THE IMPACT OF RISK ON THE DEVELOPMENTAL COURSE OF VISUAL ATTENTION IN INFANTS BORN PREMATURELY

BY

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Submitted to the graduate degree program in the Clinical Child Psychology Program and the Graduate Faculty of the University of Kansas in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

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The developmental course of attention has been documented in full-term infants, but the growth parameters of visual attention in preterm infants and the impact of medical and environmental risk on these measures have not been investigated. The purposes of the current investigation were twofold: 1) to examine the developmental course of attention over the first year of life in a sample of 71 infants born prematurely; and 2) to examine the impact of risk on these growth parameters in infants with varying levels of medical severity. Overall, the preterm sample demonstrated a general decline in peak look duration from 2- to 12-months corrected age that was best captured by a non-linear function. The construct of medical risk was not found to be significantly associated with either the intercept or slope factors in this model. Future considerations with regards to medical risk, inclusion of process environmental variables, as well as examining the relationship between these trajectories of attention and later developmental outcome, are discussed.

DEDICATIONS

This dissertation would not be complete without an expression of my utmost gratitude for those who have supported me in its completion and throughout my graduate training. First, I would like to thank my chair, Dr. John Colombo for his continued support and facilitation with this project. He has been very instrumental in seeing this project to fruition from the very first time I met with him and expressed an interest in conducting research with infants, and I am very grateful for his commitment to my training even outside the Cognitive and Developmental Programs. Next, Dr. Michael Roberts is tirelessly devoted to the training of students and has played an instrumental role in fully preparing me for a career in clinical child and pediatric psychology. In addition, his spirit and devotion to Kansas athletics increased the level of enjoyment during my graduate training. Similarly, Dr. Steele has been an exemplary mentor across many domains (i.e., teaching, advising, mentoring, supervising) and has contributed significantly to my professional development. Dr. Little has been very influential in fostering my skills in research methodology and quantitative analysis, which will be very beneficial as an aspiring researcher in an academic medical center. I am also very appreciative of Waylon Howard, graduate student in the Quantitative Psychology program, who provided hours of statistical consultation to help identify and troubleshoot modeling issues and helped increase my understanding of various imputation and latent trajectory modeling procedures. In addition, I am thankful for Dr. Wendy Turnbull who played a key role in introducing this project to staff in the special care clinic and also helping to coordinate space to allow the research to be conducted within a busy clinic setting. Finally, I would also like to thank all members of my dissertation committee members for their constructive suggestions and revisions.

In addition to those who were directly involved in my graduate training through teaching, supervising, or mentoring, I would like to express my deep appreciation for the love and support my family has provided to me. My wife, Elizabeth Aylward, has been a tremendous source of support and has been endlessly patient and understanding in seeing this project to its completion. In addition, my family and friends have also been active cheerleaders during the entire process. The skills and support I received during this project will continue to benefit me during my ongoing career as an aspiring researcher and clinician, and I am forever grateful to all those who have helped me along the way.

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This project would not have been possible without the cooperation of the staff in the Special Care Clinic at the participating hospital. Special thanks to the staff for their ongoing support and assistance in facilitating the start of this project in conjunction with the multidisciplinary clinic.

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THE IMPACT OF RISK ON THE DEVELOPMENTAL COURSE OF VISUAL ATTENTION IN INFANTS BORN PREMATURELY

The number of infants born prematurely (i.e., < 37 weeks gestational age) in the U.S. per year is increasing; in 2004, 12.5 percent of infants were born preterm (Martin, Hamilton, Menacker, Sutton, & Mathews, 2005). There also has been a dramatic increase in the survival rates of infants born prematurely, particularly with respect to infants born with extremely low birth weight (ELBW, i.e., $\leq$ 1000 g; Stoelhorst et al., 2005; Voss, Neubauer, Wachtendorf, Verhey, & Kattner, 2007). To put this into perspective, estimates of survival were less than 30% for infants with birth weights less than 1000g in the late 1970s (Doyle & Casalaz, 2001), yet more recent rates have been reported to be over 70% for survival for infants born with birth weights between 750 and 1000g, and nearly 90% for infants born between 1001 and 1250g (Hack et al., 1995; Vohr & Msall, 1997). This improved survival of preterm infants is due in part to substantial advancements made in both perinatal and postnatal medical technology (e.g., use of antenatal steroids, delivery room resuscitation, surfactant replacement; Hack & Fanaroff, 1999). As a result, however, professionals are now confronted with an increasing number of high-risk newborns that suffer from considerable neurologic morbidity associated with long-term sequelae (Anderson & Doyle, 2003; Aylward, 1997; Hack & Fanaroff, 1999).

Developmental Outcome

Given improved survival rates, particularly among infants born ELBW or 23-24 weeks gestational age, there is increased interest in the long-term developmental outcome of preterm infants (Aylward, 2002a). The primary emphasis in early studies of outcomes among infants born prematurely was on the incidence of major disabilities (i.e., moderate/severe mental retardation, sensory disorders, cerebral palsy), with incidence rates inversely related to birthweight (6-8% in low-birth weight infants (LBW, i.e., ≤ 2,500g.), 14-17% in very low birth weight (VLBW, i.e., ≤ 1500g.), 20-25% in ELBW; Bennett & Scott, 1997; Hack, Taylor, & Klein, 1995). However, improved survival rates, more advanced assessment techniques, and longer follow-up have also revealed an increase in the prevalence of low-severity dysfunctions (i.e., learning disabilities, Attention-Deficit Hyperactivity Disorder (ADHD), borderline to low average intelligence quotients, neuropsychological deficits; Aylward, 2005), with a similar inverse birth weight gradient being found (Goyen, Lui, & Woods, 1998; Taylor, Klein, Minich, & Hack, 2000). The prevalence of these difficulties may also be influenced by familial factors such as income, ethnicity, and education (vis à vis environmental risk; Aylward, 2005). Although major disabilities are often identified in infancy, these high-prevalence/low-severity dysfunctions are not apparent until school age, and are found in approximately 50-70% of very premature infants (Aylward, 2010b). For example, impairments in attention as well as deficits in executive functioning have been found in school-age children born preterm, particularly among those who were born ELBW (Anderson, Doyle, & Group, 2004; Curtis, Lindeke, Georgieff, & Nelson, 2002; Hack & Taylor, 2000).

Over the last two decades, these types of outcome studies have led to an increased interest in the research on individual differences in cognition (Colombo, Shaddy, Richman, Maikranz, & Blaga, 2004), particularly in infants at biological risk (Aylward, 2004). There is an indirect link between biological risk and subsequent outcome. In contrast with the concept of equifinality, different types of insults early in infancy do not lead to the same cognitive or behavioral outcomes later in life (Nadeau, Boivin, Tessier, Lefebvre, & Robaey, 2001). It was widely accepted through the 1970s that there was little or no relation between behavioral manifestations in infancy and later intellectual functioning in early childhood (Colombo et al., 2004). However, measures of preverbal cognition that were included in long-term outcome studies in the 1980s were found to be modestly correlated with later function in childhood (i.e., cognitive, linguistic, and overall intellectual functioning; see Bornstein & Sigmund, 1986; Colombo, 1993; Colombo & Mitchell, 1990; Fagan, 1984; McCall & Carriger, 1993; McCall & Mash, 1995). While "lagged prediction" of later cognitive function from assessments in infancy have generally been low (Colombo, 1993), the inclusion of measures such as recognition memory have improved prediction somewhat (Colombo & Mitchell, 1990). Currently, measures of attention, memory, and learning in infants and toddlers are now included in new versions of basic standardized instruments such as the Bayley Scales of Infant and Toddler Development-III (Bayley, 2006) and Mullen Scales of

Early Learning (Mullen, 1995). Inclusion of these measures approaches the goal of improving the early identification of individuals at risk for later compromised cognitive development. Ultimately, improved prediction of later cognitive functioning might aid in identifying infants in need of early intervention, the specific areas of function in need of intervention, and facilitate the development of risk phenotypes (Aylward, 1997).

Studies of children born preterm have investigated a multitude of factors spanning the pre-, peri-, and post-natal years and beyond, that ultimately contribute to variability in long-term developmental outcomes (Aylward, 2010b). As mentioned previously, there exists an inverse relationship between birth weight and gestational age with the gradient of developmental sequelae (Aylward, 2002a). Yet, the developmental outcomes of infants with the same birthweight and/or gestational age can vary markedly. Therefore, birthweight and gestational age must be considered in conjunction with other risk factors such as environmental and biologic risk factors. Citing data from the multi-site Infant Health and Development Project, Zeanah, Boris, and Larrieu (1997) suggested that contextual factors and the severity of the medical compromise may be more important than the etiology of the medical compromise itself.

Risk

Tjossem (1976) identified three categories of risk: established (medical disorder of known etiology, e.g., Down Syndrome), environmental (e.g., quality of mother-infant interaction, environmental stimulation), and biologic (exposure to noxious pre-, peri-, or post-natal developmental events, e.g., intraventricular hemorrhage (IVH), low birth weight). Preterm infants are often exposed to both environmental risk factors and non-optimal biologic factors, which can work in a synergistic fashion, often referred to as "double jeopardy" (Parker, Greer, & Zuckerman, 1988). This combination of factors can in turn place the infant at further risk for developmental problems, yet there is a ceiling effect whereby infants with the most severe biologic risk are least responsive to environmental influences (Aylward, 1992; Bradley & Corwyn, 2002).

Several independent biologic risk factors, such as low birthweight, intraventricular hemorrhage, and prolonged mechanical ventilation have been found to significantly impact long-term development (e.g., Lefebvre, Grégoire, Dubois, & Glorieux, 1998; Singer, Yamashita, Lilien, Collin, & Baley, 1997; Taylor, Klein, Schatschneider, & Hack, 1998). Given that a considerable number of infants may have more than one medical complication (i.e., these complications tend to cluster), the use of illness severity scores may be useful to quantify multiple biologic risk factors, which in turn, can be used in statistical models predicting later developmental outcomes (Aylward, 2010b). Examples of illness severity scores include the Score for Neonatal Acute Physiology (SNAP; Richardson, Gray, McCormick, Workman, & Goldman, 1993), Revised Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE-II; Richardson et al., 2001), the Neonatal Medical Index (NMI; Korner et al., 1993), Clinical Risk Index for Babies (CRIB-II; Parry, Tucker, & Tarnow-Mordi, 2003), and the Neurobiologic Risk Score (NBRS; Brazy, Eckerman, Oehler, Goldstein, & O'Rand, 1991). Generally, these scoring indices vary with respect to the total number and type of items used to calculate risk scores, the time period in which data are collected, and the weighting of different medical-related items (Aylward, 2010b).

The accuracy of these indices in predicting morbidity and mortality are generally measured by the area under the Receiver Operating Characteristic (ROC) curve (plot true positive ratio vs. false positive ratio or 1-specificity). More specifically, area under the curve (AUC) values are used to quantify the discrimination of these variables/indices in predicting outcome, with values above .80 indicating sufficient accuracy and good clinical usefulness (Swets, 1980; van Erkel & Pattynama, 1998). Overall, risk scores are generally more predictive of survival than of neurodevelopmental outcome, which may be due in part to inaccurate measurement of biomedical factors (Aylward, 2010b). Nonetheless, several of these risk indices have been found to be associated with later developmental outcome in correlation and AUC analyses, including the NMI, NBRS, CRIB, and SNAP (see Dorling, Field, & Manktelow, 2005, for further review). For example, Zaramella and colleagues (2008) found that both the NBRS and Scheiner's Perinatal Risk Inventory (PERI; Scheiner & Sexton, 1991) demonstrated sufficient accuracy (AUCs .839 and .851, respectively), in predicting abilities such as sensation and perception, memory, learning, and early language and communication, as assessed by the Mental Development Index (MDI) score on the Bayley Scales of Infant Development (BSID-II; Bayley, 1993) at 24-months of age.

While some investigations have found associations between specific biomedical factors such as birth weight, gestational age, and medical complications with later functioning on a single, global developmental index (e.g., Bayley, 1993), these composite measures may not parse out discrete developmental functions (Aylward, 2004). Furthermore, children with high-prevalence/low-severity dysfunctions will likely display much more variability in early assessments as well as in later cognitive outcome, and no good predictors of these more subtle dysfunctions have been identified during infancy or preschool age (Aylward, 2004; Hille et al., 1994). However, van de Weijer-Bergsma, Wijnroks, and Jongmans (2008) suggested that attention can serve as a potential mechanism that can help explain the within-group variability in developmental outcomes in premature infants. Research with clinical populations suggests that early problems in the regulation of attention may underlie the individual variability between premature infants and their overall risk for subsequent low-severity dysfunctions (e.g., attention difficulties) later in life (Aylward, 2002a; Davis & Burns, 2001; Lawson & Ruff, 2004). These findings, therefore, underscore the importance of examining the developmental course of attention early in life (Anderson et al., 2003; Hunnius, Geuze, Zweens, & Bos, 2008).

Attention

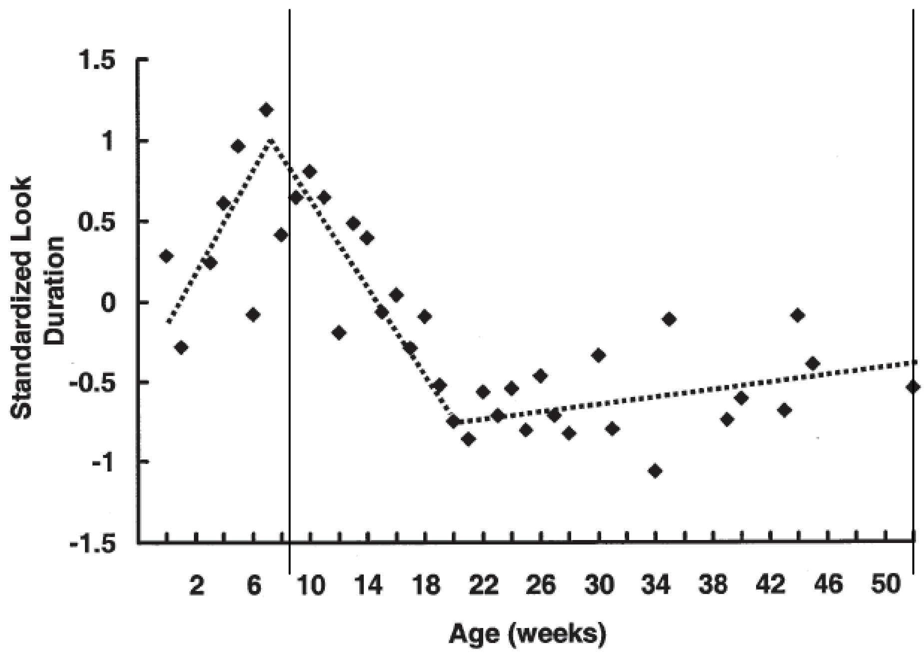
The visual habituation paradigm is among the most widely used for the study of attention, perception, and cognition in human infants (Colombo, Frick, & Gorman, 1997). Moreover, measures of visual habituation have been shown to successfully predict measures of childhood and adolescent cognition (e.g., see Bornstein, 1984;

Lewis & Brooks-Gunn, 1981; Miller et al., 1977; Slater, Cooper, Rose, & Morrison, 1989). In this paradigm, repetitive stimulus presentations are made with the expectation that the infant's attentional responses will decline in strength across presentations. This decline in attention has been theoretically attributed to cognitive processes based on Sokolov's (1963) comparator model. This model holds that the distribution of attention or strength of the orienting reflex (OR) to a stimulus is a function of the match between the stimulus and the formation of the infant's internal representation, or "engram" of that stimulus. Increased look duration indicates either a mismatch between the stimulus and engram, or a lack of an engram altogether; brief fixations imply accurate and complete representations of the stimulus. Overall, research has indicated that there is a negative correlation between the amount of attention given to a novel visual stimulus and later measures of intellectual functioning (e.g., Rose, Feldman, Futterweit, & Jankowski, 1997). As suggested by Richards (2005), infants with faster processing speeds examine a visual stimulus for a shorter period of time, and have higher intellectual abilities in early childhood and adolescence.

The visual attention paradigm can reveal many indices of attention and cognition (e.g., habituation rate, novelty preference, disengagement), yet Colombo and Mitchell (1990) argued that individual and developmental differences in visual habituation in infancy are due primarily to variations in look duration. Colombo, Mitchell, O'Brien, and Horowitz (1987) have posited that look duration: (a) is the only habituation variable that follows a consistent developmental course within the habituation paradigm, (b) has the highest test-retest reliability, and (c) contributes to variability in nearly all other parameters in the habituation curve. Although early work in the 1980s held that look duration followed a simple linear decrease during the first year of life (Bornstein, Pecheaux, & Lecuyer, 1988; Colombo & Mitchell, 1990; Mayes & Kessen, 1989), more recent data have suggested that the developmental course of look duration is not monotonically linear (Colombo, Harlan, & Mitchell, 1999; Hood, Murray, King, & Hooper, 1996). More specifically, based on a meta-analysis of developmental studies of attention in infancy, data suggest that there typically is an increase in look duration from birth to 2 months of age, followed by a decline though six months (Colombo et al., 1999). This decline in look duration has been suggested to indicate an increase in processing speed and more efficient cognitive processing (Richards, 2005). The decrease in looking duration is followed by an asymptotic period from 6 to 8 months, and then a gradual increase in looking thereafter that accelerates into the second year (see Figure 1).

Given the complex nature of the developmental course of look duration, look duration may reflect differing constructs at different points during infancy, and thus single "snapshot" measures of look duration should not be expected to account for a large proportion of variance in later intellectual or cognitive outcome (Colombo et al., 2004). The use of longitudinal data, however, allows for the examination of developmental changes in attention and may provide a more valid association with other processes (e.g., cognitive outcome), than can be seen with cross-sectional data. Ultimately, as the authors suggest, the developmental course of look duration can provide important insight into the mechanisms that underlie individual differences in visual attention and look duration in infancy. Moreover, multiple assessments that yield a profile of the developmental course of early cognition may be a more powerful or more informative indicator of later developmental outcomes (Colombo et al., 2004).

Figure 1. Developmental course of look duration (Colombo, Harlan, & Mitchell, 1999).



Note: Area between vertical bars represent approximate time period of interest (i.e., 2- to 12-months corrected age) in the current study

Prematurity and Attention. Rose, Feldman, and Jankowski (2002) underscored the fact that preterm infants tend to perform poorly on tasks that appear to involve processing speed measured indirectly via paired-comparison and habituation paradigms (e.g., Rose, Feldman, & Jankowski, 2001). More specifically, several studies have suggested that premature infants, tested at “corrected age,” take longer to habituate to novel stimuli than do full-term infants of the same post-conceptual age (e.g., Ross, Auld, Tessman, & Nass, 1992; Sigman, Beckwith, Cohen, & Parmelee, 1989; Spungen, Kurtzberg, & Vaughn, 1985). However, in contrast, Bonin, Pomerleau, and Malcuit (1998) found no significant differences in the development of visual attention between premature and full-term infants during the first six months of life; but the premature sample used in this study was free of severe medical complications (i.e., IVH, periventricular leukomalacia (PVL)) that have strong associations with developmental sequelae. Thus, as van de Weijer-Bergsma and colleagues (2008) indicated, longer look durations are more likely to be related to the severity of medical complications than prematurity itself.

The development of attention in preterm infants may be influenced by certain biological and medical factors. Generally, studies have examined the relationship between medical complications during infancy and the development of attention using summary scores of neonatal risk or illness severity or by examining the association with more specific medical complications (e.g., IVH, bronchopulmonary dysplasia (BPD); van de Weijer-Bergsma et al., 2008). For example, medical risks suffered by preterm infants, such as respiratory distress syndrome (Rose, Feldman, McCarton, & Wolfson, 1988), or subependymal or mild (Grade I) hemorrhage (Ross et al., 1992), as well as time spent on a respirator or on supplemental oxygen (Rose et al., 2001) have been shown to have a negative impact on the infant’s processing speed, or measures inferred to depend on processing speed (Rose et al., 2002). Furthermore, it may be that these factors have a more significant impact on the development of attention earlier in infancy than at later points in development during the first year of life (Rose et al., 2001). The findings with regards to summary risk scores have been mixed (e.g., Rose et al., 2002; Sun, 2003); however, medical complications often do not occur in isolation and thus should be considered together as it may be difficult to parcel out the individual contribution of a specific medical complication on indices of attention.

Study Aims

It is expected that multiple assessments which yield a profile of the individual developmental course of cognition may be more powerful indicators of later outcome than single "snapshot" measures (Colombo et al., 2004). Dynamic models that incorporate biological maturation processes appear to have better predictive ability than investigations of static constructs taken at a single time point. With preterm infants, the use of developmental trajectories from longitudinal data can aid in identifying whether there is a developmental lag or more persistent deficit in outcomes (Aylward, 2010b).

Some literature exists regarding the developmental course of visual attention and how these measures relate to later cognitive outcome in typically-developing, low-risk infants (e.g., Colombo et al., 2004). However, there are no longitudinal studies examining the developmental course of visual attention in preterm infants with varying levels of medical risk using latent trajectory modeling (LTM) techniques. Given that these infants are at risk for subsequent suboptimal developmental sequelae, including later difficulties with attention and executive functioning (Aylward, 2002a), early identification of those infants at-risk would be beneficial. Furthermore, many of the previous studies on visual habituation have been performed in laboratories and not a busy, multidisciplinary follow-up clinic. If these measures are deemed suitable to clinic practice, this could possibly lead to the inclusion of such assessments into routine developmental follow-up care, thereby affording early identification of possible risk for low severity dysfunctions later on in life.

In their review of the development of attention in premature infants, van de Weijer-Bergsma and colleagues (2008), highlight several important areas of need for future research in visual attention with infants. These areas include: 1) investigating whether patterns of change of attention in infants born prematurely show similar decline over time to that of full-term infants or evidence more of a catch-up pattern, and 2) examining the influence of biologic/medical factors over time on attention. As a result, the purpose of the present investigation was to address some of the limitations of the research on the developmental course of visual attention in infants. Representing the next logical step from earlier research (i.e., Colombo et al., 2004), the current investigation examined the developmental course of attention (gauged by peak look duration) in premature infants with varying levels of biologic risk (e.g., VLBW, IVH) enrolled in a specialty care follow-up clinic. The initial exploratory analyses examined the growth parameters of visual look duration between 2- and 12-months corrected age using latent trajectory modeling procedures. Next, we examined whether these measures of visual attention were sensitive to the medical/biologic risk (based on medical risk severity scores) of the infant.

Generally, medical-biologic factors are more strongly related to neuropsychological, motor, and perceptual-performance areas of functioning, whereas environmental factors are more related to verbal, academic, and general cognitive outcome (Aylward, 1992; Resnick et al., 1998). Although biological and environmental factors co-exist, the influence of environmental variables usually becomes more apparent between 18 to 36 months (Aylward, 1992). Given the ages of interest, the current study focused solely on the impact of medical risk on parameters of attention. It was anticipated that biological factors would negatively influence overall visual attention, such that those with higher risk status measured via risk indices would have slower rates of habituation, as reflected in longer peak look durations and a smaller slope coefficient. Moreover, it was expected that this association would be stronger at earlier points in the development of visual attention.

Method

Participants

Infants scheduled for routine clinic visits in the specialty care clinic on data collection days were screened for eligibility. Infants meeting the following inclusion criteria were recruited to participate: (a) born prematurely (i.e., ≤ 37 weeks gestation age); (b) between the ages of 2 and 12-months of age (corrected for prematurity); (c) who were enrolled in the Neonatal Follow-up Clinic; (d) English-speaking legal guardian provided consent for the infant to participate; and (e) had no known severe visual impairments (i.e., strabismus, blindness) or genetic chromosomal anomalies.

Caregivers of one-hundred and six preterm infants consented for their child to participate in the current study. Of these, 71 infants (67.0%) completed at least one valid assessment of the visual habituation paradigm. Several invalid assessments occurred when the examiner attempted to complete the visual attention assessment but testing was discontinued due to the infant becoming fussy or falling asleep during the assessment (n = 11). Other reasons for non-completion included infant falling asleep prior to beginning procedure or parent consenting to procedure, but then expressing time constraints in being able to complete experiment at particular visit. Controlling for the likelihood of Type 1 error (Bonferroni correction .05/7 = .007), independent samples t-tests revealed that there were no significant differences in medical risk scores (NMI and NRI), maternal age, infant's birthweight, gestational age, days of hospitalization, or income between those infants who were evaluated and those who did not complete a valid assessment of visual attention (all *p*s > .05). Demographic and medical characteristics of the cohort who completed the visual attention procedure are provided in separate tables below (Tables 1 and 2, respectively).

Table 1. *Demographic characteristics of the sample used for analyses.*

Variable	Mean/percentage (SD)	Range
Gender		
Female	36 (50.7%)	--
Infant Ethnicity		
White, Non-Hispanic	37 (51.4%)	--
Black	16 (22.2%)	--
Hispanic	5 (6.9%)	--
Asian	3 (4.2%)	--
Other/More than one	10 (13.9%)	--
Maternal Age (yrs; at Infant's date of birth)	27.07 (6.95)	14 – 41
Caregiver marital status		
Married, living together	36 (50.0%)	--
Married but separated	4 (5.6%)	--
Divorced	3 (4.2%)	--
Not married, living with partner	9 (12.5%)	--
Single, never married	19 (26.4%)	--
Maternal education		
Some High School	10 (13.9%)	--
High School graduate	19 (26.4%)	--
Attended college	22 (30.6%)	--

Junior college/vocational school graduate	6 (8.3%)	--
College graduate	8 (11.1%)	--
Graduate degree	5 (6.9%)	--
Gross monthly income	$ 2492.4 (2173.62)	$ 100 – $10,000

Table 2. *Medical characteristics of the sample used for analyses.*

Variable	Mean/percentage (SD)	Range
Birthweight (kg)	1.17 (0.57)	0.422 - 3.230
Gestational age (days)	196.97 (22.37)	165 – 257
Hospital stay (days)	86.65 (36.72)	24 – 190
Apgar 1	5.12 (2.35)	1 – 9
Apgar 5	7.20 (1.81)	2 – 9
NMI	3.69 (1.04)	1 – 5
NRI	3.59 (1.65)	0 – 7

Procedures

For those parents/caregivers who expressed interest, the procedures of the experiment was explained in detail by the researcher, who answered any of the questions posed by the parents. During the check-in procedure, legal guardians or parents of infants who meet screening eligibility were given a letter of introduction explaining the purposes and procedures of the study by a registered nurse or other medical provider in the follow-up clinic. If the legal guardians or parent(s) expressed interest in the study, caregiver consent was obtained by the researcher prior to the administration of the first visual attention assessment. Caregiver consent included permission for longitudinal tests of visual acuity and attention and for access to medical chart information concerning the infant's medical history and the extent and nature of any medical complications.

Tests were conducted in conjunction with normally scheduled clinic visits, typically beginning at 2-months gestation, corrected-age. Testing was conducted either prior to or after completion of routine developmental follow-up care in the specialty clinic. Over the course of the first year (corrected age), infants were continued to be followed in conjunction with regularly scheduled follow-up appointments with the specialty care clinic. The frequencies of these visits ranged from every couple of weeks to several months.

Apparatus

Infants were tested in a 10.5ft x 12ft room that was dimmed during administration of the testing procedure. Infants were positioned at midline in their caregiver's lap approximately 15 in. from a 22" Dell Widescreen Flat Panel computer monitor. Stimuli were presented using a computerized habituation program that times coded looks, keeps track of accumulated time, and controls the presentation and withdrawal of the stimuli. A second laptop was connected to a Logitech Quickcam Orbit behind the flat panel monitor which allowed for monitoring of the infant's look duration. Only the screen of the monitor and a hole which records eye movements was within the infant's field of vision. The monitor and laptop computers that run the attention tasks and allow for recording of eye movements were concealed behind a black shield.

Overview of Attention Procedures

Those parents or caregivers who agreed to allow the infant to participate and signed the consent form were brought to a room in the follow-up clinic area for testing. First, the infant was seated in their parent's lap and the researcher completed measures of visual acuity using the Teller Acuity Cards (Teller, 1989) to screen for any significant issues with visual development and assess alertness. One infant from the original 106 consented was excluded from further assessment due to significant alternating strabismus observed during the Teller Acuity procedure. After completion of this task, infants remained seated in their caregiver's lap and were moved in front of a computer screen to complete the visual attention task.

Sessions of visual attention were coded "live." Agreement assessed in laboratory sessions has been found to be typically very high, with correlations above +.95 (Colombo et al., 1987). In the current study, the primary investigator (BA) was trained for coding individual looks during habituation using videotaped sessions from a previous study. Reliability was assessed and from these training sessions, the investigator performed at levels of reliability (inter-observer $r > +.95$) reported as acceptable in previous published work. After testing, any remaining questions from the caregiver were answered. In addition, caregivers completed a demographic form that is detailed in the Appendix. The procedures of this study were approved by the

Children's Mercy Hospital Pediatric Institutional Review Board as well as the Human Subjects Committee Lawrence.

Visual Habituation Protocol. When stimuli are presented in a dark room, the infant typically fixates on the stimulus. Valid fixations are defined as looks of more than one-second in duration, and such looks are terminated when the infant looks away for one-second or more. When a look is terminated by the infant, the stimulus is withdrawn (i.e., screen goes dark) for two-seconds, and then is re-presented for another trial. Again, the infant will fixate the stimulus, but usually for a briefer duration. Over the session, the infant’s duration of looking tends to decline (“habituate”), indicating that he/she has learned/encoded the visual stimulus. A floating-point criterion was used in the current study, whereby the habituation criterion is recalculated if longer looks were encountered later during the habituation sequence (see Colombo & Mitchell, 1990). The cycle of presentation, withdrawal, and re-presentation continued until the length of the infants' fixation declined to one half of its previous longest look. At that point, a new stimulus was presented, paired with the stimulus to which the infant was habituated; each stimulus was shown to the left and right of midline with appropriate separation. Generally, the infant directs more looking to the novel stimulus under such conditions, and the expression of such a novelty preference can be taken as reflecting the infant's visual discrimination of two stimuli, as well as some recognition memory for the original one (Colombo, 1993). For the current study, only data from the habituation sequence was used.

The stimuli used in this study were drawn from a pool of stimuli used in previous studies, including slides of neutral or smiling faces, which is typical for studies of visual habituation (Colombo et al., 2004). All stimuli were presented at comfortable levels of illumination. Four-set ordered pairs of stimuli were randomized in blocks and shown to participants in sequence for the routine clinic visits.

Correction for Prematurity

To address the issue of evaluating a premature infant in comparison to his or her healthy, full-term counterpart, the use of some degree of adjustment has been standard practice (Lems, Hopkins, & Samsom, 1993). Age correction for prematurity generally consists of subtracting the number of weeks of prematurity from the infant's chronological age and is often used when following infants longitudinally (Aylward, 2010b). Despite some arguments to the contrary, the general consensus is that correction for prematurity should occur up to 2 years of age (Aylward, 2002b). It is assumed that adjustment for prematurity will help differentiate more transient effects of being born prior to 37 weeks gestation from more significant deficits (Aylward, 2005). Although some argue for incremental correction or no adjustment at all (Blasko, 1989; Ouden, Rijken, Brand, Verloove-VanHorick, & Ruys, 1991), these positions are unconvincing (Aylward, 2010b). In the current study, correction was calculated based on subtracting the number of weeks of prematurity from the infant's chronological age based on estimated gestational age by obstetrics found in the discharge summary chart or special care clinic chart.

Biologic Risk Scores

As mentioned previously, given the variability in biomedical sequelae in premature infants, illness severity scores can help to quantify these biomedical factors that can ultimately influence neurodevelopmental outcome. In the current study, two different medical risk indices were utilized to index the degree of biologic risk in participating infants as a latent construct, which allowed for the possibility to disattenuate any measurement error. Given their established association with later developmental and neurodevelopmental outcome in previous studies, the following risk indices were utilized in the current study: the Neonatal Medical Index (NMI; Korner et al., 1993) and the Neonatal Risk Index (NRI; Taylor et al., 1998). Scores for these indices were abstracted retrospectively based on the discharge summary information from the infant's respective stay in a neonatal intensive care unit (NICU). In the event that a discharge summary was not available or specific information was not present in the summary, information was culled from the special care clinic chart. De-identified discharge summaries were coded by a registered nurse (RN) with previous experience in neonatal care.

In order to establish reliability, a random sample of 25% (n = 18) of the medical charts was coded independently by the primary investigator. Coding of discharge summaries by the primary investigator was completed after all tests of visual attention were no longer being conducted to ensure rater was blind to the infant's medical status during the habituation paradigm. To assess inter-rater reliability, kappa coefficients were calculated for each medical variable (i.e., apnea, bradycardia, patent ductus arteriosis (PDA), IVH, seizures, septicemia, necrotizing entercolitis; coded 1 vs. 0) used to calculate the risk indices. In addition, reliability for continuous variables (birthweight, days on ventilation support) was calculated using Pearson correlations. The results yielded good to excellent (κs = .550 to 1.00; overall .819) agreement across raters on the seven categorical medical variables and near perfect to perfect agreement on days of ventilator support and birth weight (*r*s = .998 and 1.00, respectively). A more detailed overview of these indices is provided below.

Neonatal Medical Index (NMI). The NMI is a perinatal risk scale designed to summarize the prior medical course at the time of hospital discharge for preterm infants, and further to differentiate those who had severe perinatal complications from those with a remarkable medical course. Classifications on the NMI range from I to V (I describing those without significant previous medical complications; V those with the most severe medical complications). NMI classification is based on two overarching principles: (1) Infants with birthweights greater than 1000 grams with no major medical complications would meet NMI classification I or II. Infants born at less than 1000 grams or those above 1000 grams with severe medical complications would meet NMI classifications of III, IV, or V. (2) Need and duration of mechanically assisted ventilation (i.e., ventilator care or intubation on continuous positive airway pressure (CPAP), or mask or nasal CPAP). As outlined by Korner et al. (1993), the following are the criteria used for classifying infants' risk status on the NMI:

I. Birthweight greater than 1000 grams; free of respiratory distress or other medical complications; no oxygen required; absence of apnea or bradycardia; no patent ductus; allowable complications are benign heart murmur and need for phototherapy.

II. Birthweight greater than 1000 grams; assisted ventilation for 48 hours or less and/or oxygen required 1 or more days; no periventicular hemorrhage-intraventricular hemorrhage (PVH-IVH); allowable complications are occasional apnea and/or bradycardia not requiring theophylline or related drugs; patent ductus arteriosus (PDA) not requiring medication such as indomethacin.

III. Assisted ventilation for 3 to 14 days and/or any conditions listed under (A.) below.

IV. Assisted ventilation for 15 to 28 days and/or any conditions listed under (B.) below.

V. Assisted ventilation 29 days or more and/or any conditions listed under (C.) below.

Conditions requiring a classification of III, IV, or V regardless of duration on assisted ventilation:

(A.) Birth weight less than 1000 grams; PVH-IVH grade I or II; apnea and/or bradycardia requiring theophylline; patent ductus requiring indomethacin; hyperbilirubinemia requiring exchange transfusion. Excludes conditions listed under (B.) and (C.).

(B.) Resuscitation needed for apnea or bradycardia while on theophylline; major surgery including PDA (exclude hernias, testicular torsion and all conditions listed under (C.).

(C.) Meningitis confirmed or suspected; seizures; PVH-IVH grade III or IV; periventricular leukomalacia.

External validation of the NMI has revealed a high correlation between the NMI and the Neonatal Health Index (NHI) whose concurrent and predictive validity had already been established (Korner et al., 1994; Scott, Bauer, Kraemer, & Tyson, 1989). Furthermore, the NMI has been found to be predictive of later cognitive and motor development at 12-, 24-, and 36-months of age, particularly with infants who weighed 1500 grams or less at birth (Korner et al., 1993).

The Neonatal Risk Index (NRI). The Neonatal Risk Index is a cumulative risk index based on six medical complications. Scoring is based on adding points for each complication, with greater weights given to more severe weights of cerebral abnormalities and longer oxygen dependence given their predictive value for later outcome. The following criteria are used for the Neonatal Risk Index: apnea of prematurity = 1; septicemia = 1; jaundice of prematurity = 1; necrotizing enterocolitis = 1; chronic lung disease, defined as oxygen dependence for 28 days but not at 36 weeks corrected age = 1; chronic lung disease, defined as oxygen dependence at 36 weeks corrected age = 2; cerebral abnormality (i.e., Grade I or II intraventricular hemorrhage = 1); severe cerebral abnormality (i.e., Grade III or IV intraventricular hemorrhage, periventricular leukomalacia, or ventricular dilation = 2).

The NRI has been found to be significantly correlated with the modified Hobel Neonatal Risk Score ($r = .71$) as well as the Mental Development Index of the BSID-II at two years of age ($r = -.24$; Taylor et al., 1998).

Missing Data

Missing data in longitudinal studies with infants is typical and is one of the difficulties associated with long-term follow-up studies (Aylward, 2010b). Factors that may increase the likelihood of subject dropout or loss to follow-up include larger, less sick babies, those from lower SES households, babies born to single, young mothers, and those not born at a tertiary care hospital (Aylward, 2010b). At the current hospital, rates of missed appointments (termed "Did Not Keep Appointment"; DNKA) in the follow-up clinic overall have been reported to be around 22% (W. Turnbull, personal communication).

Periods of attention assessment for the current study occurred in conjunction with infants' normally scheduled follow-up visit to the specialty care clinic. This type of design contributed to the amount of missing data present in this study because follow-up periods typically ranged from one to four months. In addition, infants were enrolled at various ages (i.e., between 2 and 12 months corrected age), thereby adding additional points of missingness. Typical reasons for unplanned missing data included family did not keep or canceled appointment, infant becoming fussy or falling asleep prior to or during assessment of attention, or caregiver expressing time constraints with being able to procedure on data collection day. To conservatively estimate trajectories of visual attention with the available data across the first year of life, data were grouped into five separate "bins" based on visual examination of the raw data as well as prior theoretical knowledge of the course of attention: 2-3 months (time1); 4-5 months (time2); 6-7 months (time3); 8-10 months (time4); and 11-12 months (time5).

The final database was screened for outlier values, variable distributions were assessed for normality, and logarithmic transformations were calculated prior to the imputation phase.

Within the current sample, there was a moderate amount of data missing (10.28% of all data points). In order to limit the potential for biased estimates, the EM imputation algorithm was employed using SAS PROC MI to identify plausible values in the place of missing values (Graham, Cumsille, & Elek-Fisk, 2003; Hofer & Hoffman, 2007). As mentioned by Graham, Olchowski, and Gilreath (2007), multiple imputation (MI; Rubin, 1987) permits the analysis of "complete" data and allows for missing values to be entered in a way in which parameter estimates are unbiased and estimated in a reasonable way which is particularly useful in medical research (Sterne et al., 2009). Although previous researchers suggest that several imputations (i.e., 3-5) are sufficient for good statistical inference (Schafer & Olsen, 1998), more recently, Graham and colleagues (2007) recommend many more imputations (i.e., ~100) when using MI, which allows for a more representative sample to be used in the analysis as the number of data sets imputed increases.

Data Analysis Plan

The normal course of visual attention in infancy is characterized by the duration of infant looking to visual stimuli. Mentioned previously, data from healthy term infants have suggested that the developmental course of this look duration is not monotonically linear (Colombo et al., 1999). Specifically, there is typically an increase in look duration from birth to 2 months of age, followed by a decline through six months, followed in turn by an asymptotic period from 6 to 8 months, and then a gradual increase in looking thereafter that accelerates into the second year (see Figure 1).

The current project represents an important step in this area of research by extending this line of work to infants at-risk for later developmental problems. The basic design of the current study was to conduct a longitudinal assessment of attention in infants at-risk for later developmental problems or delays and examine the impact of medical and environmental risk on these trajectories. To accomplish this goal, data analyses for the current research study were conducted in two discrete stages: 1) to examine the course of attention during the first year of life in a sample of infants born prematurely using unconditional latent-trajectory models (LTM) (i.e., no correlated predictors); 2) to examine a conditional LTM to evaluate whether medical/biologic risk factors can explain individual heterogeneity in attention trajectories.

Latent trajectory profiles of visual attention were constructed using attention assessment data collected from infants during normally-scheduled visits to the developmental follow-up clinic, and modeled using structural equation modeling (SEM)-based procedures (see Nelson, Aylward, & Steele, 2008, for further review). Latent trajectory modeling estimates intra-individual developmental patterns and allows for time-varying covariates as well as the correlation of the latent intercepts and slopes across multiple variables measured longitudinally (Burchinal, Nelson, & Poe, 2006; Curran & Hussong, 2003). Further, LTM analysis techniques offer a more powerful and flexible technique to examine nonlinear trajectories and address longitudinal questions over traditional methods (e.g., ANOVA, HLM; see DeLucia & Pitts, 2007; Hancock, Kuo, & Lawrence, 2001).

Assessing model fit and interpretation of results in LTM models

The evaluation of model fit within the SEM framework has typically relied on absolute-, relative-, parsimonious-, and noncentrality-based indices such as the Chi-square goodness-of-fit test, Bentler's Comparative Fit Index (CFI), Tucker-Lewis Index (TLI), Bentler-Bonett Normed Fit Index (NFI), and Root Mean Square Error of Approximation (RMSEA). Generally, non-significant chi-square values, CFI and NFI values greater than or equal to .90, and RMSEA values less than or equal to .08 suggest acceptable to very good model fit (Bryne, 2001; Kline, 2005). The TLI is not normed from zero to one, but larger values indicate better model fit.

Evaluating model fit indices in latent trajectory models can be challenging and misspecification can occur in the within-individual covariance matrix (e.g., assuming constant residuals over time), between-individuals covariance matrix (e.g., constraining variances of growth parameters to zero), marginal mean structure (e.g., specifying incorrect functional form), or conditional mean structure (see Wu, West, & Taylor, 2009, for further review). To evaluate relative model fit indices for these types of models, some correction is required by estimating both a baseline (b) and hypothesized (h) model. The likelihood ratio test statistic (T) and degrees of freedom (df) from each model are then used to calculate the adjusted fit indices (e.g., TLI, CFI, NFI) using the following formulas:

1. TLI = $((T_b/df_b)-(T_h/df_h))/((T_b/df_b)-1)$

2. NFI = $(T_b-T_h)/T_b$

3. $D_b = (T_b-df_b)/(N-1)$ $D_h = (T_h-df_h)/(N-1)$
   If ($D_h > 0$ and $D_b > D_h$), then CFI= $1 - D_h/D_b$
   If ($D_h > 0$ and $D_b < D_h$), then CFI= 0
   If ($D_h < 0$), then CFI= 1

4. PCFI = CFI * (df_h/df_b)

Due to the nature of the models examined in the current study, these formulas were used to calculate the relative fit indices for the LTMs.

Results

Preliminary Analyses

Descriptive properties of the variables. Means and standard deviations for the manifest variables and bivariate correlations among these variables are shown in Table 3 for the sample used in the analyses. Visual depiction of the observed means revealed that the course of attention in this sample showed a general decline in mean peak look duration from time 1 (i.e., 2-3 months) until time 5 (i.e., 10-12 months).

Table 3. *Mean, Standard Deviations, and Correlations Between the Manifest Variables*

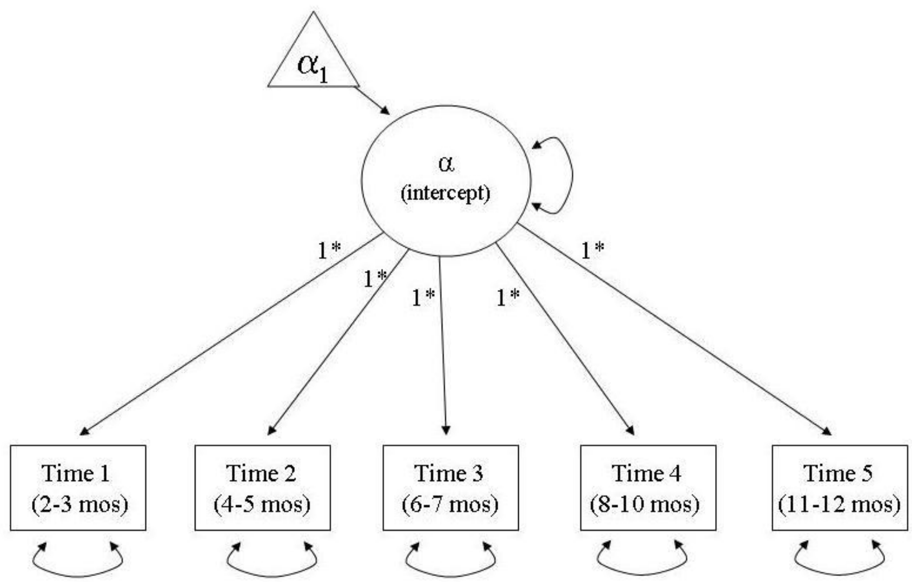
	NMI	NRI	Time1	Time2	Time3	Time4	Time5
Variable	1	2	3	4	5	6	7
1. Neonatal Medical Index (NMI)	--						
2. Neonatal Risk Index (NRI)	.601***	--					
3. Look Duration Time 1 (2-3 mos)	-.053***	.053**	--				
4. Look Duration Time 2 (4-5 mos)	.106***	-.044***	.052***	--			
5. Look Duration Time 3 (6-7 mos)	-.055***	-.108***	-.098***	-.103***	--		
6. Look Duration Time 4 (8-10 mos)	.114***	.124***	-.155***	.280***	.030*	--	
7. Look Duration Time 5 (11-12 mos)	-.012	.098***	.003	.074***	-.323***	-.093***	--
M	3.690	3.592	26.291	17.444	13.661	10.017	8.330
SD	1.029	1.641	4.600	4.990	4.150	1.451	0.412

* $p \leq .05$. ** $p \leq .01$. *** $p \leq .001$.

Trajectory Models

Baseline Model. In order to identify fit indices for the LTM that allows for valid interpretation and unbiased estimates, an unconditional baseline model was first specified (Figure 2). More specifically, the baseline model was an intercept-only growth model, where the mean of the intercept and the residual variances for the monthly assessments of visual attention were specified as the only free parameters (model based on acceptable baseline growth-curve model identified by Widaman and Thompson, 2003). With 14 degrees of freedom, the minimum fit function Chi-Square statistic (*T)* for this model was 420.303. Fit statistics from the baseline model (e.g., *df* and *T*) were then used to calculate unbiased estimates for the LTMs.

Figure 2. *Unconditional Baseline Model*



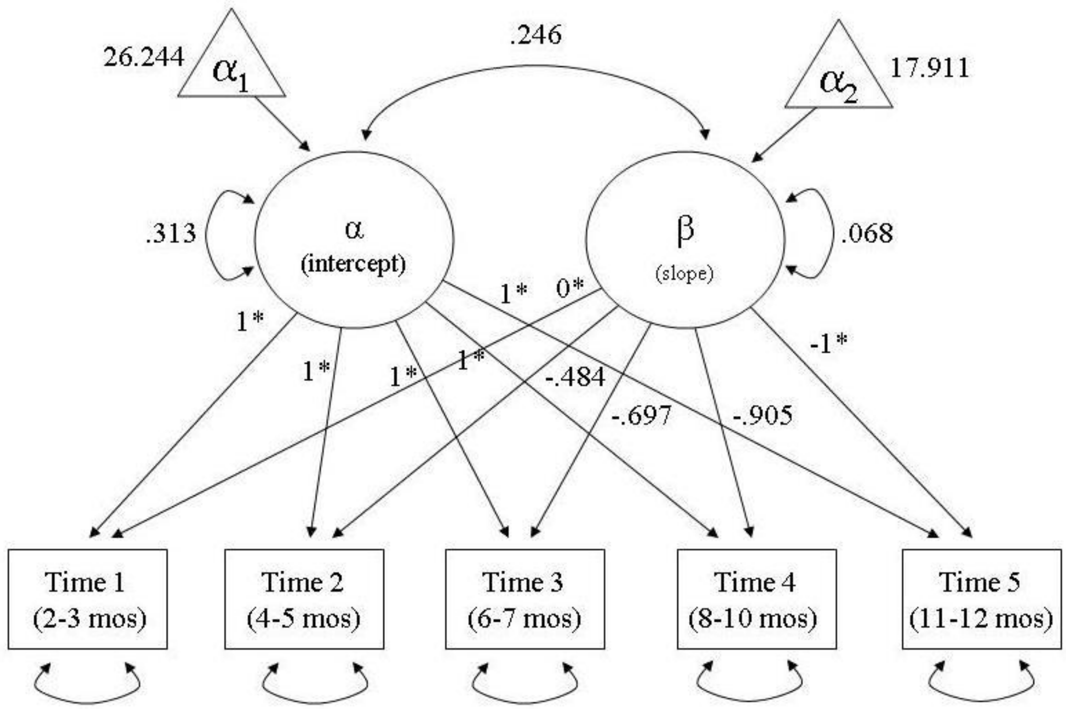
Completely latent function. Although previous studies have suggested that infants born prematurely tend to have longer look durations than their full-term counterparts, it is not entirely clear whether the course of attention over the first year follows a similar trajectory of those detailed in previous studies (e.g., Colombo et al., 2004). More specifically, previous research has not addressed whether patterns of change of attention in infants born prematurely show a similar decline over time to that of full-term infants or rather evidence more of a catch-up pattern (van de Weijer-Bergsma et al., 2008). To derive a "best fitting" curve in the current sample, a completely latent trajectory model was first modeled, whereby the functional form of data from the sample of infants born prematurely was estimated directly from the data. This allows one to freely estimate the nonlinear propensity of change that is not constrained to specific orders of curvature (i.e., linear, quadratic, cubic; Little, Bovaird, & Slegers, 2006).

Specifically, the mean intercept of visual attention, or starting point of the curve beginning at time 1 (i.e., 2-3 months bin) was captured by fixing all the loadings on this construct to 1.0. The change in the course of attention beyond two months corrected age was represented by the slope latent construct. In order to parsimoniously capture nonlinear change that is not modeled as a specific function (e.g., linear, quadratic), the time points between the first and last assessment of visual attention were estimated. More specifically, the loading of the time 1 attention bin was fixed to zero so that the intercept value was equal to the starting point of the curve at the first measurement. The loading of the last measurement of visual attention, time 5 (i.e., 11-12 months bin) was fixed to -1.0 (representing a decline in look duration across time), and the time measurements in between were estimated. The values of the loadings of the time points in between were then proportional to the change between time 1 (i.e., 2-3 months bin) and time 5 (i.e., 11-12 months bin). The factor-loading matrix for this model is provided below, where the first column represents the fixed factor loadings for the intercept factor and the second column represents the loadings for the slope factor with three points being estimated:

$$\Lambda = \begin{bmatrix} 1 & 0 \\ 1 & \lambda_{22} \\ 1 & \lambda_{32} \\ 1 & \lambda_{42} \\ 1 & -1 \end{bmatrix} \quad \begin{matrix} \text{(Months 2-3 loadings)} \\ \text{(Months 4-5 loadings)} \\ \text{(Months 6-7 loadings)} \\ \text{(Months 8-10 loadings)} \\ \text{(Months 11-12 loadings)} \end{matrix}$$

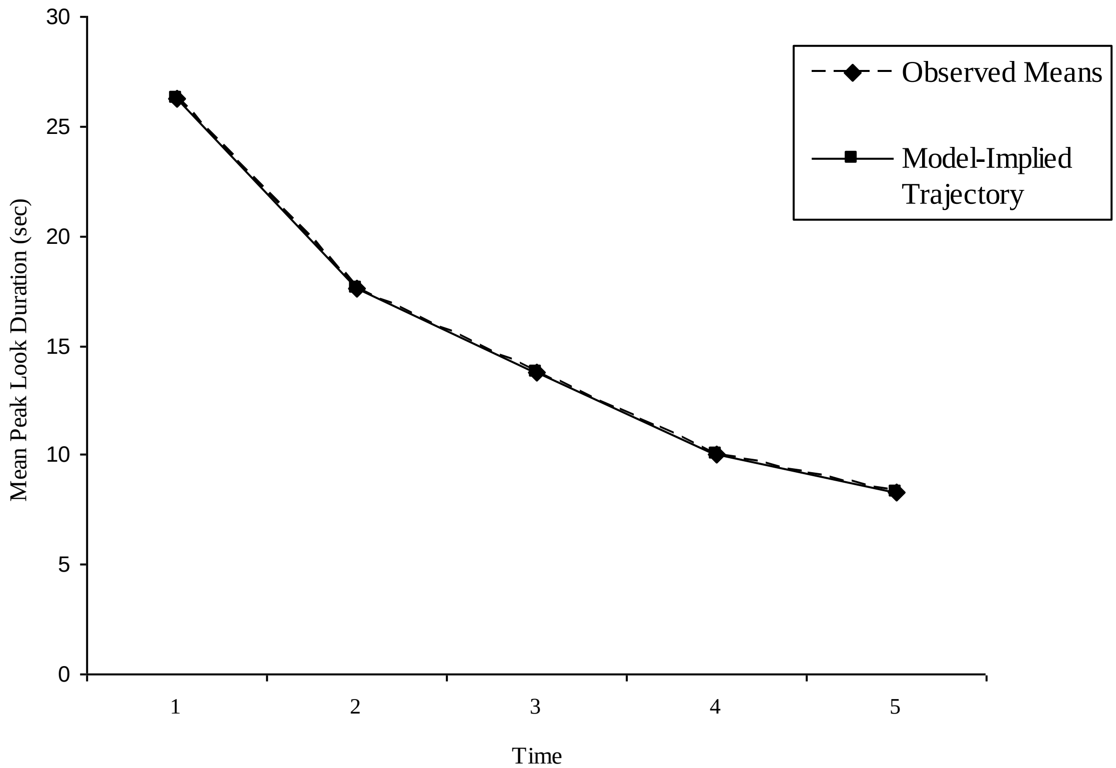
The completely latent function was compared to the baseline model to calculate adjusted model fit indices and demonstrated acceptable model fit ($\chi^2_{(7,\, n\, =\, 71)}$ = 22.790, TLI = 0.922, NFI = 0.946, CFI = 0.961). The path diagram with lambda and mean estimates is provided below (Figure 3):

Figure 3. *Completely Latent Function Model.*



The shape of the nonlinear relation of visual attention over the first year was then illustrated by using tracing rules to reproduce the means of peak look duration at each time point and plotting the values (see Figure 4).

Figure 4. *Model-Implied Unconditional Trajectory and Overall Observed Means.*



Note: Observed means are depicted but align very closely with model-implied trajectory.

Linear model. Next, based on visual depiction of the model-implied trajectory, the slope parameters were constrained to examine whether the change in average peak look duration could be adequately captured by a linear model. The factor-loading matrix for this model is provided below, where the first column represents the fixed factor loadings for the intercept factor and the second column represents the loadings for the slope factor (i.e., time 1 to time 5):

$$\Lambda = \begin{bmatrix} 1 & 3 \\ 1 & 2 \\ 1 & 1 \\ 1 & 0 \\ 1 & -1 \end{bmatrix} \quad \begin{matrix} \text{(Months 2-3 loadings)} \\ \text{(Months 4-5 loadings)} \\ \text{(Months 6-7 loadings)} \\ \text{(Months 8-10 loadings)} \\ \text{(Months 11-12 loadings)} \end{matrix}$$

This model demonstrated poorer model fit ($\chi^2_{(10,\, n\, =\, 71)}$ = 120.264, TLI = 0.442, NFI = 0.714, CFI = 0.712) and in comparing the completely latent function to the linear latent trajectory model, the difference was significant ($\Delta\chi^2_{(3,\, n=71)}$ = 97.474, $p < .01$). Therefore, the constraints were not supported and the mean trajectory was not able to be adequately captured as a linear function. As a result, the completely latent function was retained for further analysis.

Conditional piecewise LTM with Medical Risk Covariates

To better understand the individual trajectories of attention, several predictors were added to the unconditional latent model. In this analysis, the relationship between the latent construct of medical risk on the growth parameters was examined using multiple regression paths. Specifically, the risk construct, consisting of two indicators (i.e., the summary scores from the NMI and NRI risk indices) was regressed upon the latent growth parameters (i.e., slope and intercept). The resulting model demonstrated marginal fit ($\chi^2_{(16,\, n\, =\, 71)}$ = 75.918, TLI = 0.871, NFI = 0.856). Non-significant regression pathways were sequentially removed and the risk construct was found to not be significantly related to either the intercept or slope parameters (both *p*s > .10). The simplified and final model reflecting the removal of non-significant latent structural paths is presented in Figure 5. In addition, loadings, residuals, and R^2 values for each indicator are provided in Table 4.

Figure 5. *Final Conditional Latent Trajectory Model.*

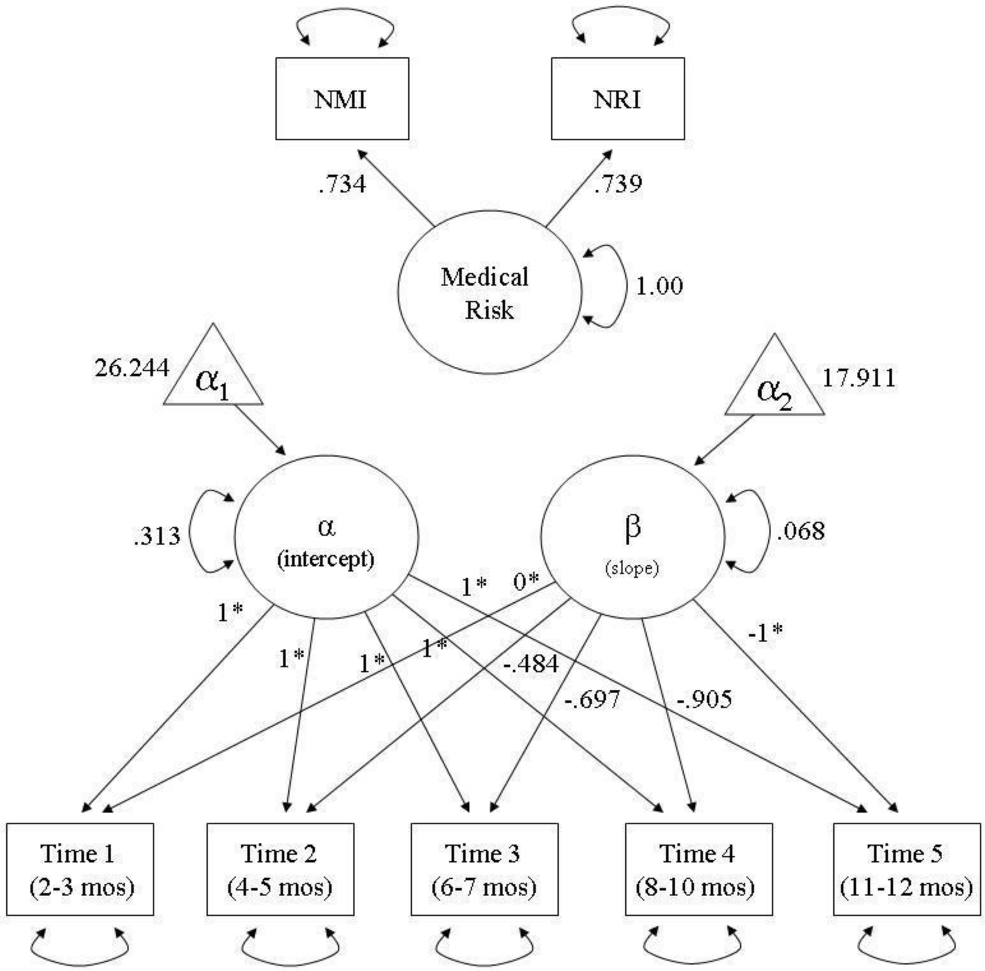


Table 4. *Loading and Intercept Values, Residuals, and R^2 Values for Each Indicator from the Structural Model for the Overall Sample*

Indicator	LISREL Estimates *Loading (SE)*	Standardized *Loading*[a]	*Theta*	R^2
Medical Risk: Estimated Latent Variance = 1.00				
NMI	1.003 (.13)	.734	0.861	.54
NRI	1.018 (.13)	.739	0.861	.55
Intercept: Estimated Latent Variance = 2.551				
Time 1	1.00	.215	24.132	.05
Time 2	1.00	.183	30.560	.03
Time 3	1.00	.200	25.371	.04
Time 4	1.00	.365	2.345	.13
Time 5	1.00	.461	0.242	.21
Slope: Estimated Latent Variance = 2.541				
Time 1	0.00	--	24.132	--
Time 2	-0.484 (.04)	-.089	30.560	.01
Time 3	-0.697 (.04)	-.139	25.371	.02
Time 4	-0.905 (.01)	-.401	2.345	.16
Time 5	-1.00	-.461	0.242	.21

[a] Completely Standardized Solution

Discussion

In their review of attention development in preterm infants, van de Weijer-Bergsma and colleagues (2008) highlighted several areas that warrant further study, including whether patterns of change or trajectories of visual attention in infants born prematurely is characterized by a decline over time, structural delay, catch-up, or some combination of these courses. The current study represents an important preliminary step in understanding the developmental trajectories of visual attention in a sample of preterm infants seen in a multidisciplinary follow-up clinic. Visual inspection of the raw means of peak look duration indicated the current sample showed a general decline from time 1 (i.e., 2-3 months) to time 5 (i.e., 11-12 months). Based on modeling procedures, this trajectory was best captured by a completely latent function which allowed the form to be freely estimated (i.e., not constrained to a linear or cubic function).

The current study also included examination of the association among medical risk factors and the growth parameters of attention during the first year of life. In contrast to our hypothesis, the latent construct of medical risk (comprised of two summary risk scores) in the current study did not account for a significant amount of variance in either the intercept or slope parameters during the first year of life. Mixed findings with regard to summary risk scores predicting early attention development has been described previously (van de Weijer-Bergsma et al., 2008) and could represent the transient nature of these measures. For example, Rose et al. (2001) found that medical risk was significantly associated with look duration at 5 months, but this relationship was not statistically significant at either 7- or 12-months of age. In addition, some factors "weighted" equally (coded 0 or 1) may have differing impact on attention development. For example, IVH can negatively impact the hippocampal region, an area posited to be related to recognition memory (Axmacher, Schmitz, Wagner, Elger, & Fell, 2008), whereas other factors (e.g., hyperbilirubinemia, cardiac anomalies) may not adversely affect attention development. In fact, Kavšek and Bornstein (2010) suggested that for infants exposed to risk factors other than IVH or RDS, the difference in habituation and dishabituation between infants born preterm and healthy term infants may be transient and be evident only during the neonatal period or start to remit around five months of age.

Patterns of Change in Visual Attention

While some studies have examined visual habituation paradigms in infants born preterm (e.g., Bonin et al., 1998; Rose et al., 2001, 2002), these studies have often relied on single "snapshots" or cross-sectional designs that have compared preterm infants to a full-term sample using some type of age matching (e.g., postmenstrual, postnatal) procedure. Due to the complexity and nonlinearity of visual attention during the first year of life, examining the course of attention may provide more insight into the study of visual attention as well as may be a stronger predictor of later outcome than single "snapshots" (Colombo et al., 2004).

Previous literature has suggested that the course of look duration in infancy is not monotonically linear (Colombo, Harlan, & Mitchell, 1999; Hood, Murray, King, & Hooper, 1996), and in fact, the constrained linear model in the current study was not tenable. The depiction of the model-based trajectory revealed that the course of visual habituation in this sample was fairly similar to previous investigations indicating longer average looking early in infancy (i.e., 2-3 months) and a general decline in mean peak look duration over time; however, unlike previous trajectories described (i.e., Colombo et al., 2004), no asymptotic period was evident, which may reflect a delay in the period corresponding to the development of endogenous attention (see Colombo, 2001b, for further review).

Attention Trajectories and Medical Risk

There is an inverse gradient between gestational age and/or birthweight with neonatal morbidity and these infants often experience a variety of medical complications (e.g., chronic lung disease, intraventricular hemorrhage; Campbell & Fleischman, 2001; El-Metwally, Vohr, & Tucker, 2000; Hack & Fanaroff, 2000), some of which have been shown to be negatively associated with indices of early attention (e.g., Landry et al., 1985; Rose et al., 2001). Several previous studies have examined the influence of medical variables on parameters of visual attention using summary risk scores, specific medical complications in isolation, or factors related to medical complications (e.g., duration of hospitalization). The advantages and disadvantages of using individual risk-variables versus a risk index as they relate to early cognitive development have been previously documented (e.g., Burchinal, Roberts, Hooper, & Zeisel, 2000). With regards to attention, the findings have been mixed across all methods. For example, significant associations have been found between specific medical variables such as intraventicular hemorrhage (Landry et al., 1985), duration of oxygen or ventilation assistance (Rose et al., 2001), and hospital stay length (Rose et al., 2002) with visual attention.

Although these studies highlight the association between specific medical variables and attention, medical complications often do not occur in isolation and thus should be considered together (Kavšek & Bornstein, 2010). Supporting this position, 85.9% of infants within the current sample had at least two of the medical complications factored into the NRI risk score, 67.6% had three or more of the medical complications, and 38.0% had four or more complications. The benefit of the algorithms used in these medical risk indices is that they "weight" the various medical complications based on their predicted impact on outcomes; yet these algorithms are generally more sensitive to prediction of mortality than morbidity, despite some modest association with developmental outcome (e.g., Scheiner & Sexton, 1991).

Also related to medical risk, previous studies examining attention in preterm infants have excluded those with such conditions as intraventricular hemorrhage greater than Grade I, gestational age less than 28 weeks, chronic lung disease (i.e., ventilation > 28 days), and/or small for gestational age (e.g., Bonin et al., 1998; Espy et al., 2002; Ross et al., 1992; Stroganova et al., 2005). Although this may allow investigators to have a more homogenous sample of low-risk infants, it may not be representative of the larger, more "typical" preterm population. To put this in perspective, if the aforementioned exclusion criteria were applied to the current sample, 47 of the 71 infants tested (66.2%) would have been excluded from the study.

Furthermore, given improved survival of infants born less than 1000 grams and/or less than 25-weeks gestation, the preterm population seen today may be markedly different than cohorts studied 20-30 years ago (Doyle & Casalaz, 2001; Vohr & Msall, 1997; Stephens, Tucker, & Vohr, 2010), including those used in early studies of attention during infancy (e.g., Landry, Leslie, Fletcher, & Francis, 1985; Rose et al., 1988). Thus, the current study allowed for examination of the attention parameters in a more representative sample seen in a hospital-based clinic setting today.

Methodological Considerations

Due to the complex nature of attention during infancy, researchers must consider a variety of factors that may provide increased precision in the analysis of attention development, particularly in preterm samples. Some of these issues are discussed below.

Stimuli and Outcomes. Previous research examining whether preterm samples, including those with high-risk infants, display slower habituation than their full-term counterparts has produced mixed results; this may reflect the type of stimuli used in the study. For example, studies employing abstract patterns have demonstrated significantly lower rates of habituation in high-risk preterm than term infants (Rose et al., 1988; Millar, Weir, & Supramaniam, 1991); however, use of naturalistic faces and/or geometric 3D forms yielded no significant differences. In addition, effect sizes for comparing term, low-risk preterm, and high-risk preterm infants have differed depending on whether the outcome focused on habituation versus dishabituation (see Kavšek & Bornstein, 2010, for further review). Thus, as these authors state, research is needed to systematically examine the role of type, number, and severity of medical complications with age, stimulus material, and outcome measures (e.g., habituation versus novelty preference) in infants born prematurely.

Psychophysiological Methods. Given the variety of functions present in the construct of attention (see Colombo, 2001b for further review), it may be important to consider convergent psychophysiological measures (e.g., heart rate, EEG, ERP) rather than relying solely on behavioral measures (i.e., look duration; Richards & Casey, 1992; Richards, 2010). These methods these can help distinguish the various components of attention reflected in visual fixation. For example, heart rate changes that occur during visual fixation can be useful in parsing infant look duration into different phases of attention (i.e., Orienting, Sustained Attention, Attention Termination; Richards, 2010). At the beginning of fixation toward a stimulus, infants often display a large deceleration of heart rate, followed by a sustained lowered heart rate during the sustained attention phase, and eventually a return of the heart rate level to the pre-stimulus level when attention termination occurs (see Richards & Casey, 1991). Moreover, these phases have been shown to be differentially organized in clusters of infants with varying courses of attention, who in turn demonstrated divergent developmental outcomes (Colombo et al., 2004).

Consistent with recommendations provided by Ricci et al. (2010), additional studies are needed to determine the specific relation between central-nervous insults, brain maturation, and visual attention. The inclusion of psychophysiological measures such as MRI and/or visual evoked potential changes may provide increased sensitivity to changes in visual changes in attention than the mere presence or absence of a particular medical condition. Moreover, these measures may allow for increased precision and a finer-grained analysis of the various components of attention (Colombo, 2001a), and allow researchers to examine the correlation between measures of visual attention and other indices of early development (Ricci et al., 2010). For example, an aberrant course in visual attention may reflect the maturation sequence of neurons in the developing brain of an infant born preterm and these measures may help elucidate the link between developmental changes in attention with related neural systems (Richards, Reynolds, & Courage, 2010); In turn, this may provide clinicians and researchers with increased understanding of the impact of central nervous system insults and the early development of attention.

Environmental Factors. The examination of environmental influences on development can include both “process” (e.g., proximal factors experienced more directly such as mother-infant interaction) and “status” features (e.g., distal or broader such as socioeconomic status, neighborhood; Aylward, 1992). Future examination of environmental process features, such as mother-infant interaction and nutritional supplementation, may be important correlates to consider given their established association with previous studies of visual attention. Ultimately, environmental factors can temper or aggravate developmental issues associated with medical complications and thus should be considered in conjunction with medical risk (Aylward, 2010a; Thompson et al., 1994). Furthermore, researchers should consider repeated measurements of environmental influences over time, given that some of these factors may be transient in nature.

Nutritional Supplementation. Long chain polyunsaturated fatty acids (LC-PUFAs), found in breastmilk and fortified formulas, are important factors that promote central nervous system development and have been suggested to help in visual function maturation (Birch, Birch, Hoffman, & Uauy, 1992), motor development (Bier, Oliver, Ferguson, & Vohr, 2002), and overall neurological functioning (Feldman & Eidelman, 2003; Lanting, Fidler, Huisman, Touwen, & Boersma, 1994). The contribution of LC-PUFAs to learning and cognition has been investigated in several studies, yet results of RCTs involving the impact of supplementation manipulation on infant development are mixed (e.g., Birch, Garsfield, Hoffman, Uauy, & Birch, 2000; Scott et al., 1998; Werkman & Carlson, 1996), which may reflect the type of dependent variable (e.g., broad, standardized tests of cognitive development versus laboratory tests tapping specific cognitive processes; see Colombo, 2001a, for further review).

Relevant to the current study, preterm infants with a higher biochemical marker of DHA have been found to demonstrate faster information processing as well as increased novelty detection during the first year of life (Forsyth & Willatts, 1996; O'Connor et al., 2001; Werkman & Carlson, 1996). Providing DHA supplementation during periods of normal increase in brain DHA (around 24 weeks gestation to greater than or equal to 2 years) might optimize development and have a positive impact on early indices of attention (Cheatham, Colombo, & Carlson, 2006). Furthermore, taking into account environmental factors, LC-PUFA supplementation may have a greater effect on those infants in which environmental quality is poor (e.g., low socioecomonic status or poor caregiver responsiveness) compared to those infants raised in more optimal environments (Colombo, 2001a).

Caregiving Environment. Factors such as quality of the home environment (e.g., Bacharach & Baumeister, 1998) and caregiver coping and psychological functioning (e.g., Veddovi, Gibson, Kenny, Bowen, & Starte, 2004) have been found to be associated with cognitive and behavioral development in infants born preterm. Somewhat intuitive, preterm infants raised in enriching and supportive environments tend to have more optimal outcomes than those infants in deprived environments (Bradley et al., 1994; Forcada-Guex, Pierrehumbert, Borghini, Moessinger, & Muller-Nix, 2006). In addition to their impact on global development, these process factors have also been shown to be related to visual attention. For example, Sun (2003) found that maternal psychological well-being was related to performance on the A-not-B task at 8-months of age in a sample of term and preterm infants. In addition, Sigman, Cohen, and Beckwith (1997) reported that fixation during infancy was significantly associated with cognitive performance at 18 years of age; this relation was moderated by early maternal stimulation such that infants with short look durations and whose mothers displayed a high vocalization rate had significantly higher cognitive scores in adolescence than those with longer fixations who experienced less maternal vocalization.

Limitations and Future Directions

The strengths of this study are in its relatively large sample of preterm infants, inclusion of infants with high medical risk (e.g., IVH grade > II, GA < 27 weeks), and use of a longitudinal design that permitted an examination of trajectories of attention during the first year of life; however, there are several limitations and challenges within this study that should be noted and warrant further discussion. First, the current study was conducted in conjunction with the infant's regularly scheduled appointment within a busy multidisciplinary follow-up clinic visit. Although the procedures for administering the assessments of visual attention were fairly standard, there was no standardization as to whether infants were seen before or after their routine physical and/or developmental evaluation. This could have played a role in the level of fatigue/fussiness during assessments as well as the parent's ability to complete the assessment on data collection days.

Second, there was a moderate amount of missing data present, which was partially due to the nature of the design within a follow-up clinic setting as well as to the characteristics of the population of interest. Periods of attention assessment occurred in conjunction with infant's normally scheduled follow-up visit to the specialty care clinic. Follow-up visits could range from 4-weeks to 3-months from the previous visit, assuming families kept their scheduled appointment. Thus, while the population under study may be more representative of preterm infants, this is one of the challenges faced in conducting this type of study in a clinic venue. There were also some missing data due to infant refusal behavior (e.g., infant falling asleep or crying prior to and/or during the procedure), which is one of the stated difficulties of working with this age-group and population. More specifically, test refusals are found more in children born at biologic risk or from low- socioeconomic households (Aylward, 2009) and subject losses in studies of infant visual perception range from 25% to 70% (Constantine, Haynes, Spiker, Kendall-Tackett, & Constantine, 1993).

Finally, the examination of medical risk was based on retrospective review of infant's discharge summary charts. Across discharging institutions, there was some variability in the presentation of information (e.g., defining septicemia or respiratory distress syndrome). In addition, the retrospective nature of this review limited the inclusion of some other risk indices (e.g., CRIB-II, NBRS), as some of these algorithms utilize lab values (e.g., pH, urine output) collected during the first 24 hours of life to calculate the risk summary score. The regular inclusion of this type of information within a discharge summary chart was uncommon.

Developmental Outcomes. The visual habituation paradigm is a rudimentary form of infant's visual learning and is often used to examine the extant cognitive abilities and skills of infants during the first year of life (Colombo, 2002). Greater declines in look duration over the first year are posited to reflect more efficient processing or disengagement of attention (Colombo, Mitchell, Coldren, & Freeseman, 1991; Frick, Colombo, & Saxon, 1999) and research findings have sparked interest in the relation between early indices of attention and individual differences in cognitive development. More specifically, indices of attention in infancy have been found to be significantly correlated with individual differences in cognitive abilities (i.e., those with steeper declines have higher developmental outcomes), accounting for 4-10% of variance in later developmental functioning (see Colombo & Mitchell, 2009 for further review).

Some research has suggested that these associations are more robust for infants born prematurely compared to a term control group (Kavšek, 2004; Ortiz-Mantilla, Choudhurry, Leevers, & Benasich, 2008). For example, in a meta-analysis on the relation between infant attention and later IQ, Kavšek (2004) found the correlation to be .50 for risk samples, whereas for non-risk infants, the correlation was .32. As part of the multidisciplinary clinic at the current site, developmental assessments using the Bayley-III are generally conducted at 6-, 12-, and 24-months of age, correcting for prematurity. Future studies will examine the relationship between early measures of attention designed to tap specific cognitive functions with the various domains of the global assessment of cognitive functioning.

In addition to examining the general relationship between trajectories of attention and standardized tests of developmental outcome, it may be important to examine whether there exist subgroups of attention trajectories. To better understand the predictive validity of the developmental function of look duration, Colombo and colleagues (2004) identified four clusters of infants with varying look duration trajectories over the first year. Those infants characterized by a non-normative pattern of looking demonstrated poorer outcomes which became increasingly divergent by 24-months of age. Future studies with a larger sample could utilize group-based trajectory modeling (GBTM; see Modi et al., 2010, for example) techniques to identify whether there are select subsets of infants who display non-normative or aberrant courses of visual attention during the first year, who in turn have poorer developmental outcomes and thus may benefit from additional early intervention services.

Conclusions and Implications for Clinical Intervention

The current study identified the developmental course of attention for a sample of infants born prematurely and serves as a preliminary step in further understanding visual attention and the nature of early cognitive functioning in this population. While previous studies have highlighted the association between prematurity and indices of attention using cross-sectional designs, this is the first study to examine the trajectories of attention during the first year of life. Moreover, the current study utilized a fairly large sample of preterm infants seen in a multidisciplinary clinic setting and can serve as a next step in translating bench science to bedside/clinical care. Future studies may provide additional answers to questions that remain regarding the varied processes that habituation encompasses, particularly in a sample of preterm infants.

The results from this preliminary research with a sample of infants born prematurely could serve as the foundation for future investigations to examine how these parameters relate to early cognitive functioning during infancy and childhood. Eventually, if the measures yield acceptable sensitivity to later development in infants with varying medical risk, then these investigations could lead to the development of a means to improve early identification of those most in need of intervention. Given that the estimated annual societal economic burden associated with preterm birth in the U.S. was over $26 billion in 2005 (Behrman & Butler, 2006), early identification is important as it affords for earlier intervention, which in turn can decrease the severity of developmental delay.

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Appendix

Record Forms

Facts about You

This information will be used to describe the participants of the study.

Date: ____/____/______

Name: ___________________ Phone (home)_____________(work)____________

Address: ____
Street

____
City State Zip Code

Infant's Name: ________________________ Date of Birth _____/____/____

What is your relationship to the infant in the follow-up clinic?
_____ Mother _____ Father
_____ Other (please specify) ____________________

If primary caregiver, what is your current marital status?
_____ married, living together _____ not married, living with partner
_____ married but separated _____ single, never married
_____ divorced _____ widowed

What is your current age? ________ Spouse's current age (if applicable) _______

What level of school have you completed?
_____ some high school
_____ high school graduate
_____ attended college
_____ junior college or vocational school graduate (e.g., associate's degree)
_____ college graduate (e.g., bachelor's degree)
_____ post-graduate work
_____ graduate degree

What level of school has your spouse completed? (if applicable)
_____ some high school
_____ high school graduate
_____ attended college
_____ junior college or vocational school graduate (e.g., associate's degree)
_____ college graduate (e.g., bachelor's degree)
_____ post-graduate work
_____ graduate degree

Estimated gross monthly income: $________.00

How would you describe **yourself**, choosing one from these categories:

_____ white, not Hispanic _____ Native American
_____ black, not Hispanic _____ Asian or Asian-American
_____ Hispanic _____ Other

How would you describe **your spouse** (if applicable), choosing one from these categories:

_____ white, not Hispanic _____ Native American
_____ black, not Hispanic _____ Asian or Asian-American
_____ Hispanic _____ Other

How would you describe **your infant**, choosing one from these categories:

_____ white, not Hispanic _____ Native American
_____ black, not Hispanic _____ Asian or Asian-American
_____ Hispanic _____ Other

With whom does the infant live?

_____ birth parents
_____ adoptive parents
_____ foster parents
_____ Other (please specify) _________________________

Difficulties during pregnancy:

For Mother? Yes ___ No___ If yes, please explain:_________________________
______

For Infant? Yes ___ No ___If yes please explain: _________________________
______

Is your baby currently on any medication? Yes No

If Yes, Please list:

Name of Medication Reason for Medication

_________________________ ____
_________________________ ____
_________________________ ____

What was the approximate date of your baby's last shots? _____/__/____

Has your baby had any ear infections? Yes No

Number of infections __________ Length of longest infection ________

Has your baby been re-hospitalized since birth? Yes No

Does your baby have any chronic health conditions? Yes No

If yes, please explain: ____
____
____
____

Did your baby sleep in the car on the way here? Yes No

Other than in the car, at what time did your baby last wake up? ___:____ A.M or P.M
(circle)

At what time was your infant last fed? _____:______ A.M or P.M (circle)

Is your infant currently in daycare? Yes No
If yes, how many hours of daycare per week? ____________

How many siblings does your infant have living at home? ________

Age	Gender	Ever hospitalized in NICU?	
_____________	_____________	Yes	No
_____________	_____________	Yes	No
_____________	_____________	Yes	No
_____________	_____________	Yes	No

Relative to contact in case of change of contact information:

Name: ________________________ Phone (home)____________(work)_____________

Address: ____
Street

____
City State Zip Code

Please initial here if you give us permission to contact this person in event of change of contact information ____________

Medical Record Information

Date: ____/___/______

Study ID # __________ Hospital ID# ________

Gender: Male Female

Date of first clinic visit: _______/___/______

Age at first visit (chronological age in months): ________________

Referral Source:

CMH NICU St. Luke's NICU Research NICU TMC NICU

Other NICU/ICU CMH PICU CMH floor Community other

Reason for Referral:

Preterm-follow-up chronic lung apnea/monitor failure to thrive/feeding

At risk for developmental delay synagis other multiple involvement

Infant's Birthweight (grams): _______________ Gestational Age (weeks): _____
Birth length (cm): __________ Birth head circumference (cm): ___________

Dates of Hospitalization: ______/___/______ to ______/___/______

Age at discharge (months): _______________

Discharge weight (grams): _________ Discharge length (cm): __________

Discharge head circumference (cm): _____________

Medications during hospitalization:

Name of Medication	Reason for Medication
____________________	________________________________
____________________	________________________________
____________________	________________________________
____________________	________________________________

Number of medications at discharge: __________

Home nursing/visits at discharge: ____________

Apgar scores: 1 minute: ________ 5 minute: ________

Medical History:

1. Chronic lung disease	yes	no	
2. GER	yes	no	
3. Apnea of prematurity	yes	no	
4. Retinopathy of prematurity (stage: _____)	yes	no	no exam
5. Laser surgery for ROP	yes	no	
6. Vision impaired	yes	no	
7. Hearing impaired	yes	no	
8. CNS findings			
IVH (grade: ________)	yes	no	
HIE	yes	no	
Cerebral infarct	yes	no	
Structural anomaly	yes	no	
Other (describe: _________________)	yes	no	
Multiple findings	yes	no	
9. Periventricular leukomalacia (PVL)	yes	no	
10. Hydrocephalus	yes	no	
11. Perinatal depression	yes	no	
12. Congenital birth defect	yes	no	
13. Congenital heart disease	yes	no	
14. Cardiac surgery	yes	no	
15. Hypothyroid	yes	no	
16. Oral feeding difficulties	yes	no	
17. Apnea	yes	no	
18. Prenatal drug exposure	yes	no	
19. Abnormal tone	yes	no	
20. Seizures	yes	no	
21. Hypoglycemia	yes	no	
22. Hypotension	yes	no	

23. Infection	yes	no
24. Hyperbilirubinemia	yes	no
25. Necrotizing entercolitis	yes	no
26. Cerebral Palsy	yes	no
27. Asphyxia/Hypoxia	yes	no
28. Meconium aspiration	yes	no

29 Other(s): ______________________________

____

____

Visual Attention Record Form

Scaled Score	Years	Months	Days
Date Tested			
Date of Birth			
Age			
Age (months and days)	(Years x 12) + months		
Adjusted for Prematurity	Through 24 mo		
Adjusted Age			

Visual Attention Test

Habituation Trial	**Looking Time**	**Novelty Preference**	**Average Looking**	**Peak Looking**
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
Novelty Preference				
Average Looking				
Peak Leaking				