full-term children reported a considerable mean difference of 10 IQ points between preterm and full-term children (Bhutta, Cleves, Casey, Cradock, & Anand, 2002). Disadvantages were most pronounced in children born extremely preterm (EPT), but they were also evident in those born very preterm (VPT), moderately preterm (MPT), and late preterm (LPT) (Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008; Johnson et al., 2015; Larroque et al., 2008).

Researchers have also shifted their attention from broad outcomes such as general intelligence to more specific domains to further characterize the vulnerabilities and difficulties of preterm children (Sansavini et al., 2011). The application of various neonatal measures has led to the documentation of alterations in neurobehavior among preterm infants, including abnormal muscle tone and movements, asymmetry, and difficulties with attention and arousal regulation (Brown, Doyle, Bear, & Inder, 2006). The motor domain has also been identified as an area of vulnerability among preterm infants. Motor development is affected by both biological (e.g., neurological injury and brain maturation) and environmental (e.g., postural limitations) constraints in the neonatal period. The prevalence of cerebral palsy is significantly higher among preterm infants (Platt et al., 2007). Moreover, differences between preterm and full-term children have been reported in relation to gross motor skills, fine motor skills, and visual motor integration. The results of a meta-analysis that focuses on preterm infants’ motor outcomes indicated delays in the attainment of early motor milestones during the first years of life. Although these children reached these milestones by their second and third years of life, difficulties related to more advanced motor skills persisted throughout their childhood and adolescence (De Kieviet, Piek, Aarnoudse-Moens, & Oosterlaan, 2009).

The language domain has also been identified as being vulnerable to long-term consequences of preterm birth. As in the motor domain, differences between preterm and full-term infants have been observed regarding various pre-language and early linguistic skills as early as in the first year of life (De Schuymer, De Groote, Striano, Stahl, & Roeyers, 2011). Although some evidence of catch-up gains over time exists in basic language skills such as receptive language (Luu, Vohr, Allan, Schneider, & Ment, 2011), many researchers have also reported growing differences in complex language functions (Sansavini, Guarini, Savini et al., 2011; Van Noort-van der Spek, Franken, & Weisglas-Kuperus, 2012; Woodward et al., 2009).

Longitudinal studies that follow preterm infants’ development at several timepoints early in life are important for understanding individual trajectories and enhancing early identification and intervention (Blauw-Hospers & Hadders-Algra, 2005; Nordhov et al., 2010). Long-term follow-up studies typically include EPT and VPT infant cohorts, whereas many studies that include MPT infants are cross-sectional. In the present study, we therefore applied the Mullen Scales of Early Learning with the aim of examining cognitive, language, and motor skills throughout the first 18 months of life in all four cohorts, namely EPT, VPT, MPT, and full-term (FT) infants. Data were collected at five timepoints throughout this period. We hypothesized that an association between gestational age will be revealed, where the EPT infants will be the most vulnerable, with the lowest MSEL scores, and the MPT infants will have more favorable outcomes compared to the EPT and VPT infants, yet lower that the FT infants.

The development of preterm infants not only tends to be less favorable than that of FT infants; it is also characterized by greater variance, which suggests that the risk associated with preterm birth is not homogenous and additional conditions may enhance or attenuate initial risk. Male gender and lower socioeconomic status (SES) have been identified as risk factors associated with less favorable developmental outcomes among preterm infants (Janssen et al., 2011; Sansavini et al., 2011). Neonatal neurobehavior has also been examined as a potential predictor of developmental outcomes, but with inconsistent results (Harijan et al., 2012; Picciolini et al., 2016; Stephens et al., 2010). The second aim of this study is therefore to examine demographic characteristics and neonatal neurobehavior as potential predictors of preterm infants’ developmental trajectories beyond gestational age (GA). We hypothesized that male gender, lower maternal education and more neonatal neurobehavior abnormalities will be associated with lower MSEL scores over time.

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