Title
Factors Influencing Early Trajectories of Adaptive Behavior in Children Born Prematurely

Author
DeBattista, Anne Michele

Publication Date
2014

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in Children Born Prematurely

by

Anne DeBattista, APRN, PNP-BC, PMHS-BC, PhD(c)

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

Nursing

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

[redacted]

Abstract

Factors Influencing Trajectories of Early Adaptive Behavior among Children Born Prematurely

Anne DeBattista

Statement of the Problem: Children born prematurely score lower on adaptive behavior measures compared to term born peers. Because adaptive behavior encompasses a broad spectrum of motor, communication, socialization, and daily living skills, deficiencies can have a significant impact on development throughout life. Achievement of adaptive behavior scores in the normative range has been expected by age 2 or 3. However, information is lacking regarding the likelihood of preterm children catching up to their peers or their trajectories of adaptive behavior over the first few years of life. Additionally, factors that may influence these trajectories are not well understood, including the impact of intervention services experienced by children in their communities. The overarching aims of this study were to describe the trajectories of adaptive behavior for preterm children from 4 to 36 months of life, to examine the influence of specific infant and family factors on these trajectories, and to determine whether amount and timing of early intervention services are associated with improvement in children's adaptive behavior over time.

Methods/Procedures: A cohort of 218 premature infants was assessed at 4 times from infancy through preschool age using the Vineland Adaptive Behaviors Scales. Hours of intervention service received by each child between assessments were recorded by participating community agencies. Additional data was collected on neonatal illness severity, infant gender and gestational age, family income, and maternal education. Multilevel modeling was used to examine the aims.

Summary of Findings: Although individual trajectories varied, mean adaptive behavior scores of children declined over time. 43 percent of the children did not achieve scores in the normative range by age 2 or 3. Younger gestational age, male sex and lower income were significant predictors of worse adaptive behavior. While amount of intervention received by children was not associated with improved adaptive behavior on average, increasing intervention was associated with some improvement in adaptive behavior as children aged. Results suggest that additional intervention might slow decline in adaptive behavior. Interventions to prevent this decline must be studied, with attention to the needs of boys born at younger gestational ages who are living in disadvantaged environments.

Acknowledgements

This dissertation was inspired by the patients and families that I have cared for over the last 30 years in both hospital and community settings. The data used in this dissertation was part of a larger database, the Preemie Project, funded by First 5 San Mateo County. I would like to acknowledge Cheryl Goldfarb-Greenwood and Nidia Floyd for their tremendous effort in collecting the data, and my psychology colleagues for their help with the adaptive behavior evaluations.

Thank you to UCSF professors Mary Lynch and Dr. Christine Kennedy for encouraging me to pursue doctoral education. I am grateful for my professors in the doctoral program for helping me understand how to address longitudinal research questions. Thank you to my dissertation committee Drs. Heidi Feldman, Abbey Alkon, Christine Kennedy for your wisdom and guidance. A special thank you to my Dissertation Chair Dr. Sandra Weiss for challenging me to think, learn, and grow; your mentorship has most certainly influenced my own developmental trajectory.

These last five years in the doctoral program and the work of this dissertation would not have been possible without the love and support of my family and friends. Thank you to my wonderful husband Manny for remaining by my side through this evolutionary and labor intensive process. My children Jayne and Brad sparked my interest in developmental trajectories as their brilliance unfolded with every milestone achieved; thank you for teaching me. To my parents Hugh and Helen, thank you for being proud of me and listening to me talk through every paper and discovery.

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General Introduction

INTRODUCTION

Innate Developmental Delay

In the United States, 12% of children are born too soon, prior to 37 weeks gestation (Foundation, 2014). They enter the world with underdeveloped bodies and their ability to function outside the womb often requires intensive medical support. The immaturity of their physiologic systems, combined with necessary medical procedures for survival, often result in damage to organs such as brain, eyes, lungs and gastrointestinal systems, particularly in infants born at the youngest gestational ages (23-28 weeks) (Saigal & Doyle, 2008). At birth, this immaturity of the nervous system results in the inability to perform developmental or behavioral skills consistent with term born peers. For example, a premature infant will stop breathing because the nervous system is overwhelmed. Or they may have delayed feeding skills because of trouble coordinating the ability to suck, swallow, and breath. Essentially, these functional skills are delayed at birth compared to term born peers, and, therefore, can be conceptualized as innate developmental delay.

Developmental Catch-up

The delays experienced by premature infants are expected to be transient. In the early years, development and adaptive behavior are often evaluated by measures that are normed on the skill progression in the general pediatric population. A child born prematurely is thought to have caught up to term born peers when their scores on these measures fall in the average range for their chronological age. For decades, families of children born prematurely have been advised to expect developmental catch-up of their child's skills by age two or three years (D' Agostino, 2010; S. L. Wilson & M. M. Cradock, 2004). Developmental catch-up in children born prematurely is often thought of as an automatic linear and sequential process (S. L. Wilson & M.M. Cradock, 2004).

The nervous system of premature infants was thought to develop sequentially, as long as brain injury was not identified (Pediatrics, 2013). Past studies report that brain injury such as white matter injury or more severe hemorrhages were significant risk factors for poor neurodevelopmental outcomes (B.R. Vohr et al., 2000). Although recent studies have identified other types of brain injuries that influence a premature infant's brain development, the lack of identification of these previously identified brain injuries on MRI or ultrasound scans often results in reassurance to families that automatic sequential catch up is anticipated.

Cerebral Dysmaturation – the Invisible Biologic Risk

The nervous system underpins the body's ability to develop and perform skills such as communication, motor, social and cognitive functions. Recently, the high prevalence of diffuse brain injury in premature infants was discovered using a 12 Tesla magnetic resonance imaging scan (MRI) (Back, 2014). These lesions may not be detected using the lower powered MRI technology available in most hospitals. This diffuse injury is thought to cause abnormal brain development resulting in a smaller adolescent or adult brain. This process of variation in the development of the premature brain is referred to as cerebral dysmaturation (Back, 2014). The smaller brain volumes resulting from this process are highly correlated with poorer developmental and adaptive behavior skills (Catherine Limperopoulos, 2010; T.M. Luu et al., 2009; Mather & Inder, 2009; Ment et al., 2006).

Long-term Outcomes Influenced by Biologic and Social Risks

Children born prematurely have a higher prevalence of developmental and adaptive behavior delays in early childhood compared with term born peers, and these differences appear to persist into adolescence and adulthood (Hack, 2009a; Sullivan, Miller, & Msall, 2012). Mean group developmental and intelligence scores of children born prematurely have been reported to be 3-17 points lower than those of term born peers (Aylward, 2002). Recent studies suggest both biologic and social risk factors are associated with poorer developmental and adaptive behavior outcomes in children born prematurely. Younger gestational age is consistently found to be associated with poorer developmental and adaptive behavior outcomes (Addison, Riesenberg, & Rosenbaum, 2004; Aylward, 2002; Cho, Holditch-Davis, & Miles, 2010; Hack & Fanaroff, 1999; Maitre, Lambert, Aschner, & Key, 2013; Mulder, Pitchford, Hagger, & Marlow, 2009; Poulsen et al., 2013; Saigal et al., 2007; Stevenson et al., 2000; B.R. Vohr, et al., 2000; Wood et al., 2005). Multiple biologic risks have been identified that are associated with illness severity, such as brain injury, sepsis, seizures, and chronic lung disease (Ambalavanan et al., 2012; S. R. Hintz, Kendrick, Vohr, Poole, & Higgins, 2005; Sullivan, et al., 2012; Volpe, 2009; Wood, et al., 2005). Male sex has is usually associated with poorer developmental and adaptive behavior outcomes (Aylward, 2002; Cho, et al., 2010; Stevenson, et al., 2000) although female sex was reported to be associated with poorer behavior scores at age two years (A. Spittle, Orton, Doyle, & Boyd, 2009).

Social risk factors such as low income levels have been associated with poor developmental outcomes in preterm infants during infancy, toddler and preschool ages (Guerra et al., 2014; Marieke R. Potijk, Jorien M. Kerstjens, Arend F. Bos, Sijmen A. Reijneveld, & Andrea F. de Winter, 2013; Tofail et al., 2012). In large scale trials of children born prematurely, low level of maternal education has been associated with poorer developmental outcomes in the first few years of life (S. R. Hintz, et al., 2005; B.R. Vohr, et al., 2000; Wang, Howe, Lin, & Hsu, 2014; Wood, et al., 2005). In contrast, a systematic review of studies of language development found children born prematurely to score significantly lower than term born peers irrespective of socioeconomic status (van Noort-van der Spek, Franken, & Weisglas-Kuperus, 2012). Few studies report the influence of these factors on outcomes as children age.

Change in the influence of risk over time may be important to consider. For instance, the influence of illness severity as a predictor of poor neurodevelopmental outcomes at 18 months becomes more significant over the neonatal hospitalization (Ambalavanan, et al., 2012). However, beyond the neonatal period, there is a paucity of scientific literature evaluating change in risks on developmental trajectories. Understanding whether a risk factor becomes more significant over the first three years of life may provide important information to consider when planning interventions designed to ameliorate risk.

Early Intervention and Neuroplasticity

Early intervention (EI) services are designed specifically to improve developmental skill progression in children from birth to three years of age. Although many studies have reported long term developmental, social, functional, educational, occupational and behavioral outcomes of children born prematurely, most do not consider early intervention service receipt as a factor in the analysis. EI services provide experiences designed to facilitate neuroplasticity and aid in the progression of developmental and adaptive skills from birth to three years of age (Rosenberg, Robinson, Shaw, & Ellison, 2013). Neuroplasticity is a process of recovery from brain injury and progression toward age appropriate skills (Cicchetti & Cohen, 2006). Brain development is supported by visual, auditory, or somatosensory input acquired through experience (Cuppini, Magosso, Rowland, Stein, & Ursino, 2012). Recent studies report better brain maturation or improved outcomes with developmental interventions provided in the first months of a preterm infant's life (R. Feldman, Z. Rosenthal, & A. I. Eidelman, 2014; Milgrom et al., 2010; Scher et al., 2009). Additionally, a recent Cochrane Review reported that early intervention programs implemented in the first year of life have a positive impact on cognitive and motor developmental outcomes at preschool age (A. Spittle, et al., 2009). One study found that the influence of receipt of any EI services over the first three years positively influenced trajectories of mental development from 16 through 36 months, although investigators did not account for the timing when EI occurred (McManus, Carle, & Poehlmann, 2012).

Early Intervention Service Delivery through IDEA- Part C

Federal Legislation for Early Intervention services is outlined under the Individuals with Disabilities Education Act- Part C (IDEA Part-C) for children ages birth to 3. Although these services are mandated at the federal level, the implementation of regulations and services provided varies widely (Center, 2007; Dunst & Bruder, 2002; Mott & Dunst, 2006; Rosenberg, et al., 2013; Rosenberg, Zhang, & Robinson, 2008; Tang, Feldman, Huffman, Kagawa, & Gould, 2012; C.J. Wang et al., 2009). Less than a handful of states currently provide EI services based on the eligibility category of "At Risk". Access to services by this category provides an avenue for premature infants with biologic risk factors to obtain EI services that begin in the first year of life. Without it, children need to have an established developmental disability or have developmental scores" delayed enough" to qualify. The percentage of delay needed to qualify for Part C eligibility varies by state. Additionally, for children born prematurely, scores based on expectations for adjusted age (higher scores) are used to calculate the level of delay. This results in children born prematurely needing to be more delayed than term born peers in order to qualify. By the time many qualify, they are in their second year of life, leaving little time to receive services before they age out of their eligibility for services at 3.

While the scientific literature suggests receipt of developmental interventions shortly after birth results in better brain development and outcomes (R. Feldman, et al., 2014; A. Spittle, et al., 2009), in 2012, less than 1% of the pediatric population in California received Part C services in the first year of life (OSEP, 2013). Although exact numbers of children born prematurely are not specified, 10% of the pediatric population was born prematurely, suggesting a significant gap in service receipt in their first year of life (Foundation, 2014). Other evidence for this gap was provided in a recent report which noted that a large percentage of children in California was not referred to EI services in the first year of life, although they were presumably eligible by developmental scores reflecting percentage of delay (Tang, et al., 2012). Additionally, on a national scale, only 53% percent of the most vulnerable of premature infants, born at less than 28 weeks gestation, received any early intervention by 18 months adjusted age (S.R. Hintz, Kendrick, Vohr, Poole, & Higgins, 2008).

Investment in EI services for children has decreased significantly over the last 12 years, with the dollar amount of EI services spent per child going from $1697 to $1257 (Lazara, Danaher, & Goode, 2014). These investment rates are consistent with amounts spent in 1992, and over the last four years, the number of children receiving EI services has consistently declined (Lazara, et al., 2014). However, the timing when services are provided has not been studied, in order to understand whether more services are being provided at certain developmental periods than others.

PROBLEM STATEMENT

Children born prematurely have innate delays in adaptive behavior skills. Although many are likely to experience cerebral dysmaturation and persistent delays, catch-up of these children to same aged peers has been expected by most clinicians by age 2 or 3 years (Back, 2014; Pediatrics, 2013). However, information is lacking regarding the likelihood of achieving adaptive behavior scores in the average range by age 2 or 3 years. The development of individual and between-child trajectories of adaptive behavior in the first three years has not been described, and there is a paucity of information regarding the influence of risk factors and receipt of EI services. Although studies suggest that early timing and amount of service provision improve outcomes in children born prematurely, there are currently no reports of the influence of these factors experienced by children in their communities.

RESEARCH AIMS

Aim 1: To describe the proportion of children who scored in the expected normative range in late infancy, as toddlers, and in preschool

Aim 2: To evaluate the likelihood of preterm children achieving adaptive behavior scores in the normative range by toddler and preschool periods

Aim 3: To describe the trajectory of adaptive behavior for children born prematurely over their first 3 years of life

Aim 4: To examine the influence of gestational age, illness severity, sex, family income and maternal education on variation in adaptive behavior trajectories from infancy to preschool periods

Aim 5: To describe the amount and timing of early intervention services received by children born prematurely from hospital discharge to age three years

Aim 6: To determine whether the amount and timing of early intervention service hours received by children born prematurely are associated with change in their adaptive behavior skills over the first three years of life.

THEORETICAL FRAMEWORK

The theoretical framework of this dissertation research is more complex than past theories of automatic sequential developmental catch-up in children born prematurely. This framework focuses on the importance of environmental experiences as factors that dynamically shape outcomes and create variation in trajectories of adaptive behavior. It highlights the importance of children's experiences and interactions within their environment as significant facilitators of change in their overall brain development and function.

Cicchetti's Theory of Neuroplasticity

Cicchetti's theory of neuroplasticity was used to inform this dissertation. Cicchetti defines neuroplasticity as a modification of the brain and central nervous system structures, as a result of experiences, with the assumption that such modification is adaptive for the continued survival or optimal function of the organism (Cicchetti & Cohen, 2006). The goal of the theory of neuroplasticity is to explain the biological and behavioral response to environment and injury. As shown in Figure 1, the theory includes the following key concepts: 1) experience, 2) level of change, 3) outcome, 4) contextual factors, and 5) dynamic self-organization. Neuroplasticity is consistent with the idea of self-organization of the brain, but in contrast to the theory of automatic sequential developmental catch-up, it includes the influence of environmental experience, variation in levels of biological and behavioral responses, and the importance of timing.

The key concept of experience is defined by interactions between person and environment that comprise complex types of stimulation for the brain. The model for neuroplasticity (Figure 1) shows experiences are classified under the following domains: sensory experiences (hearing, vision, touch, taste, motion & smell), socialization with other humans, emotional responses, motor activities, and lastly, injury. Level of change describes the target areas changed by interaction with experience: genetic, neurochemical, synaptogenesis (or the connection of nerve cells in the brain), cellular, anatomical or behavioral systems. In Cicchetti's model, level of change signifies the fundamental idea that all levels of the central nervous system exhibit a "bottom up" neuroplasticity, with changes at lower levels (cellular, neurochemical and synaptogenesis) precipitating outcome changes at a higher level (e.g. behavior). Outcomes listed in Cicchetti's model are the resultant short and long term changes from interaction with experience and range from individual genetic expression to neural changes and enhanced adaptive functioning. Contextual factors in Cicchetti's model include genetic inheritance as well as potential developmental supports/constraints and the time course of neural change. The concept of dynamic self-organization implies a dynamic feedback system, whereby any change in the central nervous system can bring about further instances of neural plasticity in a self-organized fashion. In summary, this model of neuroplasticity portrays human development as influenced by a complex matrix of the individual's level of biological and psychological organization, experiences, social context, timing of the adverse event(s) and experiences, and the developmental history of the individual (Cicchetti & Cohen, 2006).

The theory has the following key propositions: 1) Neuroplasticity is a dynamic and nonlinear function that constantly reshapes and organizes the brain through a reciprocal relationship between neurobiological development and experience, 2) Sensory, motor, injury, social, and emotional experiences are influenced by the contextual factors of genetic inheritance, biological developmental periods, and critical developmental periods, 3) Experience influences change in the molecular, physiological and structural properties of neural pathways and in behavior, 4) The levels of neural change result in simple to higher order outcome changes in these areas, ultimately resulting in changes in adaptive function, and 5) This complex and dynamic process of human development produces varied trajectories of adaptation and maladaptation.

In contrast to the concept of developmental catch-up in preterm infants as a biologically based automatic and sequential process, Cicchetti's theory of neuroplasticity is based on interactions between environmental experience and neural and behavioral change. The dynamic feedback system describes the process of continual change; specifically, how outcomes influence further experiences which in turn result in further changes in outcomes. The complexity of the theory captures biological and environmental determinants, timing of these determinants, and the dynamic and evolving interaction of these determinants (including the frequency of interaction, or dosage) to support outcomes.

Contextual factors can be both biologically driven and environmental in nature. As a contextual factor, genetic inheritance can determine sex as well as vulnerability to early birth and neonatal illness. The concept of sensitive periods, another contextual factor, can refer to the timing of biological mechanisms that require a fine tuned orchestration of high quality and specific synaptic connections to support brain capacity (Braun, 2011). Sensitive periods can also represent developmental stages that are most susceptible to environmental experience. Thus, sensitive/critical periods can be explained by the co-occurrence of synaptogenesis (production of nerve synapses) and activity-dependent and experience-dependent pruning of synapses. Activity-dependent neuroplasticity is a key concept in supporting brain development through early environmental intervention as well as through risk factors in the environment that may inhibit brain development. The mechanism for synaptic plasticity, first described by Donald Hebb in 1949, is an increase in synaptic efficacy (based on amount of stimulation) from the presynaptic cell's repeated and persistent stimulation of the postsynaptic cell. The often cited Hebbian phrase "cells that wire together, fire together" underscores this process (Galtier, Faugeras, & Bressloff, 2012). This critical time of overproduction of neurons is thought to be adaptive for the brain by creating a reservoir that is available to repair injury. A prolonged period of overproduction and pruning of synapses in children and young adults, contributes to their capacity for learning, increased cortical thickening, and correlates with scores of superior intelligence (Koziol, Budding, & Chidekel, 2010). In contrast, lack of stimulation stemming from a disadvantaged environment may disrupt these therapeutic neural processes.

The word "dynamic" implies constant looping of the mechanism and constant change in progress. The frequency and duration of stimulation and the practicing of new learning are hypothesized to advance skills and adaptive function. Through cerebral-cerebellar circuits and sensory information from the environment, the cerebellum builds on working memory to create automaticity of behavior independent of cortical control and working memory (Koziol, et al., 2010). Functional MRI studies have demonstrated that functions for motor and cognition are segregated and specialized in the human cerebellum (Koziol, et al., 2010). The processes involved in attaining developmental and adaptive behavior skills requires automaticity in functioning, dependent on cerebellar activity that becomes increasingly refined as behaviors are practiced and repeated. With practice, the speed, focus, rate, rhythm and overall refinement of movement, thought, and emotional/affective tone become more adaptive (Baillieux, De Smet, Paquier, De Deyn, & Marien, 2008; Bolduc et al., 2012; Hautzel, Mottaghy, Specht, Muller, & Krause, 2009; Koziol, et al., 2010; Catherine Limperopoulos, 2010).

Application of Cicchettis' Theory to this Study

Current knowledge of brain development provides support for the utility of Cicchetti's theoretical model for use in research evaluating risk factors and environmental interventions that may influence adaptive behavior in children born prematurely. The primary focus of this research is on Cicchetti's concepts of experience, contextual factors, and outcome. The experience of key interest is the amount of early intervention for children. Contextual factors of interest involve the timing of the intervention, the infant's sex, gestational age and illness severity, and family-related indices of a potentially advantaged or disadvantaged environment (including income and maternal education). The outcome of interest in this research is adaptive behavior development in the early years of life of children born prematurely.

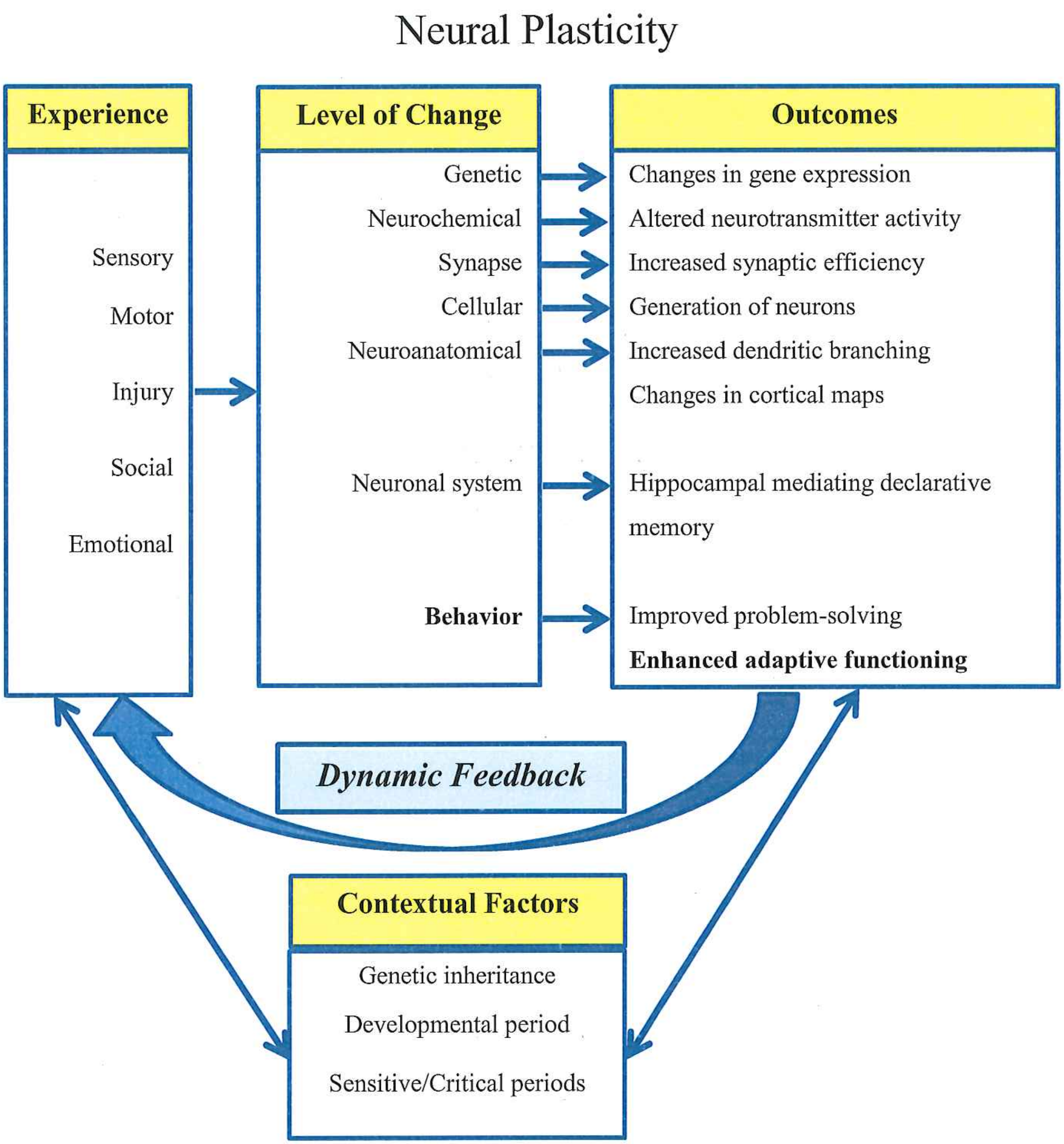
SIGNIFICANCE

Prematurity is a serious chronic health condition associated with lifelong developmental morbidities. Advancements in neurocognitive science have increased our understanding of brain injury and long-term neurodevelopmental morbidities associated with prematurity including cerebral palsy, cognitive impairment, specific learning differences, and behavioral disorders (de Kieviet, van Elburg, Lafeber, & Oosterlaan, 2012; de Kieviet, Zoetebier, van Elburg, Vermeulen, & Oosterlaan, 2012; Johnston, 2009; Johnston et al., 2009; Catherine

Limperopoulos, 2010; Mather & Inder, 2009; Volpe, 2009). Often, the difficulties experienced by children born prematurely are not recognized until learning demands become more complex (Feldman et al., 2012; Loe, Lee, Luna, & Feldman, 2012). Fewer children born prematurely are receiving EI, and there is an overrepresentation needing special education assistance (Klouda, Hacker, Kretlow, & Mikos, 2009; T.M. Luu, et al., 2009; Saigal & Doyle, 2008). This study addresses the question of whether premature children do catch up by age two or three years. It also informs us about factors that influence the adaptive behavior trajectories of children born prematurely, including early intervention services as well as contextual factors in the child's biologic history and social life. Understanding effects of these factors will address significant gaps in the literature to improve knowledge regarding the development of adaptive behavior of children born prematurely over the first 3 years of life.

The following chapters present research findings specific to the aims of the study. Chapter 2 examines the proportion and likelihood of children catching up to same age term born peers over the first 3 years of life (Aims 1 & 2). Chapter 3 describes the adaptive behavior trajectories in children born prematurely and examines whether gestational age, illness severity, sex, family income and maternal education influence these trajectories in the first three years (Aims 3 and 4). Chapter 4 describes the amount and timing of early intervention services received by children born prematurely and examines whether the amount of EI service hours received over time is associated with changes in adaptive behavior over the first 3 years of life (Aims 5 and 6). Chapter 5 identifies key findings for each aim and what the findings suggest for pediatric clinicians, providers of early intervention for children born prematurely. Additionally, the study's limitations and implications for future research are discussed.

Figure 1.1



Developmental Psychopathology Developmental Neuroscience 2nd Edition, Cicchetti, 2006

Two

Likelihood of Demonstrating Adaptive Behavior in the Normative Range

BACKGROUND & SIGNIFICANCE

When should children who are born prematurely be expected to function with the same developmental and social proficiency as their same age peers? This question continues to plague providers who are asked to predict such outcomes. Significant advances in neonatal care have been made over the past 40 years, with increased survival rates of infants born at younger gestational ages (S. R. Hintz et al., 2011). At the same time, families are given a message that is unchanged over the past four decades – that is, most children born prematurely catch up by age two or three years (Pediatrics, 2013). Catch-up is defined by the chronological age at which the premature child's standard developmental scores are in the average range for same age peers (Dimes, 2008; Pediatrics, 2013).

A child's adaptive behavior is an important part of his/her overall catch-up. The construct of adaptive behavior has been defined as the performance of daily activities required for personal and social sufficiency, which is dependent to a great extent on the child's ability but also changes in response to the environment (Cicchetti & Cohen, 2006; S. Sparrow, Cicchetti, & Balla, 2005; S. S. Sparrow & Cicchetti, 1985). Adaptive skills follow a developmental continuum whereby they improve and become more complex as individuals age. Adaptive function is thought to be sensitive to change in skills over time (Rosenbaum, Saigal, Szatmari, & Hoult, 1995; Snider, Majnemer, Mazer, Campbell, & Bos, 2009; Sullivan, et al., 2012). In the early years of life, adaptive behavior skills represent developmental function, the foundational skills for personal and social sufficiency (S. Sparrow, et al., 2005; S. S. Sparrow & Cicchetti, 1985). Compared to term born peers, children born prematurely demonstrate more impaired adaptive behavior skills; in cross-sectional studies, this finding has been demonstrated at school-age [Hack 1994; Rosenbaum, 1995; Taylor 2006] and adulthood (Saigal & Doyle, 2008).

There are few reports of adaptive function in prematurely born children during the first three years of life (Boyd et al., 2013; Snider, et al., 2009). Cho et al. evaluated adaptive behavior in infancy- and toddler-aged children born prematurely (Cho, et al., 2010). At six months, the mean score for adaptive behavior was in the middle of the normative range; by 16 months, mean scores trended down to the bottom of the normative range. This downward trend in early adaptive behavior scores, appears consistent with previous reports of worsening cognitive and neuropsychological outcomes over time in children born prematurely (Aylward, 2002).

Providers counsel families to adjust age level expectations for their prematurely born children by subtracting the number of weeks that the child was born prematurely from the child's chronological age (Pediatrics, 2013). However, the evidence that supports this clinical recommendation is difficult to find. One recent systematic review concluded that there is evidence to support adjusting age expectations until age 12 months (D'Agostino, 2010). Another systematic review reported that there is evidence to support adjusting age expectations until age two years for infants born at 35 weeks gestational age, but not for those born at younger gestational ages (S. L. Wilson & M. M. Cradock, 2004). Long-term outcome studies report continued lower mean neurodevelopmental and behavioral scores into adulthood, suggesting that individuals born prematurely may never fully catch up over time (Hack, 2009a; Luu, Vohr, Allan, Schneider, & Ment, 2011; Saigal, et al., 2007). Findings to date indicate that further research is needed to support the policy and practice of adjusting age expectations in prematurely born children (D'Agostino, 2010; D'Agostino et al., 2013; S. L. Wilson & M. M. Cradock, 2004).

A major limitation in previous research has been the use of cross sectional analysis at different points in time to compare developmental scores of preterm children to term born norms (Dahl et al., 2006; Hack et al., 2009; Rosenbaum, et al., 1995; Saigal, et al., 2007). As an exception, one study did use a multilevel statistical model to evaluate individual level change and group change over time, producing outcome trajectories for language development of prematurely born children from 3 through 8 years of age (T. M. Luu et al., 2009). However, no studies have used this method to examine trajectories for adaptive behavior in very young prematurely born children. There are two aims to this study of children born prematurely: 1) to describe the proportions of children who scored in the expected normative range in late infancy, as toddlers, and in preschool, and 2) to evaluate the likelihood of achieving adaptive behavior scores in the normative range by age two or three years. Multilevel logistic regression modeling was employed to examine the probability of achieving scores in the normative range.

METHODS

Sample

This cohort study followed children born between 2000 and 2006. Inclusion criteria for infants were low birth weight (<2500 grams), prematurity (<37 weeks gestation), and at least 1 of the California Children's Services (CCS) criteria for risk of later neurodevelopmental complications (e.g. prolonged perinatal hypoxemia, seizures, intracranial abnormality). Families who were not living in San Mateo County were excluded from participation. If they consented and later moved out of county during the study, they were no longer eligible.

Procedure

Parents of babies who met the inclusion criteria were approached by the study coordinator for consent to participate in the study. Consents were in English and Spanish and all meetings with families who spoke a language other than English were conducted with an interpreter. Letters were sent to hospital intensive care nurseries in San Mateo County inviting them to refer infants who met the inclusion criteria. Demographic data was collected at entry to the study. Adaptive behavior data was collected at 4 time points: baseline infancy (4-5 months adjusted age), late infancy (12 - 13 months adjusted age), toddler (18 - 22.5 months adjusted age), and preschool (32 - 35 months chronological age). Chronological age was used to calculate scores for adaptive behavior at each assessment time period. Adaptive behavior data was collected during visits to the High Risk Infant Follow-up Clinic or by telephone interview. This study was approved by the Institutional Review Boards of Stanford University and the University of California, San Francisco.

Measures

Gestational age as well as medical information needed for inclusion criteria and calculation of illness severity were acquired through review of the medical record. Illness severity while in the neonatal intensive care unit (NICU) was summarized with the Neonatal Medical Index (NMI). The NMI has good predictive and concurrent validities in discriminating abnormal neurodevelopmental and functional outcomes (Korner et al., 1993; Wang, et al., 2014). Other demographic data, including maternal age, education level, family composition and income level, were collected by the study coordinator at the baseline visit.

The Vineland Adaptive Behavior Scales (VABS) were used to measure adaptive behavior. The VABS is a norm-referenced instrument designed to assess the developmental and social proficiency of children in the context of their environment. It consists of 297 interview items that are responded to by a parent or primary caretaker. The instrument measures adaptive behavior in several dimensions relevant to children's function (communication, daily living skills, socialization and motor domains) and provides an overall adaptive behavior composite (ABC) score of these four domains that can be compared to normative population values (Cho, et al., 2010; S. Sparrow, Cicchette, & Balla, 1989). The VABS ABC score will be used in this analysis. The mean normative composite score is 100 with an average range of 85 to 115. A score of 85 is considered the cut off for achieving normative expectations at each specific development level. At each data collection time point, a structured interview with the primary caretaker was conducted by a clinical psychologist or nurse practitioner trained to administer the VABS. The interview typically took around 30 to 45 minutes to conduct.

There is evidence for concurrent and predictive validity of the VABS in children born prematurely (C. Limperopoulos, Majnemer, Steinbach, & Shevell, 2006; Rosenbaum, et al., 1995; Weiss, Wilson, Seed, & Paul, 2001). The reliability of the VABS is also well established, with coefficient alphas greater than .80 for the ABC for all age ranges under 3 years and with test-retest reliability coefficients of .78-.93 (S. Sparrow, et al., 1989). Equivalence reliability with telephone administration has also been established (C. Limperopoulos, et al., 2006). While the initial psychometric properties of the Vineland were established many years ago, it remains one of the standard tools of assessment used today (Gleason & Coster, 2012; Scattone, Raggio, & May, 2011).

Data Analysis

For each developmental period -- late infancy, toddlerhood, and preschool-aged – we used descriptive analyses to determine the percentage of children who met the criterion for catch-up (i.e., achieving VABS ABC scores in the normative range). To evaluate the likelihood of obtaining a composite score for adaptive behavior in the normative range (i.e. greater than or equal to 85), a multilevel logistic regression was performed using STATA/SE Release 12 (StatCorp, 2011). This analysis tested both linear and quadratic change over time in a VABS dichotomized ABC score; the binary score was based on achieving normative range (i.e., VABS ABC score of ≥85) or not. Change in age across 8-month increments was estimated (this increment approximated intervals between data collection time points). We controlled for gestational age at birth and centered the analysis at the assessment in late infancy because there is some evidence to support adjusted age correction to 12 months (D'Agostino, 2010). Multilevel logistic estimation in Stata uses full maximum likelihood with numerical integration and adaptive quadrature to linearize the relationship between the dichotomous dependent variable and the continuous independent variable. Additionally, the use of full maximum likelihood produces unbiased estimates and accounts for missing data. Descriptive statistics were analyzed using SPSS version 21.

RESULTS

The convenience sample largely comprised infants born at Lucile Packard Children's Hospital. 218 infants were enrolled in the study. Table 2.1 presents key sample data. The mean gestational age at birth was 31 weeks (± 2.99). The range of gestational ages at birth was 23 weeks to 36 weeks, and 70% of the sample was less than 33 weeks gestation at birth. The average maternal age at delivery was 31 years (± 6.6), with a range of 16 to 48 years. 47% of mothers had not attained a college degree. 42% of mothers self-identified as Caucasian, 34% Hispanic, and 28% as Other. 42% of subjects were covered by government-sponsored insurance. 43% of families had an annual income of less than 50,000. 89% of the infants had two parents involved in their lives at the time of enrollment. Based on scores from the Neonatal Medical Index (Korner, et al., 1993), the majority of infants had experienced some medical complications. However, severity of illness had a fairly even distribution across the sample.

Children Demonstrating Adaptive Behavior in the Normative Range, By Developmental Period

Table 2.2 shows group means for VABS ABC scores and percentage of children who achieve scores in the normative range across developmental periods. The overall percentage of children scoring in the normative range declines from Infancy to Toddler periods. Although the ranges are wide, the means for children at both toddler and preschool age are 1 point above the cut-off for achieving expected norms.

Likelihood of Demonstrating Adaptive Behavior in the Normative Range

The initial unconditional logistic regression model testing linear change in adaptive behavior indicated that the odds of getting a score ≥ 85 for adaptive behavior declines by .75 (SE .05) with each additional increase in age by 8 months ($z=-4.66$, $P<.001$). When gestational age (GA) in weeks was added to the model to control for its effects, no major change in these odds occurred. However, gestational age itself was a significant predictor of adaptive performance; the odds of achieving a score ≥ 85 increased by 1.2 for every additional week of gestational age at birth ($z=3.25$, $P=.001$). The interaction between gestational age and chronological age of the child was added to the model to evaluate whether GA might moderate improvement or decline in adaptive behavior at different points in development. The interaction was not significant ($z = -1.02$, $P=.307$).

Results for the quadratic (non-linear) logistic regression model show a somewhat different picture. A quadratic time variable captures the rate of change (acceleration or deceleration) over the measurement time points. In this model, the odds of demonstrating adaptive behavior in the normative range increased by 1.2 for each successive 8-month increase ($z=4.58$, $p < .001$). This model showed effects similar to the linear model with regard to gestational age ($z=3.13$, $P=.002$) and for the interaction between gestational age and chronological age ($z=.44$, $P=.657$).

Data for the most parsimonious model are shown below in Table 2.3. The -Log likelihood (indicating goodness of fit) of the model was -355.11, $p< .001$. It includes linear and quadratic effects, controlling for gestational age. In the linear model, the odds of demonstrating adaptive behavior in the normative range decline over time (odds ratio = 0.46). In the curvilinear (quadratic) model, the odds demonstrating adaptive behavior in the normative range decrease until around 22 months and then increase (odds ratio = 1.17). A graph of this model is displayed in Figure 2.1. The odds of demonstrating adaptive behavior in the normative range increase with greater gestational age (odds ratio = 1.16).

DISCUSSION

Results suggest that almost half of the children born prematurely are not "catching up" and that 'catch up' may not be a sequential process to be expected over time. A significant number of children have scores in the lower end of the average range at the preschool period. The data also imply that assessments of adaptive behavior in early infancy are not necessarily predictive of or consistent with later assessment results.

Our findings highlight the importance of looking beyond differences in group mean scores when evaluating outcomes. For children born prematurely, the probability of achieving an adaptive behavior score in the normative range declines over time and then begins to increase. The quadratic effect in the probability model suggests that when children are toddlers, the decline stabilizes but then improves into the preschool period. Regression findings also show that babies born at older gestational ages had a better chance of achieving adaptive behavior outcomes in the normative range by the preschool period.

Results of the initial decline in adaptive behavior are consistent with Cho and colleagues who also found mean scores for adaptive behavior that were lower in toddler ages than at infancy (Cho, et al., 2010). To our knowledge the quadratic effect has not been reported, although variations in patterns of development have been previously described (Aylward, 2002). Lastly, our findings are consistent with lower outcome scores associated with younger gestational ages that have been described in the literature (Aylward, 2002; B. R. Vohr et al., 2000).

Implications for Future Research

Long-term outcome research of children born prematurely most often reports aggregated group differences from term born controls using methods such as cross sectional differences at two points in time, or with repeated measures ANOVA. Repeated measures ANOVA of longitudinal data simply describes a series of observed group changes at fixed points in time. In contrast, multilevel modeling examines how the developmental process unfolds for each individual and then uses the estimated parameters for within-person change as dependent variables to examine the effects of factors that may differ across individuals. The use of multilevel modeling and other related methods for longitudinal studies of children born prematurely would provide more information about the rate and pattern of change across time points.

Our results raise questions regarding various predictors, other than gestational age, that may influence the rate and pattern of adaptive behavior change over time. Illness severity, gender, maternal education, and family income, are just a few of the variables thought to explain variances in outcomes. Findings also indicate the need to better understand exactly what occurs at the beginning of the second year of life that may enhance or impede their continued development of adaptive behavior skills. Our data suggest that this may be a significant point in time. Problems arising at that developmental phase could reflect a sensitive period at which certain interventions could be especially important. Lastly, our study does not provide information on trajectories beyond the preschool period. Further research is needed to determine whether the changes we found in the infants' adaptive behavior trajectory continue or not.

Limitations

This sample of children born prematurely may not be representative of the broader population of children born prematurely. Additionally, this analysis does not account for the influence of variables such as early intervention services, sex, poverty, illness severity or other biological risk factors.

IMPLICATIONS FOR PRACTICE

Our data challenges the theoretical assumption for children born prematurely that catch-up is a biologically based sequential phenomena that occurs automatically by age 2 or 3. The decline in scores over the first 24 months suggests that clinicians should refrain from reassuring families based on normative outcomes obtained in infancy. Our study used chronologic age scores to evaluate change in true age scores. If we adjusted age expectations in the sample, they would look even better at the first visit, thereby augmenting the decline between the first assessment and the lower unadjusted preschool visit. Age adjustment may hide true delays and lead to overconfidence in the child's skill progression.

The assumption of automatic catch-up has also influenced eligibility for federally funded early intervention services designed to help children with delayed development. Many states use adjusted age (higher scores) to determine eligibility for EI based on percentage of delay from the norm (Schakelford, 2006). This practice requires that children born prematurely need to be more delayed than term born peers. Often children are turning two by the time they are delayed enough to qualify. Recent literature highlights the limited access to EI services that children born prematurely experience, particularly in the first two years of life (S.R. Hintz, et al., 2008; Lazara, et al., 2014; Tang, et al., 2012; C. Jason Wang et al., 2009). Assumptions of catch-up and ensuing practices may be contributing to the decreased numbers receiving EI services and ultimately smaller numbers catching up.

CONCLUSION

We have described change in adaptive behavior for a cohort of preterm infants over the first 3 years of life, along with proportions that achieve normative expectations by preschool. These findings require corroboration in larger prospective studies and validation by more sensitive diagnostic testing. However, data suggest that it may not be wise for clinicians to provide reassurance that children born prematurely will catch up to same age peers by age 2 or 3 years. Our data support the need for further evaluation of factors that influence adaptive behavior trajectories and the need to reconsider the practice of age adjustment for prematurely born children.

Table 2.1

Family and Child Demographic Characteristics

Characteristic (n)	n (%)
Annual Family Income (196)	
>50k	111 (57%)
<50k	85 (43%)
Insurance (206)	
MediCal/Medicaid	87 (42%)
Private	119 (58%)
Maternal Race/Ethnicity (218)	
Caucasian	92 (42%)
Hispanic	73 (34%)
African American	12 (5%)
Asian Pacific Islander	25 (11%)
other	16 (8%)
Gender Male (218)	109 (50%)
Birthweight in grams (218)	(Mean=1479,SD=500)
ELBW <1000	45 (20%)
VLBW 1000-1499	73 (34%)
LBW 1500-2499	100 (46%)
Gestational Age in weeks (218)	(Mean=31 weeks, SD=2.99)
23-29	72 (33%)
30-32	82 (37%)
33-36	64 (30%)

Table 2.2

Group Means for Adaptive Behavior Scores and Percent of Subjects Scoring in the Average Range at Each Developmental Period

		Mean Score (S.D.)	**Range**	**Total percent ≥ 85 (n)**
Infancy	**(n=197)**	93 (9.68)	60-117	84 (166)
Late Infancy	**(n-154)**	91 (9.84)	64-119	73 (113)
Toddler	**(n=162)**	86 (9.17)	64-113	57 (92)
Preschool	**(n=101)**	86 (9.62)	68-116	57 (58)

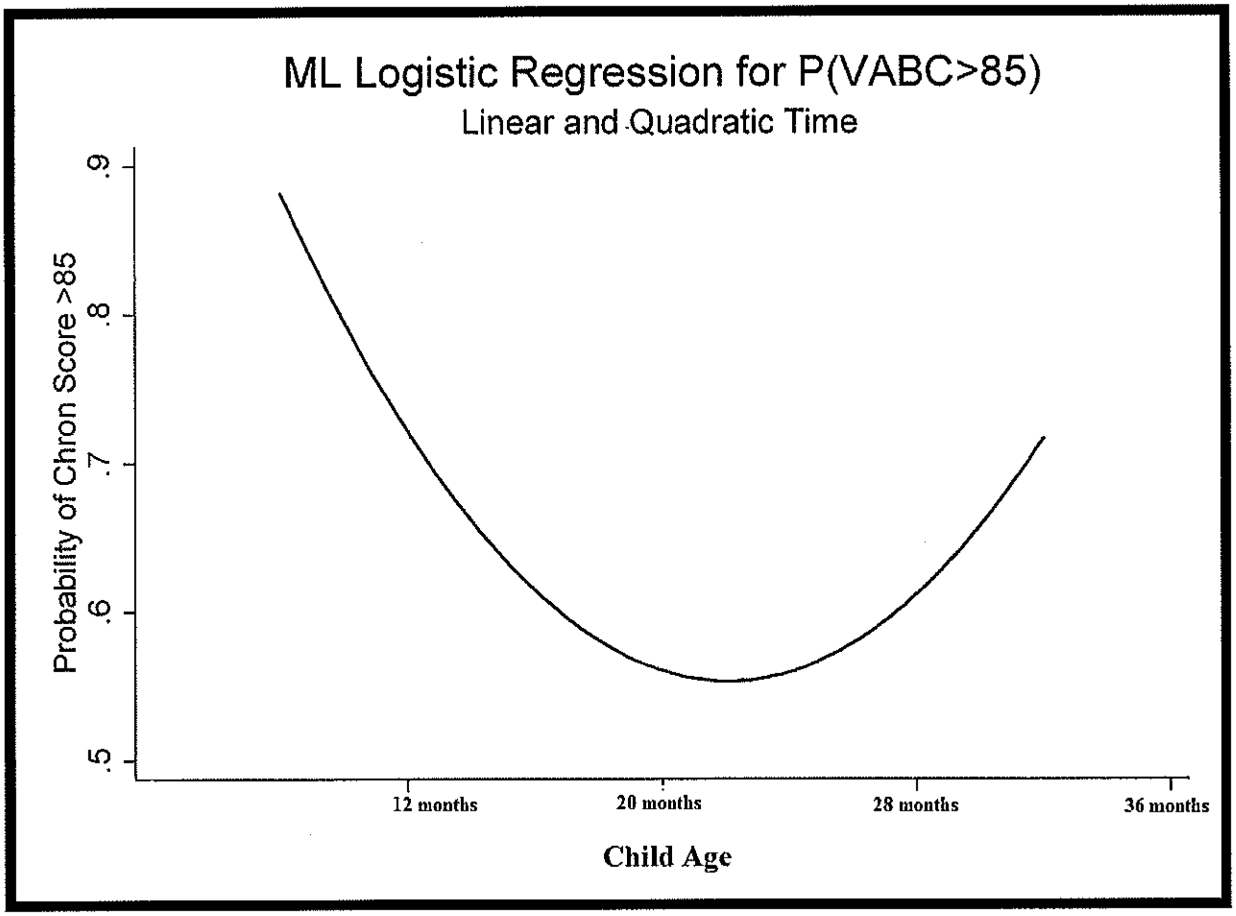
Table 2.3

Effects of Gestational Age and Development Over Time of Achieving Normative Expectations For Adaptive Behavior Composite

	Odds Ratio	**Std. Error**	**WALD z**	**p**	**Confidence Interval**
Linear Time	.4570	.0607	-5.90	<.001	.3523-.5929
Quadratic Time	1.170	.0408	4.50	<.005	1.093-1.253
Gestational Age	1.156	.0537	3.13	.002	1.056-1.266
cons	.0396	.0560	-2.28	.022	.0025-.6326

Figure 2.1

Multilevel Logistic Regression for Probability of Achieving Vineland Adaptive Behavior Composite Score in the Normative Range



Three

Factors that Influence Early Adaptive Behavior Trajectories

INTRODUCTION

Many children born prematurely have difficulties with adaptive behavior. Adaptive behavior reflects functional abilities in communication, social, daily living (self-care and coping), and motor skills (S. Sparrow, et al., 2005; S. S. Sparrow & Cicchetti, 1985). Adaptive behavior involves skills that a child demonstrates in his/her natural setting on a daily basis; these skills change over time and in response to the environment. In the early years of life, adaptive behavior skills are indicative of developmental function, representing foundational skills for personal and social sufficiency (S. Sparrow, et al., 2005; S. S. Sparrow & Cicchetti, 1985). Compared to term born peers, children born prematurely demonstrate more impaired adaptive behavior skills; in cross-sectional studies, this finding has been demonstrated at school-age (Hack 1994; Rosenbaum, 1995; Taylor 2006) and adulthood (Saigal & Doyle, 2008).

Only one recent study has addressed change over the early years of life in adaptive behavior skills of children born prematurely. Cho et al reported that, over a 10-month period during later infancy, preterm children showed a decline in adaptive behavior scores (Cho, et al., 2010). A downward trend in adaptive behavior scores, if further substantiated, would be consistent with the decreasing mean developmental standard scores consistently reported in children born prematurely over the first few years of life (Aylward, 2002; Greene, Patra, Silvestri, & Nelson, 2013; Harris, Megens, Backman, & Hayes, 2005).

It is not clear why some children born prematurely develop more or less optimal adaptive behavior or developmental skills than others. Previous research suggests that both biological factors and social factors may influence these outcomes. Given the paucity of research on adaptive behavior function per se in children born prematurely, we also consider research regarding factors that influence developmental domains that comprise the construct of early adaptive behavior (communication, social, daily living and motor skills). The combination of biologic and social risk factors for children born prematurely has been referred to in the literature as double jeopardy (Jobe, 2013). It has been proposed that social factors, such as poverty and maternal education, influence communication function, while biologic factors are more strongly related to motor function (Aylward, 2002).

Results of previous research regarding biological contributions to developmental and adaptive behavior outcomes indicate that gestational age, neonatal illness severity, and sex are significant predictors. Poorer outcomes in children born at younger gestational ages have been highlighted in the scientific literature for decades (Hack, 2009a; Saigal, 1986; Saigal & Doyle, 2008; Vohr, Stephens, & Tucker, 2010). Recently, reports have highlighted the high prevalence of developmental and adaptive behavior delays in infants born between 32-36 weeks gestational age, often referred to as late preterm (Chyi, Lee, Hintz, Gould, & Sutcliffe, 2008; Guerra, et al., 2014; M. R. Potijk, J. M. Kerstjens, A. F. Bos, S. A. Reijneveld, & A. F. de Winter, 2013). Potijk reported that younger gestational age was associated with delays in fine motor, communication, and personal social domains, but not gross motor (M. R. Potijk, et al., 2013). Several recent studies report younger gestational age as a significant predictor of poorer outcomes in social competence (Jones, Champion, & Woodward, 2013; A. J. Spittle et al., 2009) self-care skills (Verkerk et al., 2013), and communication (Greene, et al., 2013; Thuy Mai Luu et al., 2009; van Noort-van der Spek, et al., 2012).

Another common biological risk factor for preterm infants is increased medical complications, or illness severity. Degree of illness severity has been associated with increased risk for brain injury and resulting poorer neurodevelopmental and adaptive behavior outcomes (Back, 2014; Johnston, 2009; Volpe, 2009). Several recent studies highlight the high incidence of white matter injury in preterm infants, and it's value as a predictor of poorer outcomes in social (Jones, et al., 2013; C. Limperopoulos et al., 2008), communication (Feldman, et al., 2012; Mather & Inder, 2009) and motor (Mirmiran et al., 2004) domains. Another recent large multicenter study evaluated the trajectories of prognostic indicators for neurodevelopmental impairment at 18 months, and reported that the importance of illness severity increased as a prognostic indicator over the NICU course (Ambalavanan, et al., 2012). This study not only validates the importance of illness severity as a prognostic indicator, it highlights the significance of evaluating the change in influence of predictors over time. Spittle et all (2009) have also found brain injury, lower birth weight and postnatal steroid administration to be associated with poorer social and behavioral competence for prematurely born children at age two (A. J. Spittle, et al., 2009).

A frequent biological predictor of development and adaptive behavior in studies of children born prematurely is sex. Although the results are inconsistent, most studies report that boys have worse outcomes than girls (Aylward, 2002; Cho, et al., 2010; Gargus et al., 2009; Kerstjens et al., 2013; Mulder, et al., 2009; Stevenson, et al., 2000; Wood, et al., 2005). Cho et al evaluated the impact of sex on adaptive behavior in children born prematurely during early life and found male sex to be a significant predictor of poor cognitive and adaptive behavior outcomes. Adaptive behavior scores at 6 months trended downward to the bottom of the normative range by 16 months (Cho, et al., 2010). In a study of 908 children born at less than 28 weeks gestation, male sex was associated with delays in communication, motor, cognitive and social domains at age two (Boyd, et al., 2013). A large longitudinal study of preterm infants born less than 28 weeks gestation reported triple the prevalence of sensory, motor or developmental impairments in boys than in girls (21 vs. 7%) at 5 years of age (Walther, den

Ouden, & Verloove-Vanhorick, 2000). The male disadvantage did not change after adjustment for gestational age and variables indicative of illness severity such as respiratory distress. In contrast, Spittle et al. (2009) found that female sex was a significant predictor of poorer social and behavioral competence at age 2 years.

Results of previous research indicate that social risk factors may adversely influence development and adaptive behavior for children born prematurely. Recent studies have linked low income to poor developmental outcomes in preterm infants at 10 months, 2 and 4 years (Guerra, et al., 2014; M. R. Potijk, et al., 2013; Tofail, et al., 2012). Low maternal education has been associated with poorer motor skills at age 2, and with overall development at age 4 (M. R. Potijk, et al., 2013; Wang, et al., 2014). Luu et al evaluated language trajectories from age 3 through 12 years in children born prematurely and reported that maternal education accounted for more variance in receptive language development than history of severe brain injury (Thuy Mai Luu, et al., 2009). In a study of language trajectories between ages 8 and 16 years in children born prematurely, a higher level of maternal education was associated with gains in language skills between ages 8 and 16 years of age (Caskey & Vohr, 2013). In contrast, a systematic review of studies of language development in preterm children found that they scored significantly lower than term children, but that outcomes were independent of socioeconomic status (van Noort-van der Spek, et al., 2012).

In summary, findings regarding the effect of biologic and social factors on early adaptive behavior of children born prematurely has been limited and not been entirely consistent. The most consistent findings are for the influence of gestational age and neonatal illness severity. Lower gestational age overall is consistently a risk, but late preterm gestation is also identified to be a risk. Male sex is frequently identified as a risk, but female sex has also been significant in predicting poorer outcome. Socioeconomic risks related to lower income and limited maternal education are often significant predictors, but not always. Some studies have found SES to have more influence than biologic risk (Thuy Mai Luu, et al., 2009). Of most importance is that studies evaluating adaptive behavior trajectories in the early years of life have not been conducted. Overall, there is a paucity of research in children born prematurely on the early development of adaptive behavior skills and factors that may influence their trajectories. The purpose of this study was to address these gaps in the literature. There are two aims in this study of children born prematurely: 1) to describe adaptive behavior trajectories over the first three years of life, and 2) to examine whether gestational age, illness severity, sex, family income, and maternal education, together or independently, predict these trajectories.

METHODS

Sample

This cohort study followed children born between 2000 and 2006. Inclusion criteria for infants were low birth weight (<2500 grams), prematurity (<37 weeks gestation), and at least 1 of the California Children's Services (CCS) criteria for risk of later neurodevelopmental complications (e.g. prolonged perinatal hypoxemia, seizures, intracranial abnormality). Exclusion criteria included all other infants that did not meet criteria above and were not living in San Mateo County. If families consented and moved out of county during the study, they were no longer eligible.

Procedure

Letters were sent to hospital intensive care nurseries in San Mateo County inviting them to refer infants who met the inclusion criteria. Parents of babies who met the inclusion criteria were approached by the study coordinator for consent to participate in the study. Consents were in English and Spanish and all meetings with families who spoke a language other than English were conducted with an interpreter. Demographic data, including maternal education and family income, was collected at entry to the study. Medical information, including gestational age, birth weight, sex, and illness severity was collected from the medical record after consent to the study. Adaptive behavior data was collected at 4 time points: baseline infancy (4-5 months adjusted age), late infancy (12 - 13 months adjusted age), toddler (18 - 22.5 months adjusted age), and preschool (32 - 35 months chronological age). Chronological age was used to calculate scores for adaptive behavior at each assessment time period. Most adaptive behavior data was collected during visits to the High Risk Infant Follow-up Clinic. Some adaptive behavior data was collected by telephone interview. This study was approved by the Institutional Review Boards of Stanford University and the University of California, San Francisco.

Measures

Medical information for inclusion criteria and calculation of the Neonatal Medical Index was acquired through review of the medical record. The Neonatal Medical Index (NMI) classifies illness severity for babies in the neonatal intensive care unit and has been shown to have good predictive and concurrent validities in discriminating abnormal neurodevelopmental and functional outcomes (Korner, et al., 1993; Wang, et al., 2014). External validity was established on 512 low birth weight children born prematurely with the most consistent predictability in cognitive and motor outcomes at 12 and 24 months for those with birth-weights less than 1500 grams (Korner, et al., 1993). The NMI classifications range from I to V, with I describing preterm infants with very few medical problems and V describing infants with the most serious complications.

The Vineland Adaptive Behavior Scales (VABS) were used to measure adaptive behavior, which in the early years of life measures key domains of overall infant development (S. Sparrow, et al., 2005; S. S. Sparrow & Cicchetti, 1985). The VABS is a norm-referenced instrument designed to assess the developmental and social proficiency of children in the context of their environment. It consists of 297 interview items that are responded to by a parent or primary caretaker. The instrument measures several dimensions relevant to children's function (communication, daily living skills, socialization and motor domains) and provides an overall Adaptive Behavior Composite (ABC) score that represents the 4 adaptive behavior domains and can be compared to normative population values (Cho, et al., 2010; Rosenbaum, et al., 1995; S. Sparrow, et al., 1989). The mean normative ABC score is 100 with an average range of 85 to 115. A score of 85 is considered the cut off for achieving normative expectations at each specific development level. At each data collection time point, a structured interview with the primary caretaker was conducted by a clinical psychologist or nurse practitioner trained to administer the VABS. The interview typically took around 30 to 45 minutes to conduct.

There is evidence for concurrent and predictive validity of the VABS in children born prematurely (C. Limperopoulos, et al., 2006; Rosenbaum, et al., 1995; Weiss, et al., 2001). The reliability of the VABS is also well established with coefficient alphas greater than .80 for the ABC scale for all age ranges under 3 years and with test-retest reliability coefficients of .78-.93 (Rosenbaum, et al., 1995; S. Sparrow, et al., 1989). Equivalence reliability with telephone administration has also been established (C. Limperopoulos, et al., 2006). While the initial psychometric properties of the Vineland were established many years ago, it remains one of the standard tools of assessment used today (Gleason & Coster, 2012; Scattone, et al., 2011).

Data Analysis

Descriptive statistics were employed to examine sample characteristics. Assumptions of bivariate normality and linear relationships were examined and met. Multilevel Mixed Model estimation with full maximum likelihood was used to evaluate the influence of predictors on ABC trajectories. The use of full maximum likelihood accounts for missing data and variation in assessment ages, producing unbiased estimates from slight differences in age of each assessment and the fact that not all children had reached the ages of later assessments by the end of the study.

A two-level polynomial model was fitted to the data. At Level 1, each child's successive ABC scores were examined by individual growth trajectory. To allow visual inspection of the data and appreciation of variability among children, a spaghetti plot also was computed to graph the trajectories of each individual subject's ABC scores from Infancy to the Preschool period. At Level 2, trajectory differences between groups of individuals were examined by adding the between-subject predictors to the model. We proposed that ABC score and its pattern of change would vary across individuals and that this variation would in part be explained by gestational age, level of illness severity, sex, family income, and maternal education. Data were analyzed using SPSS version 21.

RESULTS

The convenience sample was made up largely of infants born at Lucile Packard Children's Hospital. 218 infants were enrolled in the study. Table 3.1 presents key descriptive data. The mean gestational age at birth was 31 weeks ($\pm$ 2.99). The range of gestational ages at birth was 23 weeks to 36 weeks, and 70% of the sample was less than 33 weeks gestation at birth. The average maternal age at delivery was 31 years ($\pm$ 6.6), with a range from 16 to 48 years. 47% of mothers had not attained a college degree. 42% of mothers self-identified as Caucasian, 34% Hispanic, and 28% as other. 42% of subjects were covered by government-sponsored insurance. 43% of families had an annual income of less than 50,000. 89% of the infants had two parents involved in their lives at the time of enrollment. Based on scores from the Neonatal Medical Index (Korner, et al., 1993), the majority of infants had experienced some medical complications. However, severity of illness had a fairly even distribution across the sample. On average the ABC score for the baseline Infancy Assessment was 93, with a range in scores of 60-119.

In the unconditional repeated measures model, time was centered at 4 months chronological age to provide a constant baseline for all infants. Time intervals were set for 8 months to coincide with approximate ages at each assessment period. As shown in Table 3.2, the linear model for time demonstrated significant variation in linear growth trajectories. The growth rate was negative, implying that on average, ABC scores decline over the first three years of life ($B=-4.61$, $p<.001$). Also shown in Table 3.2, the addition of a higher order time variable, quadratic (nonlinear) time, accounted for changes in growth rate. The quadratic growth curve includes the square of the time variable, which represents the degree of acceleration or deceleration in growth at different points in time. The quadratic estimate was also significant and positive indicating that the growth rate was not constant ($B=.63$, $p<.001$). On average, the ABC score initially declined but showed a slight increase around 28 months. This trajectory of Average ABC scores is shown in Figure 3.1.

Inclusion of both linear and quadratic estimates was the most parsimonious model (Akaike's Information Criterion (AIC) = 4925), in contrast to a linear model alone. The spaghetti plot in Figure 3.2 shows the degree of individual variation in linear and quadratic growth trajectories over the first 3 years. Lines in the plot indicate that, for the majority of children, ABC scores gradually decreased over time; however, there are children with sharp increases or decreases in scores. The majority of trajectories cluster in the lower end of the average range (85-90) for ABC scores. The red curvilinear line represents the mean group trajectory for ABC score. Given this apparent variation in growth trajectories, an Intraclass Correlation Coefficient (ICC) was calculated (ICC = 21.762 / 100.287 = .217) to determine actual variance in ABC scores among the children. The ICC demonstrated that the proportion of variance due to differences between children was 22 percent. The unconditional repeated measures model, spaghetti plot, and ICC, all showed significant variability in ABC scores, indicating that examination of a conditional model was warranted to identify factors that might explain the variability.

The following biologic and social predictors were added to the Level 2 conditional growth model separately: gestational age, illness severity, sex, family income, and maternal education. In the single predictor model, gestational age had a significant effect at baseline, but the cross-level interaction demonstrating the effect over time was not significant. Similarly, NMI category had a significant effect at baseline; however, the effect over time was not significant. Male sex did not have a significant effect at baseline, but was significant predictor over time. Neither family income nor maternal education was a significant predictor at baseline or across time.

Following the single predictor models, all predictors and any significant cross-level interactions were simultaneously entered in a composite model with linear and quadratic functions. Table 3 displays this Level 2 Linear Quadratic composite model. The model demonstrated improvement in model fit with a lower AIC deviance statistic (4035) and lower residual (54.15) suggesting that these predictors explained more individual and between individual variance than the unconditional model. As in the single predictor model, gestational age had a significant effect at baseline, but not over time. Consistent with the single predicator model, male sex did not have a significant effect at baseline, and the cross-level interaction was significant (see Figure 3.3). As illustrated in the figure, the difference between ABC scores for males and females was not apparent at 4 months of age, but the difference increased over time, with boys scoring significantly lower than girls. Consistent with the single predictor models, the NMI and maternal education did not have significant effects in the composite model. Although family income did not have a significant effect at baseline in either the single or composite model, the interaction between income and time was significant in the composite model. With all predictors in the model, lower income was a significant predictor of lower ABC scores over time. The difference in ABC score trajectories by family income is shown in Figure 3.4.

DISCUSSION

Findings from this study highlight the significant variability in adaptive behavior trajectories of children born prematurely. Some children started with low scores and achieved scores in the normative range (above 85) by age 3. These trajectories are consistent with current expectations that preterm children catch-up to term born peers by age 2 or 3 (Pediatrics, 2013). Other children initially scored in the normative range and their scores dropped below average over time. However, the majority of children clustered around the lower end of the average range and trended downward over time. The average of all the trajectories was a negative mean linear trend in scores down to the lowest end of the average range. This pattern is consistent with previous studies in children born prematurely (Mwaniki, Atieno, Lawn, & Newton) except that the small positive trend (the quadratic effect) is a new finding that has not been previously reported.

The biologic and social risk factors added to the model at Level 2 provide important information regarding factors that may influence individual differences in adaptive behavior trajectories. Consistent with the literature, we found gestational age to be a significant predictor. On average, children's trajectories differ based on gestational age at birth, with each additional week of gestational age resulting in improved adaptive behavior.

Surprisingly, illness severity was not a significant predictor of adaptive behavior over time. In previous research, Wang et al (2013) found the NMI to predict fine motor function using a tool specific to the measurement of motor function at age 4. This could suggest that the ABC score may not be sensitive enough to detect this level of effect on fine motor. It is also possible that the NMI did not capture the specific types of morbidity that have major effects on adaptive behavior. Lastly, because illness severity was significant in the single model, it is possible that gestational age accounted for much of the variance reflected in the illness severity measure when these variables were examined together in the composite model.

It is interesting that the sex of a premature infant was not associated with group differences in adaptive behavior scores at 4 months, but became a significant predictor over time. On average over the first three years, females demonstrated more positive gains while males dropped below the lower end of the average range. Our finding is consistent with reports that males often have poorer outcomes than females and it appears that this difference is independent of illness severity or gestational age. However, results of our study shed new light on the timing when these differences may emerge. At about 28 months to 36 months, girls experience an upswing in their adaptive behavior while boys continue to decline.

Our findings also indicate that the effect of income on adaptive behavior becomes more significant as a child ages. At about 24 months, children from families with annual incomes less than 50 thousand dollars a year dropped below the average range for adaptive behavior skill. At about 28 months, this sharp decline slowed but continued to decline. In contrast, children from families with higher income experienced a positive upswing in their trajectories at about 28 months. Aylward (2002) has also noted that the effects of income become increasing apparent between 18 and 36 months, with 24-months being an age that is cited frequently as a turning point.

Our lack of any significant findings for maternal education is consistent with most literature in the field, although some studies have reported its influence on language and motor domains (M. R. Potijk, et al., 2013; van Noort-van der Spek, et al., 2012; Wang, et al., 2014). The lack of effect for maternal education in our research could be explained by our quite highly educated sample, with over 50% of our mothers achieving at least a college education. A better distribution of educational levels would have provided more power to identify any effect.

In summary, our results show that children born prematurely have varied adaptive behavior trajectories over their first few years of life. This variation is initially influenced by their gestational age; however, the biologic risk of male sex and the social risk of poverty become significant predictors of poorer adaptive behavior outcomes as these children develop. On average, the development of adaptive behavior is increasingly worse until about 28 months of age when trajectories start to improve slightly. The timing of this upswing is consistent with improvements found for females and for the higher income group. However, the final group mean score is 86, 14 points lower than standardized norms. This finding suggests that a significant proportion of children born prematurely are not achieving adaptive behavior skills consistent with term born peers by age 3 years.

Limitations

Limitations of this study should be considered. While the Vineland Adaptive Behavior Scales have been validated for children of the age range in this study, the domains of daily living skills and social competence are not typically evaluated in children born prematurely at this age. Therefore, inclusion of an additional measure of adaptive behavior would have been useful to support findings from the Vineland Scales. Although we included predictors in our study that have been noted in previous research, other important variables may have been missing from the model, contributing to potential error variance. Lastly, our sample may not be representative of the broader population of children born prematurely.

Future Research

Further investigation is needed to understand the initial negative linear trend and slight upward gain for adaptive behavior skills in the second year of life. It may be important to consider additional predictors that vary over time, such as receipt of early intervention services designed to improve outcomes in children with developmental delays. In addition, biological markers of brain development would be important predictors to consider and could substantially influence our understanding of adaptive behavior trajectories (Back, 2014; de Kieviet, Zoetebier, et al., 2012; Dean et al., 2014; Johnston, 2009; Catherine Limperopoulos, 2010; Volpe, 2009). It may also be important to evaluate factors that influence trajectories of different domains of adaptive behavior (such as social skills or motor function).

Clinical Implications

In children born prematurely, the combination of biologic and social risk appears to have an increasingly negative influence on adaptive behavior trajectories over the first three years of life. This decline over time is not consistent with theories of developmental catch up to same age peers by ages 2 or 3 years (Pediatrics, 2013). It may be time to reconsider the practice and purpose of adjusting age level expectations. Follow-up programs use adjusted and chronological scores to monitor progress towards catch-up to term born peers; however, determination of need for services designed to assist developmental progression is often based on consideration of delays significantly below adjusted age development. This practice means that a child born prematurely has to be more delayed in development than a term born child in order to receive help. The results of this study not only challenge the longstanding theory that children born prematurely automatically and sequentially catch-up to term born peers by age 2 or 3, but they highlight the importance of addressing both biologic and social risk in the design of interventions to improve outcomes of children born prematurely.

Table 3.1

Family and Child Demographic Characteristics

Characteristic (n)	**n**	**%**
Annual Family Income (196)		
>50k	111	(57%)
<50k	85	(43%)
Maternal Education (206)		
less than College degree	84	(47%)
College or graduate degree	112	(54%)
Gender (218)		
Male	109	(50%)
Female	109	(50%)
Gestational Age in weeks (218)	(Mean=31 weeks, SD=2.99)	
23-29	72	(33%)
30-32	82	(37%)
33-36	64	(30%)
Neonatal Medical Index (218)		
Fewest medical complications	30	(14%)
Fewer medical complications	41	(9%)
Some medical complications	86	(40%)
More medical complications	24	(11%)
Many medical complications	35	(16%)

Table 3.2

Best Fitting Unconditional Model of Adaptive Behavior with Linear and Quadratic Time and Random Intercepts and Coefficients

Parameter	Estimate	Std. Error	t	Sig.	Confidence Interval	
Intercept	94.0317	.7801	120.54	.000	92.4998	95.5635
Linear Time	-4.6133	.6195	-7.45	.000	-5.8304	-3.3962
Quadratic Time	.6286	.0999	6.29	.000	.4323	.8250

Table 3.3

Effects of Sex, Gestational Age, Illness Severity, Income and Maternal Education on the Development of Adaptive Behavior in the First 3 Years

	Estimate	Std. Error	t	Sig.	Confidence Interval	
					Lower	Upper
Intercept	66.1464	7.3305	9.023	.000	51.6905	80.6022
Linear Time	-5.7631	1.0554	-5.461	.000	-7.8378	-3.6885
Quadratic Time	.8875	.2359	3.762	.000	.4236	1.3513
Male sex	-.9662	1.2042	-.802	.423	-3.3428	1.4105
Gestational Age	.9474	.2026	4.677	.000	.5479	1.3469
Illness Severity	-.0493	.4782	-.103	.918	-.9929	.8944
Family Income	2.6201	1.5501	1.689	.092	-.4348	5.6750
Maternal Education	-.1327	.4562	-.291	.771	-1.0321	.7668
Linear time x Male	1.7782	.6166	2.884	.005	.5574	2.9991
Linear time x Income	-1.7079	.62450	-2.733	.007	-2.9448	-.4710

a. Dependent Variable: Vineland Adaptive Behavior Composite chronologic age score.

Figure 3.1

Linear and Quadratic Change in Average Adaptive Behavior Composite over First 3 years

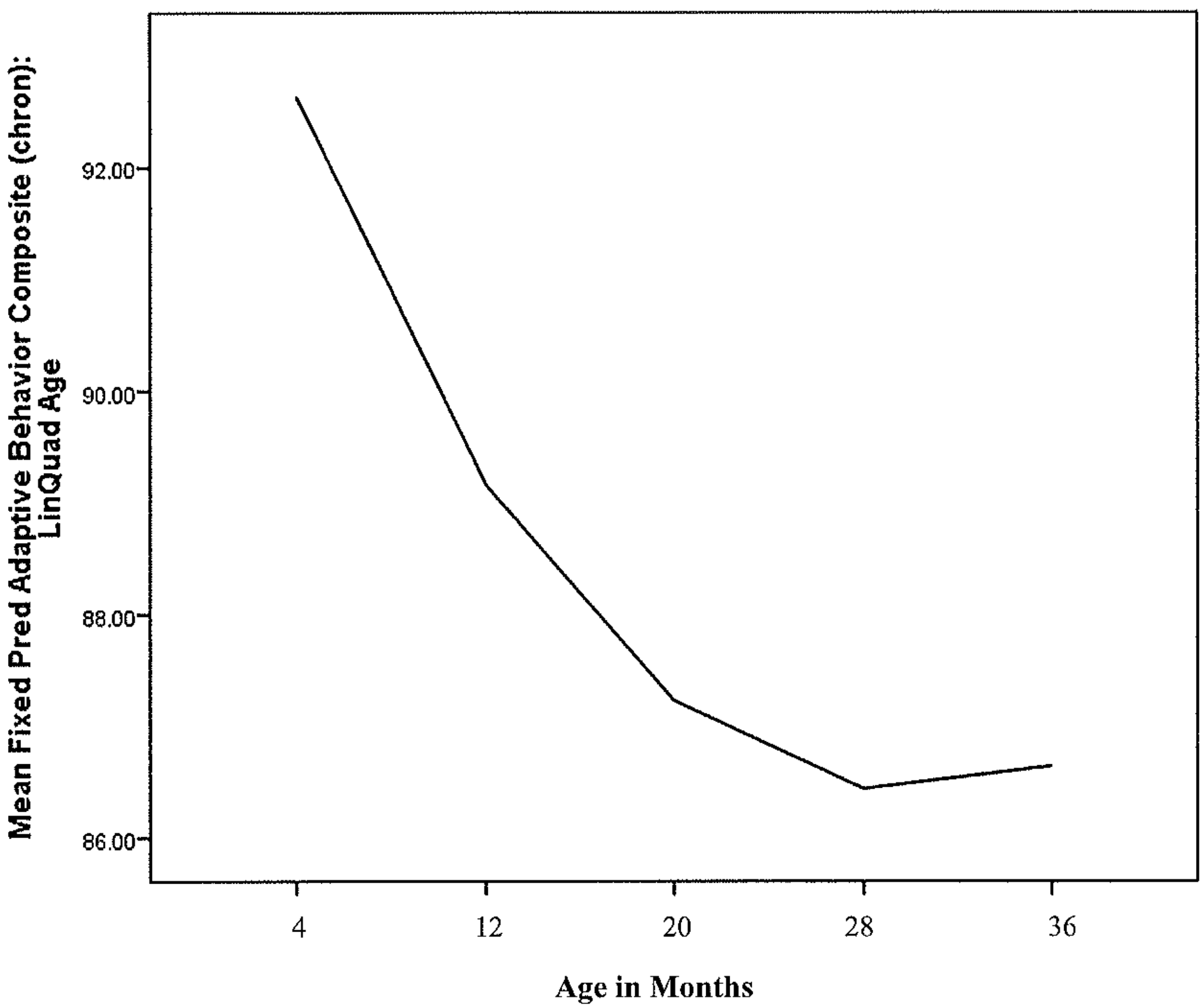


Figure 3.2

Spaghetti Plot Cohort Individual Curvilinear Adaptive Behavior Composite Trajectories over the First Three Years

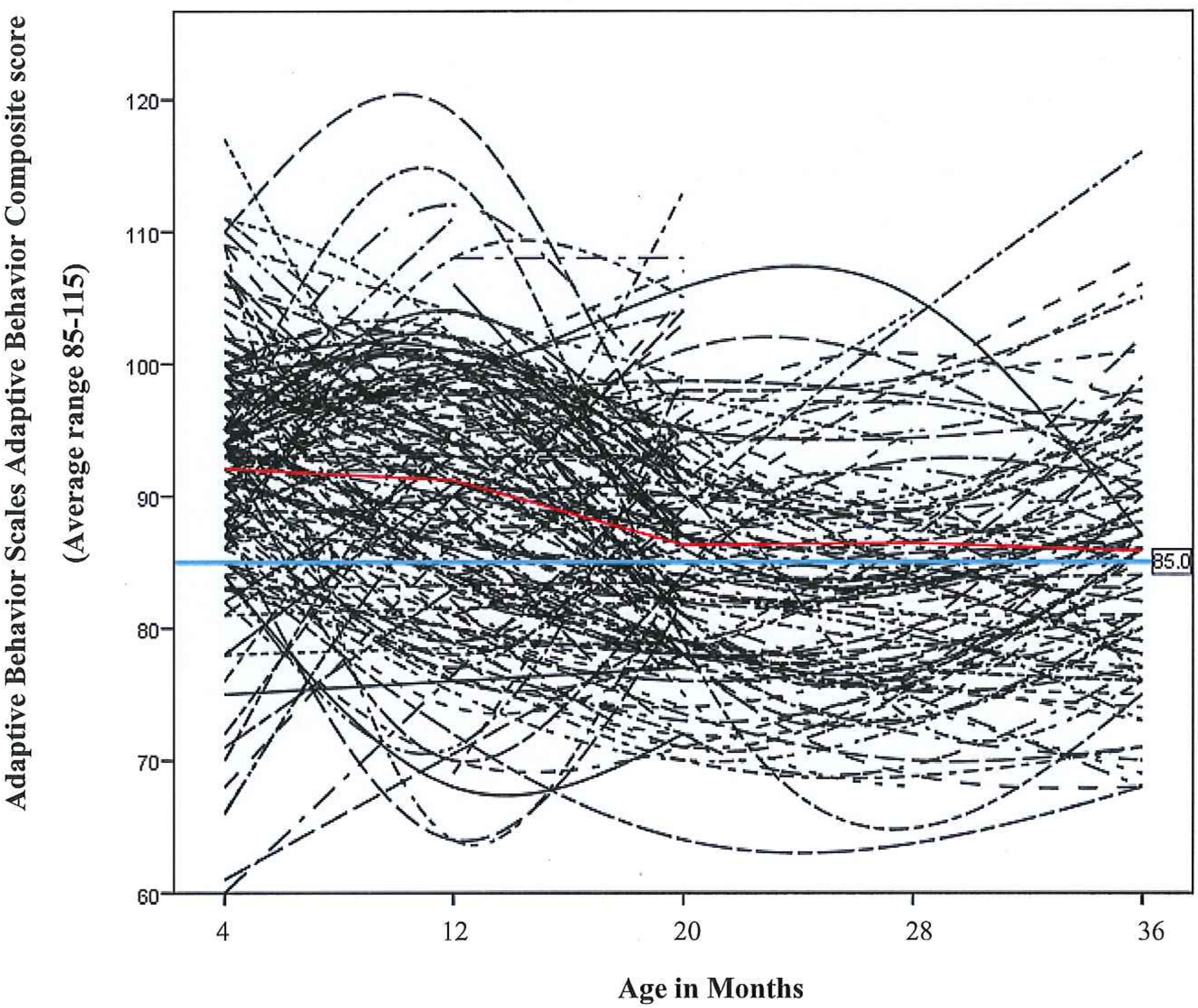


Figure 3.3

Interaction of Sex and Linear Adaptive Behavior Composite Score

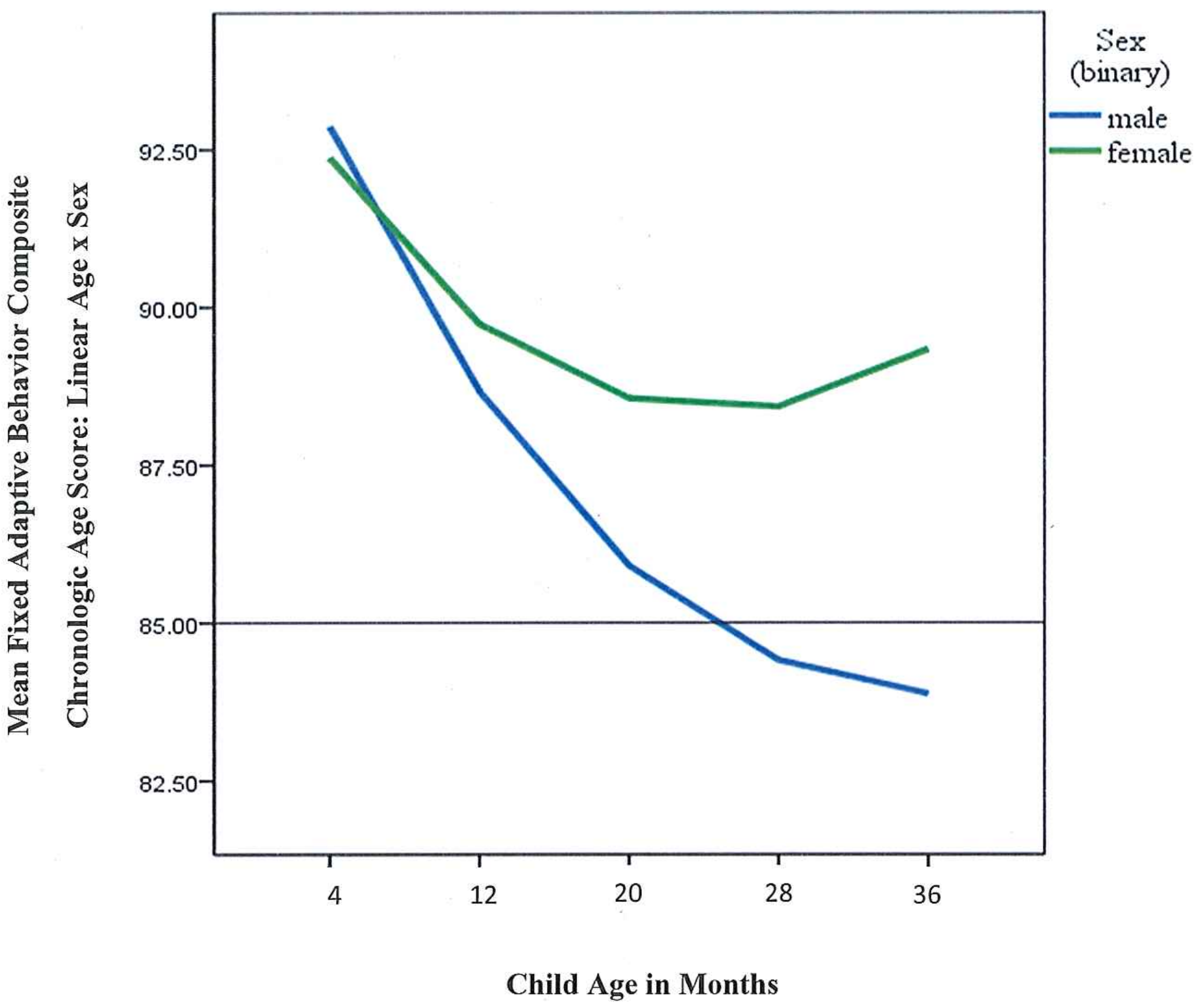
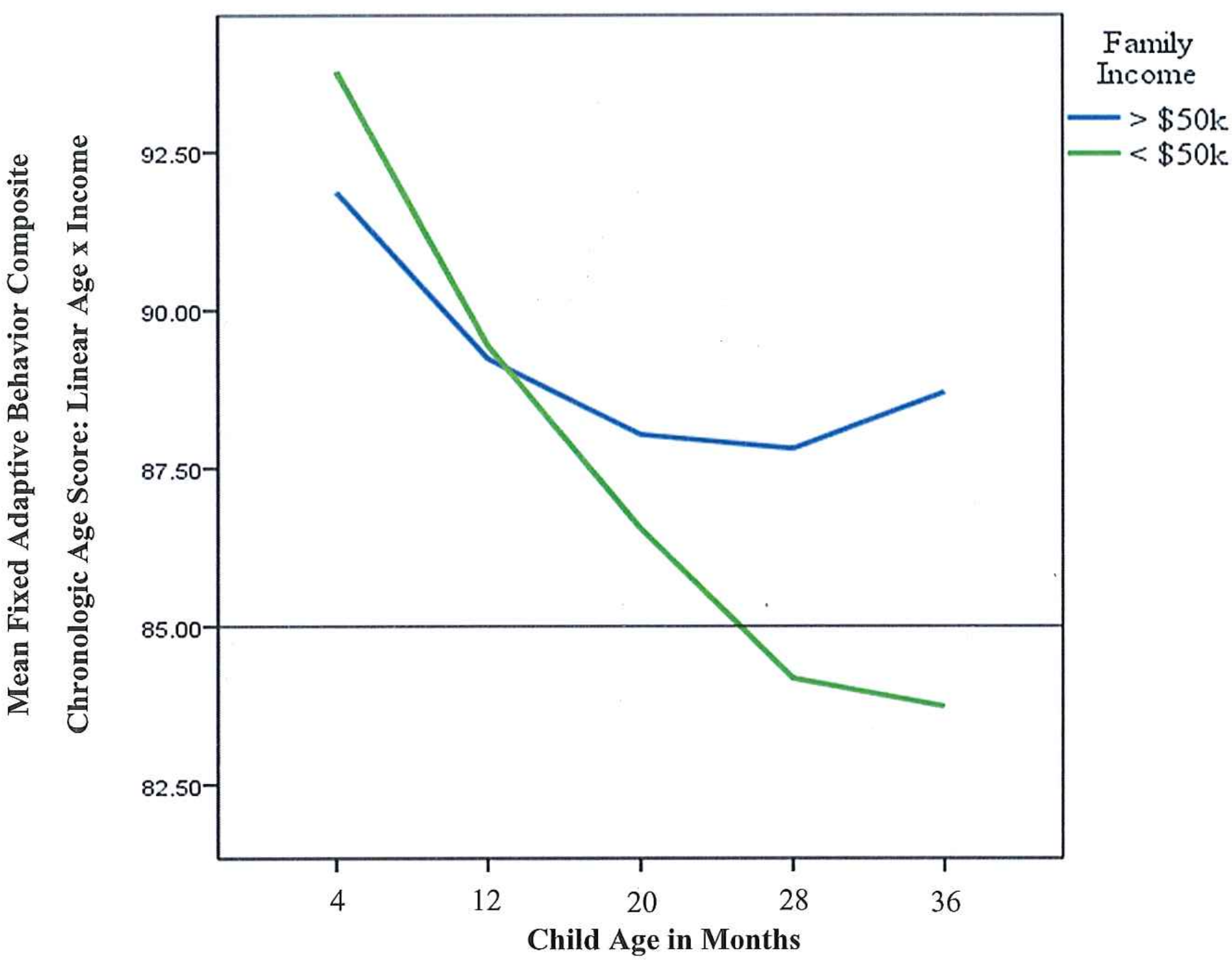


Figure 3.4

Interaction of Income and Linear Adaptive Behavior Composite Score



Four

Early Intervention Amount of Service as a Time Varying Predictor

INTRODUCTION

Research has shown that, compared to term born peers, children born prematurely have lower group mean scores on measures of intelligence, social-emotional competence, and adaptive behavior function; these differences persist from the early years through adolescence and adulthood (Hack, 2009a; T.M. Luu, et al., 2009; Saigal, et al., 2007; Sullivan, et al., 2012; Wood, et al., 2005). Early intervention (EI) services are designed to address these disparities by providing experiences that promote brain development and skill advancement. EI services may include physical, occupational or speech therapy, or education targeting specific aspects of development. The provision of EI services for children birth to 3 years of age with developmental delays or disabilities is mandated through the Individuals With Disabilities Education Act (IDEA) Part C federal legislation (Rosenberg, et al., 2013; Schakelford, 2006; C. Jason Wang, et al., 2009). However, the effectiveness of EI in children born prematurely continues to be debated in the literature (Hack, 2009a). Uncertainty regarding effectiveness has coincided with restrictions in financial investment, as federal and state budget cuts continue to impede the provision of EI services (Lazara, et al., 2014). These restrictions result in limited access and deferred entry of children into EI services. A later start decreases the amount of services a child can receive before age 3, at which point they are no longer eligible for services. However, it is unknown whether start time and amount of EI service influence outcomes of children born prematurely.

Recent research suggests that timing of interventions designed to improve development may be important. Several studies have demonstrated that interventions provided to premature infants shortly after birth are associated with better brain maturation and neuro-developmental outcomes (Effenberger et al., 2011; Ruth Feldman, Zehava Rosenthal, & Arthur I. Eidelman, 2014; Guzzetta et al., 2011; Milgrom, et al., 2010). A recent study measured the actual amount of intervention (i.e. the number of words spoken to the premature infant) and demonstrated that a greater number of words provided to infants was associated with better language and cognitive function at 18 months (Caskey & Vohr, 2013). Similarly, research has shown that a greater amount of tactile stimulation over the first 6 months of life helps to compensate for early neurosensory deficits (especially visual and motor skills) and promote neurodevelopment for preterm, low birth weight children (Weiss, Wilson & Morrison, 2004). A Cochrane Review supports such findings, indicating that early intervention provided to preterm infants in the first year of life has a positive effect on motor and cognitive outcomes at preschool age (A. Spittle, et al., 2009).

Seminal research of community-based interventions also suggests that amount of services received may improve outcomes of prematurely born children. The Infant Health and Development Project (IHDP) was conducted in the late 1980's and is referenced as the largest U.S. multicenter randomized controlled trial of EI in children born prematurely (McCormick et al., 2006). Studies from IHDP that considered the amount of intervention received showed favorable and sustainable effects of the intervention (Hill, Brooks-Gunn, & Waldfogel, 2003; Ramey & Ramey, 1992). However, most long-term studies of children born prematurely have not examined amount of EI service as a potential factor that may contribute to outcomes (Hack, 2009b; T.M. Luu, et al., 2009; Saigal et al., 2003).

One particular area where timing and amount of services may be important is the child's development of adaptive behavior skills. Adaptive behavior measures are used to assess overall function in children with neurosensory impairment, and include functional developmental domains such as communication, social skills, ability to manage activities of daily life, and motor development (Rosenblum, Saigal, Szatman, & Hoult, 1995; Scattone, Raggio, & May 2011).

To our knowledge, there have been no studies describing the amount and timing of EI services being provided to children born prematurely by community delivery systems over the child's first few years of life. Additionally, it is unknown whether early access (younger age receipt of EI) or amount of EI service provision in the community improves adaptive behavior outcomes in children born prematurely. Our study attempted to address these gaps in the field through two primary aims: 1) to describe the amount and timing of EI services received by children born prematurely over their first 3 years of life, and 2) to determine whether the amount and timing of early intervention service hours received by children born prematurely are associated with change in their adaptive behavior skills over the first three years of life

PATIENTS AND METHODS

Sample

This cohort study followed 216 children born between 2000 and 2006. Inclusion criteria for this convenience sample of infants were low birth weight (< 2500 grams), prematurity (< 37 weeks gestation), and at least 1 of the California Children's Services (CCS) criteria for risk of later neurodevelopmental complications (e.g. prolonged perinatal hypoxemia, seizures, intracranial abnormality). Exclusion criteria included all other infants that did not meet criteria above and were not living in San Mateo County. If families consented and moved out of county during the study, they were no longer eligible.

Procedure

The study was approved by the Institutional Review Boards of Stanford University and the University of California, San Francisco. Letters were sent to hospital intensive care nurseries in San Mateo County inviting them to refer infants who met the inclusion criteria. Parents of babies who met the inclusion criteria were approached by the study coordinator for consent to participate in the study. Consents were in English and Spanish and all meetings with families who spoke a language other than English were conducted with an interpreter. Demographic data was collected at entry to the study. Data on adaptive behavior was collected at 4 assessment points: baseline infancy (4-5 months adjusted age), late infancy (12 - 13 months adjusted age), toddler (18 - 22.5 months adjusted age), and preschool (32 - 35 months chronological age). Chronological age was used to calculate scores for adaptive behavior at each assessment point. Most data was collected during visits to the High Risk Infant Follow-up Clinic. Some data were collected by telephone interview.

For the purposes of this study, early intervention was defined as therapeutic services specifically provided to address risk for or actual delays in development and adaptive behavior. The EI data collected is representative of both public and private EI services received by children born prematurely in their communities. In California, two entities provide public EI services: California Children's Services (CCS) Medical Therapy Program (MTP) and the California Early Start Program (ESP). CCS MTP is a Title V program and provides physical and occupational therapy (PT/OT) for children with chronic neuromuscular diagnosis, or for children under age 3 with early signs of cerebral palsy (California, 2014). ESP is mandated by federal legislation under the Individual with Disabilities Education Act-Part C (IDEA-Part C) to provide EI services for children birth to 3 (Services, 2014). ESP EI and CCS MTP are considered public programs because they are government funded and access is not restricted by financial eligibility. Additionally, because they are regulated and have experienced pediatric providers, they are the primary source for referrals if children meet medical and developmental eligibility criteria.

Referrals for EI services were made either at hospital discharge or in the follow-up clinic. Referrals were made to the ESP upon hospital discharge if infants had two medical risk factors for developmental disability (e.g. brain hemorrhage and prematurity less than 32 weeks gestation). This ESP eligibility category is referred to as "at risk". ESP services provided to infants at risk generally included developmental monitoring and teaching about activities designed to promote development. Referrals to ESP were made in the follow-up clinic if children appeared eligible by categories of "developmental delay" (i.e., percentage of delay compared to norms) or "established risk" (e.g., Down syndrome, cerebral palsy). When ESP confirmed child eligibility, ESP would refer the child to a community program that provided EI services; community programs provided EI services through EI professionals, including physical or occupational therapists, speech pathologists, vision specialists, teachers or nurses trained in early childhood development; services were delivered in the home or community center. In the event that children demonstrated delays in development, but did not appear eligible for public CCS MTP or ESP services, direct referrals, using medical insurance, were made for private therapies (physical, occupational and speech/language).

Community programs participating in the study signed a contract in which they agreed to collect data about all services provided to children enrolled in the study. EI professionals completed a quarterly data sheet quantifying hours of services provided to each child. Every three months, EI professionals submitted EI service data (details below) to research project staff.

Measures

Descriptive data regarding gestational age, birth weight, gender, and neonatal illness severity was acquired through review of the medical record. Descriptive data on maternal education and income was collected at the time of consent or at the baseline (i.e., early infancy) assessment point.

Early Intervention. The quarterly data sheets of EI services were labeled by season and year and included the dates for 3 months of weekly slots. Early Intervention data included referral and re-referral dates, service start and discontinuation dates, agency and professionals providing services, and weekly number of hours of service provided per child. Case management and public health prevention program service hours were not considered specific interventions targeting developmental and adaptive behavior delay, and, therefore, were not included in this study. To examine service provision by types of early intervention services, we grouped services in alignment with the EI service delivery system in California: 1) Community Programs provided for children meeting ESP eligibility criteria in an eligibility category other than "at risk", 2) Motor Therapies (PT/OT) targeting abnormal neurological exams or motor delays and provided by public or private funding sources, 3) "At risk" eligible ESP services.

The EI score for each child consisted of the number of hours of EI received during four service periods (i.e., time between assessment points). Scores were developed for total number of hours received for each service period: 1) hospital discharge to early infancy (period 1), 2) early infancy to late infancy (period 2), 3) late infancy to toddler (period 3), and 4) toddler to preschool (period 4). These 4 scores served as a time varying predictor of the amount of EI hours received over time for each child.

Adaptive Behavior. The Vineland Adaptive Behavior Scales (VABS) were used to measure adaptive behavior. The VABS is a norm-referenced instrument designed to assess the developmental and social proficiency of children in the context of their environment. It consists of 297 interview items that are responded to by a parent or primary caretaker. The instrument measures adaptive behavior in several dimensions relevant to children's function (communication, daily living skills, socialization and motor domains) and provides an overall Adaptive Behavior Composite (ABC) score that can be compared to normative population values (Cho, et al., 2010; S. Sparrow, et al., 1989); the ABC score was selected for use in this study. The mean normative ABC score is 100 with an average range of 85 to 115. A score of 85 is considered the cut off for achieving normative expectations at each specific development level. At each data collection time point, a structured interview with the primary caretaker was conducted by a clinical psychologist or nurse practitioner trained to administer the VABS. The interview typically took around 30 to 45 minutes to conduct.

There is evidence for concurrent and predictive validity of the VABS in children born prematurely (C. Limperopoulos, et al., 2006; Rosenbaum, et al., 1995; Weiss, et al., 2001). The reliability of the VABS is also well established with coefficient alphas greater than .80 for the Adaptive Behavior Composite for all age ranges under 3 years and with test-retest reliability coefficients of .78-.93 (S. Sparrow, et al., 1989). Equivalence reliability with telephone administration has also been established (C. Limperopoulos, et al., 2006). While the initial psychometric properties of the Vineland were established many years ago, it remains one of the standard tools of assessment used today (Gleason & Coster, 2012; Scattone, et al., 2011).

Data Analysis

To address Aim 5, descriptive statistics were employed to describe the amount and timing of early intervention services. Multilevel modeling (MLM) was used to examine Aim 6 - to determine whether the amount and timing of early intervention service hours received by children born prematurely are associated with change in their adaptive behavior skills over the first three years of life. The multilevel analysis involved several models to estimate the following: 1) the change in adaptive behavior scores of children as they aged (i.e. over time), 2) the association between adaptive behavior and the amount of EI services received by different children after Late Infancy (between-child effects), 3) the association between average amount of EI hours received over time and adaptive behavior scores (the main effect of EI hours), and 4) whether the association between adaptive behavior and time-varying EI hours changed over time (the interaction between changes in EI hours and changes in adaptive behavior over time). When looking at the main effect or average association between adaptive behavior and EI as a time-varying predictor, the estimated relationship remains constant across time. Creating an interaction term between time (age) and the time-varying predictor allows for understanding specific predictor effects at specific time points (Singer & Willet, 2003). The between-child analysis was grand mean centered at late infancy. Centering for the within-child analysis was based upon average EI hours for each child over the 3 years. Multilevel estimation in SPSS uses full maximum likelihood, contributing to unbiased estimates and accounting for missing data. The aims were analyzed using SPSS version 21.

RESULTS

The convenience sample was made up largely of infants born at Lucile Packard Children's Hospital Stanford. Table 4.1 presents key data about the overall sample (n=218). The mean gestational age at birth was 31 weeks (± 2.99). The range of gestational ages at birth was 23 weeks to 36 weeks, and 70% of the sample was less than 33 weeks gestation at birth. The average maternal age at delivery was 31 years (± 6.6), with a range from 16 to 48 years. 47% of mothers had not attained a college degree. 42% of mothers self-identified as Caucasian, 34% Hispanic, and 28% as other. 42% of subjects were covered by government-sponsored insurance. 43% of families had an annual income of less than 50,000. 89% of the infants had two parents involved in their lives at the time of enrollment. Medical record data indicated that the majority of infants had experienced some medical complications. However, severity of illness had a fairly even distribution across the sample.

Tables 4.2 through 4.4 present findings related to Aim 1. Table 4.2 shows mean ABC scores at each assessment point for children who received any services and those who received no EI services. Children who did not receive EI services had a slightly higher group mean ABC score than children who received services at the Early Infancy assessment point. By the end of the study, scores for children in both groups had declined and were quite similar.

The range and mean hours of early intervention received by children during each service period are shown in Table 4.3. In general, the total hours of service delivered to all children receiving EI services during each service period increases over time, while the number of children receiving services declines after the Late Infancy assessment point. The average number of EI hours received per child increases over time from 4 hours per child during Period 1 (NICU Discharge → Early Infancy assessment) to 59 hours per child during Period 4 (Toddler assessment → Preschool assessment). The range in hours of EI services received by children also increases after the Early Infancy assessment point.

Early Intervention services provided by different service groups are shown in Table 4.4. Some children received services from more than one group at a time. The largest number of children (n=136) received Public ESP services by At Risk Eligibility; on average, they received the fewest total hours of service (5 hours/child). The smallest number of children (n=36) received public and private Motor Therapy services; on average, they received an intermediate number of hours of service (61 hours/child). Eighty-four children received Community EI; on average, they received the most total hours of service (106 hours/child).

Table 4.5 presents findings related to Aim 2. The main effect of age is significant and negative, indicating that, on average, ABC scores declined over the first 3 years of life. The estimate for amount of EI hours that a child received after late infancy (between-child effects) was also significant and negative, suggesting that receipt of more EI hours by children was associated with lower ABC scores over the first 3 years of life. Similarly, the average number of EI hours received by children from birth to 3 years (within-child effects) was associated with lower adaptive behavior scores. However, when looking at the interaction between changing amounts of EI services provided over time and the change in adaptive behavior over time, there was a significant positive effect of EI on adaptive behavior ($t = 2.16$, $p<.031$). The estimate for this interaction term in Table 4.5 indicates that every additional hour of EI service resulted in a small positive change in adaptive behavior for children. Figure 4.1 shows this small improvement (the difference between the red and blue lines) in the trajectory. The blue line indicates the relationship of average EI over time to adaptive behavior scores over time while the red line indicates the association between changing EI hours over time and the change in adaptive behavior over time (estimate for the interaction).

DISCUSSION

Amount and Timing of Early Intervention Services

Results related to Aim 1 indicate that about half of the children born prematurely did not receive any EI services. This finding supports recent studies that suggest the lack of access to early intervention services is a nationwide issue (Rosenberg, et al., 2013). For children who did receive EI services, the largest proportion (136 of 216) received At Risk services, which comprised few service hours. At the time the study was conducted, California was one of a handful of states that provided Part C services for infants At Risk (Services, 2014). This may explain why our findings contrast with previous reports of fewer numbers of children receiving services in the first two years (S.R. Hintz, et al., 2008; C. Jason Wang, et al., 2009). Recent studies (S.R. Hintz, et al., 2008; Schakelford, 2006; C. Jason Wang, et al., 2009) indicate that more children begin to receive EI service after the Toddler period. Although only 4 % of the California pediatric population receives ESP between age two and three years, the number served is 57% of the total number served for all three years (Foundation, 2014; OSEP, 2013). In contrast, only 12% of the total number served is receiving services in the first year (Foundation, 2014; OSEP, 2013). The clinical practice of using adjusted age scores (higher scores) to determine the need for referral to EI or the eligibility for public EI services may explain this low rate of EI service receipt.

The overall limited amount of EI service hours received is another important finding. On average children received less than 3 total service hours a month in the first year of life. Between the Toddler and Preschool periods, the average amount of service hours received increased to about 6 hours a month. A few children received about 25 hours a month while some children received only one total hour between assessment periods. The progression of the total number of service hours is included to provide a virtual estimate for the total cost of services (or investment) provided to the children in our study. The cost of EI services provided appears disproportional to the usual initial investment in intensive care.

Effects of Amount and Timing of EI Services on Change in Adaptive Behavior Skills

With regard to Aim 2, our data indicate that the more hours of EI services a child receives after the first year of life, the lower are the child's adaptive behavior scores over time. This finding was unexpected. One interpretation of these findings is that EI services are detrimental to the child's development of adaptive behavior. Clearly, this would be an unwarranted conclusion. Alternatively, results suggest that the most delayed and vulnerable children are receiving the greatest number of services. In addition, the low dosage of services received may not be enough to shift the trajectory in a positive direction. When looking at the association of average EI hours from birth to 3 years to adaptive behavior scores over time, results also show that a greater number of EI hours continued to be associated with worse adaptive behavior. It is likely that more EI services were planned for children who showed lower levels of function. However, the amount of services provided were not adequate to fully turn around a child's trajectory of poor adaptive behavior. Unfortunately, the data did not allow us to examine the effect of EI service hours on children born prematurely whose delays were not "delayed enough" to have been referred for EI services. It is also possible that we examined the effects of EI in too global a manner to capture its impact. For instance, physical therapy may have had a strong impact on motor skills but we did not look at these more specific relationships.

Importantly, however, the interaction analysis showed a small positive improvement in adaptive behavior over time that was related to amount of intervention hours received.

Additional hours of intervention over time appeared to slow the decline in adaptive behavior skills. This finding may indicate the importance of continued EI for preterm children. The number of EI hours received by each child was substantially greater during the toddler to preschool period of development. For those children who were fortunate enough to continue receiving services over time, the increased dose of EI they received may have been especially meaningful. In sum, although children born prematurely begin life with innate delays in developmental skills compared to their term born peers, our results indicate that most children do not receive intervention services early enough or of adequate amount to help them catch-up.

Limitations of the Study

The use of real service delivery data poses several challenges. Because of funding restrictions, families that moved out of the county were no longer eligible for the study and were lost to follow up. Most of the children in our sample did not receive high dosage EI services in the first year of life. As a result, we were not able to fully examine the effect of early intensive EI on adaptive behavior. The receipt of EI services is dependent on several factors including insurance authorization for private therapies, transportation services, occupations that allow families to participate in EI during the work week, and professional agreement regarding level of delay. While the statistical methodology accounts for missing data, there were a few children who received EI services from professionals outside the study; there were no controls for this potential confound. In addition, the study did not account for receipt of developmental interventions in the NICU (e.g. skin to skin holding) which has been demonstrated to improve neurodevelopmental outcomes in children born prematurely. We also did not account for the amount of time parents spent reinforcing EI activities when EI professionals were not present.

Future Research Implications

Findings of this study emphasize the need for further research to examine the impact of high dose intervention on adaptive behavior. Future research is also needed to determine whether receipt of high dosage early interventions beginning after birth and continuing through the first 3 years of life can prevent decline in adaptive behavior and enable children born prematurely to achieve norms consistent with term born peers. Lastly, implementation of EI services varies widely. The effects of EI services by professional, setting and curriculum need to be examined. For instance, services provided by a developmental teacher versus an occupational therapist may have uniquely different effects on adaptive behavior over time. Similarly, different components of adaptive behavior should be examined to see if motor skills, social skills or other aspects of adaptive behavior are influenced by EI in different ways.

CONCLUSION

We have described the amount of EI received by a cohort of preterm children and the influence of this intervention on changes in their adaptive behavior trajectories over the first 3 years of life. Although recent studies have documented the efficacy of EI provided in the first year of life, results of our study suggest that the amount of EI children are receiving is inadequate to counteract their increasing deficits in adaptive behavior skills. However, results suggest that a greater amount of EI services may positively influence a child's individual adaptive behavior trajectory. Overall, results indicate the need for a renewed investment in the early provision of EI services for children born prematurely and appropriate research designs to evaluate individual and group effects over time.

Table 4.1

Family and Child Demographic Characteristics

Characteristic (n)	n	%
Annual Family Income (196)		
>50k	111	(57%)
<50k	85	(43%)
Insurance (206)		
MediCal/Medicaid	87	(42%)
Private	119	(58%)
Maternal Education (206)		
less than HS degree	38	(18%)
HS degree	25	(18%)
Partial college	21	(11%)
College degree	64	(30%)
Graduate degree	48	(24%)
Maternal Race/Ethnicity (218)		
Caucasian	92	(42%)
Hispanic	73	(34%)
African American	12	(5%)
Asian Pacific Islander	25	(11%)
Other	16	(8%)
Family Parent Involvement (218)		
2 Parent	194	(89%)
1 Parent	17	(8%)
Foster Care	6	(3%)
Gender (218)		
Male	109	(50%)
Female	109	(50%)
Gestational Age, in weeks (218)	(Mean=31, SD=2.99)	
23-29	72	(33%)
30-32	82	(37%)
33-36	64	(30%)
Neonatal Medical Index (216)		
Fewest medical complications	30	(14%)
Fewer medical complications	41	(9%)
Some medical complications	86	(40%)
More medical complications	24	(11%)
Many medical complications	35	(16%)

Table 4.2

Mean Adaptive Behavior Scores for Children Born Prematurely Who Did and Did Not Receive Early Intervention Service

	Early Infancy Mean (S.D.) (total n=196)*	**Late Infancy Mean (S.D.)** (total n=154)*	**Toddler Mean (S.D.)** (total n=162)*	**Preschool Mean (S.D.)** (total n=101)*
EI	91 (16.24)	88 (10.08)	85 (10.16)	87 (9.48)
% of n	(44%)	(49%)	(51%)	(46%)
No EI	94 (9.17)	94 (8.64)	88 (7.76)	85 (9.68)
% of n	(56%)	(51%)	(49%)	(54%)

*Sample size differences are due to missed assessment visits or loss of eligibility for services.

Table 4.3

Mean and Range of Early Intervention Service Hours Received by Children by Service Period

	Period 1 NICU discharge to Early Infancy	Period 2 Early Infancy to Late Infancy	Period 3 Late Infancy to Toddler	Period 4 Toddler to Preschool
Number of children to whom EI services were delivered	87	96	77	77
Total hours of EI service delivered to all children	358	2048	2315	4502
Mean hours of EI service received	4	21	30	59
Range of EI service hours	1-20	1-143	1-132	1-253

Table 4.4

Early Intervention Provided by Different Service Types

N=218	Distribution	Length of Open Case (in months)	Service Amount (in hours)
Service Type	Number of Children*	Average Number of Months Between Case Open and Case Close	Average Number of Service Hours Per Child
IDEA Part C other EI	84	18	106
Motor Therapies (CCS & private)	36	27	61
IDEA Part C 'At Risk'	136	19	5

*Children may have been enrolled in more than one service

Table 4. 5

Effect of Early Intervention (EI) Hours on Adaptive Behavior Over Time

	Estimate	t	p	95% Confidence Interval	
Intercept	90.1672	187.76	<.001	89.2204	91.1139
Age of child	-1.5160	-4.81	<.001	-2.1395	-.8925
EI hours between-child	-.1059	-4.72	<.001	-.1501	-.0616
EI hours within-child	-.0667	-2.76	.006	-.1141	-.0193
Age x Changing EI hours across time	.0219	2.16	.031	.0020	.0418

Figure 4.1

Linear-Quadratic Change in Average Adaptive Behavior Composite over First 3 years

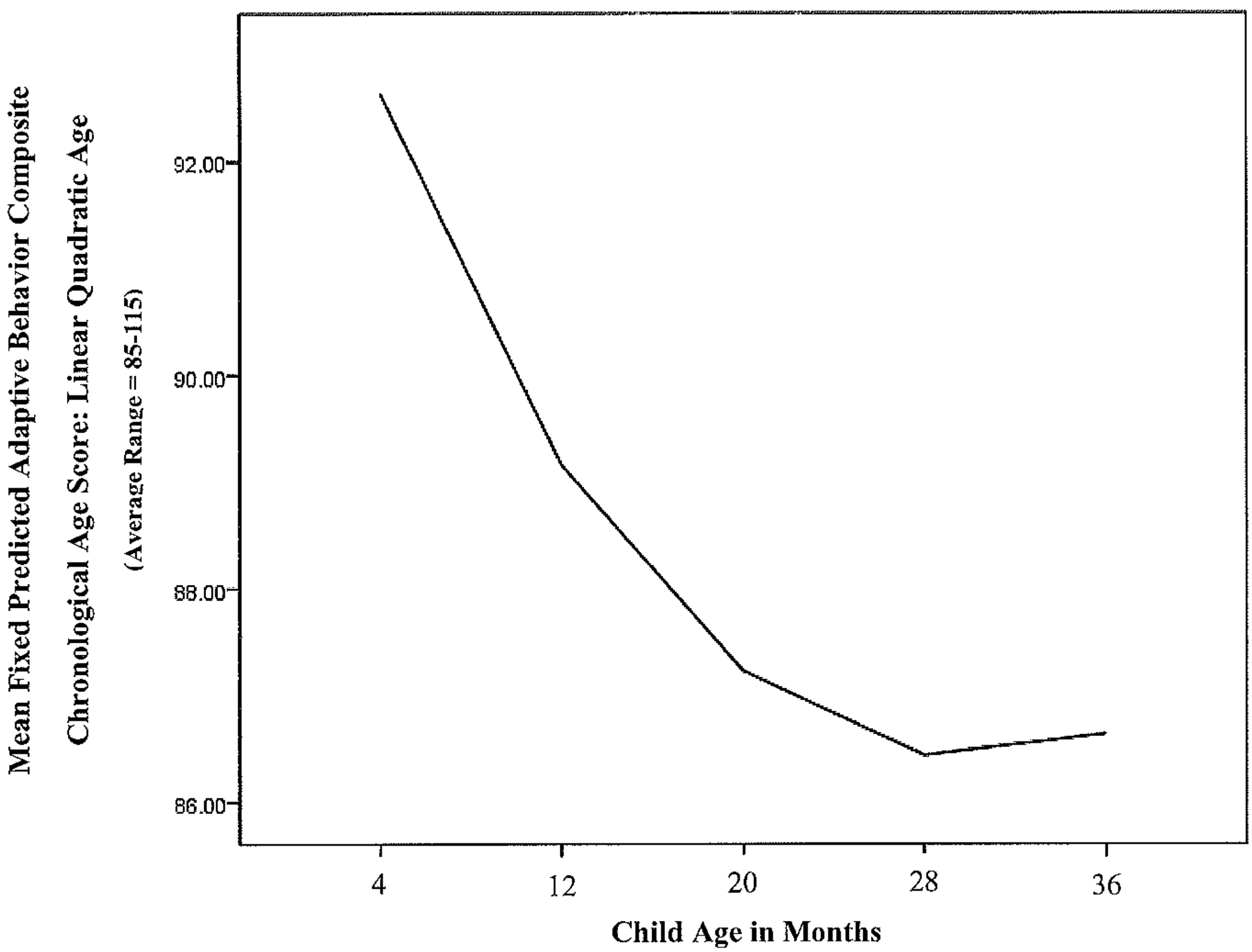
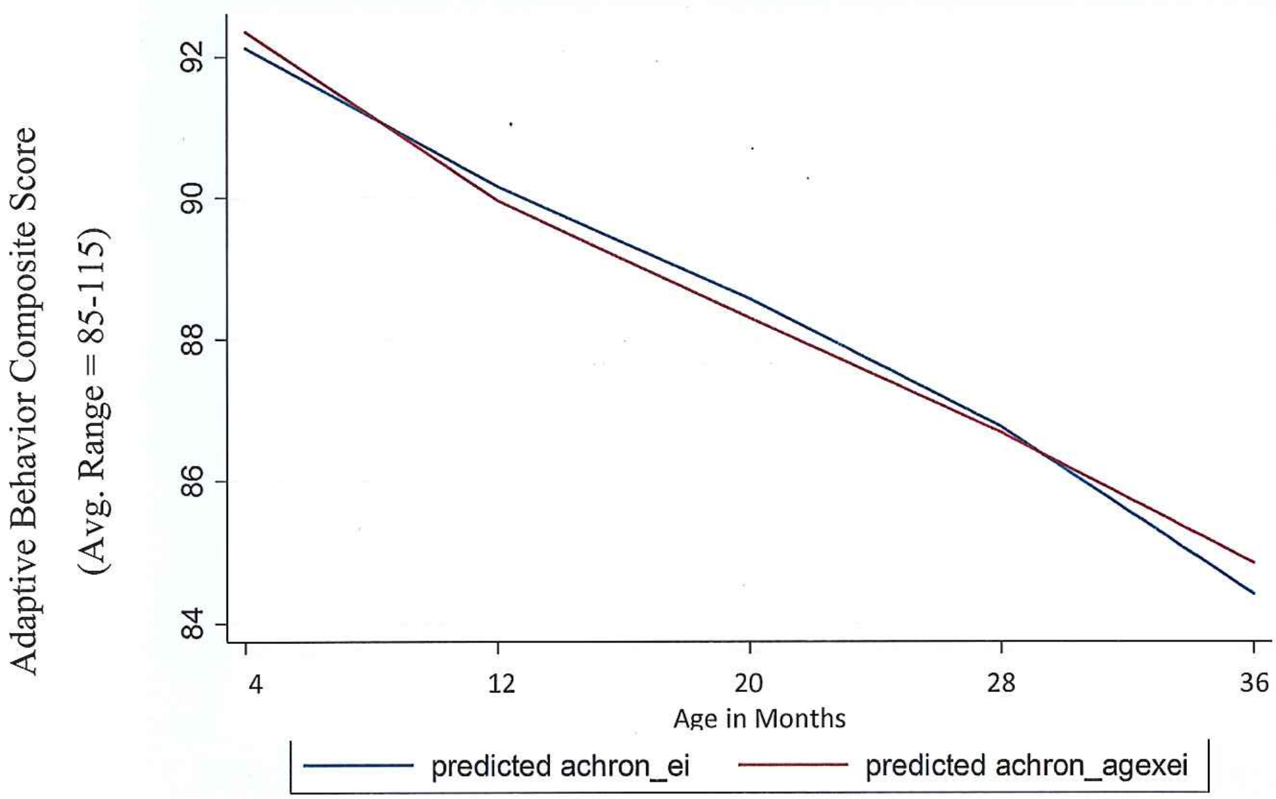


Figure 4.2

Effect of Amount of Early Intervention Service Hours on Adaptive Behavior over Time When Estimating Average Within-Child EI Changes Versus Time-Varying EI Changes



Five

General Discussion

This dissertation has examined adaptive behavior trajectories across the first three years of life for children born prematurely as well as various risk and protective factors that may influence these trajectories. The introductory chapter presented the contributions of past studies and a theoretical framework that clarifies the importance of neuroplasticity to adaptive behavior outcomes and informs an understanding of how various experiential and contextual factors can influence adaptive behavior of children born prematurely. The scientific literature and theoretical framework led to the formulation of the research aims of this dissertation. Additionally, information was provided about the significance of these aims and the innovation of the study. Chapter 2 described the proportion of children who scored in the expected normative range in late infancy, as toddlers, and in preschool and evaluated the likelihood of preterm children achieving adaptive behavior scores in the normative range over the first three years of life (Aims 1 and 2). Chapter 3 examined the degree of variability among children born prematurely in their adaptive behavior trajectories and whether gestational age, illness severity, sex, family income and maternal education influence these trajectories in the first three years (Aims 3 and 4). Chapter 4 described the amount and timing of early intervention services received by children born prematurely and whether amount and timing of service hours are associated with change in adaptive behavior of the children over the first 3 years of life (Aims 5 and 6). In this chapter, key findings for each aim will be synthesized, along with their relevance to clinical practice. Additionally, the study's limitations and implications for future research are discussed.

Aims 1 & 2

Aim 1: To describe the proportion of children who scored in the expected normative range in late infancy, as toddlers, and in preschool. Findings show that 43% of children born prematurely did not achieve scores in the normative range by toddler or preschool periods. The group mean was lower at the Toddler period than in Early Infancy. Additionally, the group mean score for the preschool period was only one point above the lower end of the average range, suggesting a large proportion of children scored below the average range. The results suggest that developmental catch-up is not an automatic sequential process that should be expected. However, the range in scores was wide from Infancy through Toddler assessment periods, suggesting variation in children's achievement.

Aim 2 was to evaluate the likelihood of preterm children achieving adaptive behavior scores in the normative range by Toddler and Preschool periods. Findings indicate that the probability of achieving scores in the normative range declined over time. However, there was a slight improvement that occurred in their likelihood of achieving normative adaptive behavior from about 24 to 36 months. These findings suggest that the period between toddler and preschool may be a window of opportunity for supporting and increasing children's adaptive behavior skills. Data also indicate that each week of gestation in utero increased the odds of achieving adaptive behavior scores in the average range. Results are consistent with other outcome studies of children born prematurely, suggesting that many children do not catch up to their term born peers as is assumed in clinical practice.

Aims 3 & 4

Aim 3 was to describe the degree of variability among children born prematurely in their adaptive behavior trajectories over the first 3 years of life. Data showed a large variation in individual trajectories of adaptive behavior, there were children with sharp increases or decreases in scores. The majority of trajectories clustered in the lower end of the average range for adaptive behavior. On average, the ABC score initially declined but showed a slight increase around 28 months. The proportion of variance in the multi-level model that was due to differences between children was 22 percent.

Aim 4 was to examine the influence of gestational age, illness severity, gender, family income or maternal education on variation in adaptive behavior trajectories of children born prematurely. As indicated earlier, findings supported the influence of gestational age as a significant biologic predictor of change in trajectories of adaptive behavior over the first three years of life. Younger gestational age was associated with worse adaptive behavior outcomes over time; this effect applied across time and did not have a particular impact at any specific time period in the adaptive behavior trajectory. The infant's sex, another biologic predictor, became significant over time. Results show that beginning in the first year of life, the gap gradually began to widen between boys and girls in their adaptive behavior development. On average, girls stayed within the normative range for adaptive behavior skills across the developmental trajectory. However, by the time children became toddlers, boys had declined substantially in adaptive behavior and were below expected norms for adaptive behavior between 28 and 36 months of life. A similar pattern of change over time was found for family income. At 12 months of age, children whose families had incomes above and below $50,000 per year showed no differences in adaptive behavior skills. However, after that time, income difference emerged and increased over time. By the toddler period, average scores indicate that children whose families had annual incomes below $50,000 were not achieving normative expectations for adaptive behavior while those above $50,000 were meeting normative standards and actually improving in their adaptive behavior skills. Overall, the gap was widest between income groups at 36 months, suggesting that the influence of poverty became more significant for children as they aged. Neither severity of the child's illness as a neonate nor maternal education showed any impact on the child's achieving normative expectations for adaptive behavior over time.

Aim 5 & 6

Aim 5 was to describe the amount and timing of early intervention (EI) services received by children born prematurely from hospital discharge through age 3 years. Results show that roughly half the sample did not receive any EI services. The number of children who received EI services declined from Late Infancy to the Preschool period, while the average EI hours received increased over time. Thus, the number of EI hours for children receiving services during the toddler and preschool periods was substantially greater than during earlier development. The largest proportion of children received services through IDEA Part C- At Risk eligibility; however, children eligible by At Risk criteria received on average only 5 total service hours.

Aim 6 was to determine whether amount and timing of early intervention service hours received by children born prematurely were associated with change in their adaptive behavior skills over the first three years of life. Initial descriptive data indicated that the average adaptive behavior skills of children who did not receive EI services were higher during infancy than the adaptive behavior skills evidenced for children who did receive services. This difference was most likely related to the lower degree of assessed delay or risk present among children who did not receive EI services. However, these group mean differences were less during the toddler and preschool periods. Results of multi-level modeling indicated that the more hours of EI services a child received during the first year of life, the lower the child's adaptive behavior scores over time. These results suggest that the most delayed and vulnerable children were receiving the greatest number of services. However, the amount of services provided did not appear to be enough to fully turn around a child's trajectory of poor adaptive behavior. There was, however, a small upward trend in adaptive behavior that was related to amount of intervention during the toddler to preschool period. For children who continued to receive services during this period, additional hours of intervention they received appeared to slow their decline in adaptive behavior skills to a small extent. This finding may indicate the importance of continued EI for preterm children during the 3rd year of life. In addition, for those children who were fortunate enough to continue receiving services from 28 to 36 months of age, the increased dose of EI they received may have been especially meaningful. In sum, although children born prematurely begin life with innate delays in developmental skills compared to their term born peers, our results indicate that most children do not receive intervention services early enough or of adequate intensity to help them catch-up.

Implications for Clinical Practice

As introduced in the theory section of the first chapter of this dissertation, neuroplasticity is influenced by a complex interplay of contextual factors and experiences (Cicchetti & Cohen, 2006). Consistent with this theory, our findings suggest a reevaluation of the practice of predicting that children born prematurely catch up by age two or even three years. Even qualified reassurance for infants who do not appear to have brain injury should be cautioned; research studies using more powerful MRI magnets have detected brain injury that is not identifiable on MRI machines available in most hospitals (Back, 2014). Although our data suggests that the likelihood of achieving ABC scores in the normative range declines over the first 24 months of life and then increases slightly, exact individual outcomes of children born prematurely cannot currently be predicted.

A large percentage of children born prematurely do not achieve scores in the average range by the Preschool period. This finding suggests the clinical practice of using adjusted age scores should be reconsidered. Age level expectations are adjusted for children born prematurely by subtracting the number of weeks born before 40 weeks gestation to create an age adjustment consistent with expectations of a younger child. Many follow-up clinicians use adjusted age scores until age 2 or 3 to monitor progress and assess need for intervention. Our findings are consistent with the literature that highlights the lack of scientific evidence to support this practice (Aylward, 2002; D'Agostino, 2010; S. L. Wilson & M. M. Cradock, 2004). Close follow-up of skill progression is impeded by the assumption that achieving adaptive behavior skills for adjusted age ensures that a premature infant will continue to progress and automatically catch-up. Often, managed care practices will not authorize insurance coverage for future follow-up assessments for high risk premature infants if they are found to be functioning at a level consistent with their adjusted age at the Early Infancy assessment period. Our study used chronologic age scores to evaluate change in true age scores. If we adjusted age expectations in the sample, the scores would look even better at the first visit, thereby augmenting the decline between the first assessment and the lower unadjusted preschool assessment. Age adjustment may hide true early delays and lead to overconfidence in the child's skill progression.

Adjusted age scores are also frequently used to determine access to, or need for, early intervention services (Schakelford, 2006). This practice requires that children born prematurely need to be more delayed than term born peers. The term "adjusted" or "corrected age" is not included in IDEA Part-C federal regulations guiding the determination of percent delay needed to qualify for EI services. In accordance with the law, the standard definition of age is chronological age; therefore, our findings support that these scores should be used to determine eligibility for Part C services by percentage of delay.

In children born prematurely, clinical concern should increase for children born at younger gestational ages, males, and children living in poverty. Our findings suggest the threshold for referral to private EI services should be lower and based on chronological age scores. This study also suggests that mandates guiding the provision of EI services should consider the combination of biologic and social risk in the determination of eligibility. The data demonstrates the influence of combined risk for persistent delay. Although there are separate public services for children living in poverty that are designed to enhance developmental experiences, they often do not provide therapy and instruction targeting specific delays in development. Consideration of the combined influence of biologic risk with poverty may improve service delivery by eliminating the need for multiple referrals, assessments, and the need for communication between providers and agencies.

Although the significance of early intensive EI services on improved adaptive behavior trajectories could not be demonstrated, the data indicate that very few children received an intensive amount of early EI hours. Additionally, the overall group mean score has shifted to the lower end of the average range by the Preschool period, over ten points lower than the pediatric population average. Past and recent studies have demonstrated the importance of amount of EI services and early receipt in the first year of life on better cognitive and motor outcomes (Hill, et al., 2003; Ramey & Ramey, 1992; A. Spittle, et al., 2009). Our findings highlight the discrepancy in amount of services in these studies and those received by children in our study. Additionally, Cicchetti's theoretical model of neuroplasticity supports the relationship of early and intensive environmental experiences in facilitating early development and adaptive function. Our data describes the reality of service receipt experienced by children born prematurely and implies that a redesign of the EI service provision system is needed. Children in this study did not receive intensive early and sustained EI services over the first three years of life. A large percentage of children born prematurely did not receive any EI services. Consistent with nationwide numbers the bulk of EI services are provided between ages 2 and 3 years. Although the system is intended to provide services early, the majority of children receiving a greater amount of services are getting a late start. The EI service data highlighted in this dissertation suggests that change in both access (e.g. calculation of delay from chronological age scores to qualify, recognition of prematurity as an Established Risk eligible condition) and amount of service delivery (more service hours provided early in life and continuing through the 3rd year of life) are needed.

Life sustaining care provided to children born prematurely is expensive for families and society (Clements, Barfield, Ayadi, & Wilber, 2007). Consistent with the literature on EI costs for children born prematurely, our data suggests that the initial significant financial investment of intensive care to reduce mortality and morbidity in premature infants is not sustained after discharge from the hospital (Clements, et al., 2007). The first 3 years of life are a critical time period of rapid brain development and neuroplasticity influenced by environmental experiences (Cicchetti & Cohen, 2006; Johnston, 2009). Our findings suggest many children born prematurely experience limited continued investment in amount of early intervention service hours (environmental experiences) targeting neuroplasticity and adaptive behavior over the first years of life, and that a reinvestment in IDEA Part-C service delivery is indicated.

LIMITATIONS OF THE STUDY

Our model did not account for all of the contextual factors presented in the theoretical model. We did not evaluate changes in brain development over time, or the influence of genetic inheritance. Additionally, we did not have a measure for the change in gene expression based on environmental sensory experiences. These factors may have explained more of the variance in adaptive behavior trajectories. While the Vineland Adaptive Behavior Scales have been validated for children of the age range in this study, the domains of daily living skills and social competence are not typically evaluated in children born prematurely at this age. Therefore, inclusion of an additional measure of adaptive behavior would have been useful to support findings from the Vineland Scales. Although we included predictors in our study that have been noted in previous research, other important variables may have been missing from the model, contributing to potential error variance. Additionally, our sample may not be representative of the broader population of children born prematurely.

The use of real service delivery data poses several challenges. Because of funding restrictions, families that moved out of the county were no longer eligible for the study and were lost to follow up. Most of the children in our sample did not receive high dosage EI services in the first year of life. As a result, we were not able to fully examine the effect of early intensive EI on adaptive behavior. The receipt of EI services is dependent on several factors including insurance authorization for private therapies, transportation services, occupations that allow families to participate in EI during the work week, and professional agreement regarding level of delay. While the statistical methodology accounts for missing data, there were a few children who received EI services from professionals outside the study; there were no controls for this potential confound. In addition, the study did not account for developmental interventions received in the NICU (e.g. skin to skin holding) which have been demonstrated to improve neurodevelopmental and adaptive behavior outcomes in children born prematurely (Ruth Feldman, et al., 2014; Milgrom, et al., 2010; Weiss, et al., 2001). We also did not account for the amount of time parents spent reinforcing EI activities when EI professionals were not present.

IMPLICATIONS FOR FUTURE RESEARCH

It will be important to consider research design and methodology in future studies. Long-term outcome research of children born prematurely most often reports aggregated group differences from term born controls using methods such as cross sectional differences at two points in time, or with repeated measures ANOVA. Repeated measures ANOVA of longitudinal data simply describe a series of observed group changes at fixed points in time. In contrast, multilevel modeling examines how the developmental process unfolds for each individual and then uses the estimated parameters for within-person change as dependent variables to examine the effects of factors that may differ across individuals. The use of multilevel modeling and other related methods for longitudinal studies of children born prematurely would provide more information about the rate and pattern of change across time points.

Our results raise questions regarding various predictors, other than gestational age, sex, and income, which may influence the rate and pattern of adaptive behavior change over time. Biological markers of brain development would be important predictors to consider and could substantially influence our understanding of adaptive behavior trajectories (Back, 2014; de Kieviet, Zoetebier, et al., 2012; Dean, et al., 2014; Johnston, 2009; Catherine Limperopoulos, 2010; Volpe, 2009).

Our findings indicate the need to better understand exactly what occurs at the beginning of the second year of life that may enhance or impede continued development of adaptive behavior skills. Our data suggest that this may be a significant point in time. Problems arising at that developmental phase could reflect a sensitive period at which certain interventions could be especially important. Our study does not provide information on trajectories beyond the preschool period. Further research is needed to determine whether the changes we found in the infants' adaptive behavior trajectory persist or not. Services may be stopped before the child reaches a sensitive period when the potential impact may be the greatest for some children.

It may be important to examine effects of more specialized EI services at the agency level or by type of professional. For instance, developmental interventions provided by an EI teacher versus an occupational therapist may have uniquely different effects on adaptive behavior over time. Similarly, different components of adaptive behavior should be examined to see if motor skills, social skills or other aspects of adaptive behavior are influenced by EI in different ways. Lastly, future research is needed to determine whether receipt of more EI service hours beginning after birth and continuing through the first 3 years of life can prevent decline in adaptive behavior and enable children born prematurely to achieve norms consistent with term born peers.

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