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Research Article

Adaptive Behavior Trajectories in Children Born Prematurely: The Influence of Biologic and Social Risk Factors over the First Few Years of Life

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- Prematurity
- Adaptive behavior
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Abstract

Introduction: Preterm infants are expected to achieve skills consistent with term born peers by age 3. The purpose of this study was to describe trajectories of adaptive behavior for preterm children, examining the influence of gestational age (GA), illness severity, sex, family income, and maternal education.

Method: 218 children (birth weight < 2500 grams, GA < 37 weeks) were evaluated four times over 36 months with the Vineland Adaptive Behavior Scales. Multilevel modeling was used to assess individual growth trajectories and between-group differences on the adaptive behavior composite score of the Vineland Scales.

Results: Individual trajectories of children varied. On average, adaptive behavior composite scores declined to the low end of the average range until about 28 months of age when trajectories showed slight improvement ($t=6.29$, $p<.001$). Older gestational age was associated with better scores ($t=4.68$, $p<.001$). Male sex ($t=2.77$, $p=.005$) and poverty ($t=-2.73$, $p=.007$) were significant predictors of poorer adaptive behavior as children aged.

Discussion: Results suggest that a lower threshold for referral to early intervention may be prudent, especially for premature male infants who live in poverty. Research is needed to understand and address the causes of decline in adaptive behavior over time, especially among the large proportion of children born preterm who do not achieve adaptive behavior scores consistent with term peers by age 3 years.

ABBREVIATIONS

VABC: Vineland Adaptive Behavior Composite Score

INTRODUCTION

Many children born prematurely have difficulties with adaptive behavior [1]. Adaptive behavior reflects functional abilities in communication, social, daily living (self-care and coping), and motor 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 [2]. Compared to term born peers, children born prematurely demonstrate more impaired adaptive behavior skills at school-age [3,4].

However, little is known regarding the adaptive behavior skills of preterm children over their early years of life. Cho *et al.,* reported that, over a 10-month period during later infancy, preterm children showed a decline in adaptive behavior scores [5]. This finding of a downward trend in adaptive behavior scores, if further substantiated, is consistent with the decreasing mean developmental standard scores over the first few years of life that has consistently been reported in children born prematurely [6,7].

It is not clear why some children born prematurely develop more or less optimal adaptive behavior but previous research suggests that both biological factors and social factors may influence developmental outcomes in general. The combination of biologic and social risk factors for children born prematurely has been referred to in the literature as double jeopardy [8].

Previous research indicates that gestational age, neonatal illness severity, and sex are significant biologic risks. Poorer outcomes in children born at younger gestational ages have been highlighted in the scientific literature for decades [9,10]. Recent reports have emphasized the high prevalence of developmental and adaptive behavior delays in infants born between 32-36 weeks gestational age (often referred to as late preterm) [11-13]. Potijk reported that younger gestational age was associated with delays in fine motor, communication and personal social domains [11]. Several studies report that younger gestational age is also associated with poorer outcomes in social competence [14,15] self-care skills [16], and language [17,18].

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 neurodevelopment and adaptive behavior outcomes [19-21]. Several recent studies highlight the high incidence of white matter injury in preterm infants, and its value as a predictor of poorer outcomes in social [14,22], language [23,24] and motor [25] domains. Another recent large multicenter study evaluated the trajectories of prognostic indicators for neurodevelopment impairment at 18 months, and reported that the importance of illness severity increased as a prognostic indicator over the NICU course [26]. This study not only validates the importance of illness severity as a prognostic indicator, it highlights the significance of evaluating the changing influence of predictors over time. Spittle *et al.,* have also found brain injury and lower birth weight to be associated with poorer social and behavioral competence for prematurely born children at age two years [15].

In numerous studies of children born prematurely, child sex has been demonstrated to be a biological predictor of development and adaptive behavior. Although the results are inconsistent, most studies report that boys have worse outcomes than girls [5,6,27-31] Cho *et al.,* evaluated the impact of sex on adaptive behavior in children born prematurely and found male sex to be a significant predictor of poor cognitive and adaptive behavior outcomes in early life [5]. Adaptive behavior scores at 6 months trended downward to the bottom of the normative range by 16 months. 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 years [32]. 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 [33]. 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.,* [15] 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 also 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 [11,12,34]. Less maternal education has been associated with poorer motor skills at age 2, and with overall development at age 4 [11,35] 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 [17]. 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 [36]. In contrast to studies that show low income and less education to be risks, 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 [18].

In summary, knowledge regarding the effect of biologic and social factors on early adaptive behavior of preterm children is limited, with findings that have not been entirely consistent. The most consistent findings are for the negative influences of younger gestational age and increased neonatal illness severity. While younger gestational age is consistently noted as a risk, late preterm gestation has also been linked to worse outcomes. 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 socioeconomic status (SES) factors to have more influence on development than biologic factors [17]. Overall, there is a paucity of research on the early development of adaptive behavior among children born prematurely and factors that may influence their trajectories. The purpose of this study was to address these gaps in the literature. The specific aims were: 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.

MATERIALS AND 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 one of the California Children's Services (CCS) criteria for risk of later neurodevelopment complications (e.g. prolonged perinatal hypoxemia, seizures, intracranial abnormality).

Procedure

Letters were sent to hospital intensive care nurseries in the county where the study was conducted, 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. 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, were 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 four 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). Scores for adaptive behavior were calculated 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

A demographic questionnaire acquired self-report data on family income and maternal education. Family income had the following choice of categories: 1) less than 5k, 2) 5k to 9,999, 3) 10k to 19,999, 4) 20k to 29,999, 5) 30k to 39,999, 6) 40k to 49,999, 7) greater than or equal to 50k. Categories for maternal education included: 1) less than high school degree, 2) high school degree, 3) partial college, 4) college graduate, 5) graduate degree. Gestational age and sex of the infant were extracted from the medical record. Medical information for inclusion criteria and calculation of the Neonatal Medical Index also 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 neurodevelopment and functional outcomes [35,37]. 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 [37]. The NMI classifications range from I to V, with I describing preterm infants with fewest medical complications and V describing infants with many medical 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 [2]. 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 4 dimensions relevant to children's function (communication, daily living skills, socialization, and motor domains). It provides an overall Adaptive Behavior Composite (ABC) score that represents the 4 adaptive behavior domains and can be compared to normative population values [3,5,38]. 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.

There is evidence for concurrent and predictive validity of the VABS in children born prematurely [3,39,40]. 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 [3, 38]. Equivalence reliability with telephone administration has also been supported [39]. While the initial psychometric properties of the Vineland were established many years ago, it remains one of the standard tools of assessment used today [41, 42].

Data Analysis

Descriptive statistics were employed to examine sample characteristics. Assumptions of bivariate normality and linear relationships were examined and met. Multilevel model estimation with full maximum likelihood was used to describe adaptive behavior trajectories and evaluate the influence of predictors on these trajectories. The use of full maximum likelihood accommodates missing data (cases with missing assessments are retained in the analysis) and variation in assessment ages, producing unbiased estimates over time even with differences in age of assessment and different numbers of assessments (e.g., not all children had reached the ages of later assessments by the end of the current study).

A two-level polynomial model with linear and quadratic effects was fit 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 generated to display the trajectories of each individual subject's ABC scores from Infancy to the Preschool period. At Level 2, trajectory differences were examined by adding the subject-level predictors to the model. We proposed that the ABC score and its pattern of change would vary across individuals and that this variation would be explained, in part, by gestational age, level of illness severity, sex, family annual income, and maternal education. Data was analyzed using IBM SPSS Statistics for Windows version 21.

RESULTS AND DISCUSSION

The convenience sample was comprised largely of infants born at Lucile Packard Children's Hospital. 218 infants were enrolled in the study (Table 1) presents key descriptive data. The mean gestational age at birth was 31 weeks (SD 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 races or ethnicities. 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 [37], 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 model to estimate the best fitting change trajectory, 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 2), the linear model for time demonstrated significant variation in linear growth trajectories. The growth rate was negative, implying that, on average, ABC scores declined over the first three years of life (B= -4.61, p<.001). Also shown in (Table 2), the addition of a quadratic effect, which represents the degree of acceleration or deceleration in growth at different points in time, was also significant and positive indicating that the growth rate was not constant (B=.63, p<.001). On average, the adaptive behavior composite score declined from 4 to 28 months but showed a slight increase around 28 months. This trajectory of average scores is shown in (Figure 1)**.**

Inclusion of both linear and quadratic estimates of the average change trajectory fit the data better than a linear model alone, based on Akaike's Information Criterion (AIC = 4925). The curvilinear spaghetti plot in (Figure 2) shows the individual variation in linear and quadratic growth trajectories over the first 3 years**.** Lines in the plot indicate that, for the majority of children, adaptive behavior scores gradually trend toward the lower end of the average range 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). The red curvilinear line represents the mean group trajectory for adaptive behavior. Given this apparent variation in growth trajectories, an Intra class Correlation Coefficient (ICC) was calculated (ICC = 21.762 / 100.287 = .217) to determine actual variance in adaptive behavior scores due to differences among the children; the ICC indicated that 22% of the variance in adaptive behavior was due to different characteristics of children. The unconditional model, spaghetti plot, and ICC, all showed significant variability in adaptive behavior scores; thus, a conditional growth model was examined to identify factors that might explain the differences between children in change over time.

The following biologic and social predictors were added to the Level 2 conditional growth model separately: gestational age, illness severity (i.e., NMI category), sex, family income, and maternal education. In the single predictor model, gestational age had a significant effect at baseline (four months of age), but the cross- level interaction testing the effect of gestational age 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 a significant predictor over time, indicating that the change trajectories for males and females differed. Neither family annual 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

Table 1: Family and Child Demographic and Clinical Characteristics.

Characteristic (n) **Family Annual Income (196)**	**n**	**%**
≥ $50,000	111	(57%)
< $50,000	85	(43%)
Maternal Education (206)		
less than College degree	84	(47%)
College or graduate degree	112	(54%)
Sex (218) Male	109	(50%)
Female	109	(50%)
Gestational Age in weeks (218)		
	23-29	72 (33%)
	30-32	82 (37%)
	33-36	64 (30%)
Neonatal Medical Index (218)		
I - Fewest medical complications	30	(14%)
II - Fewer medical complications	41	(9%)
III - Some medical complications	86	(40%)
IV - More medical complications	24	(11%)
V - Many medical complications	35	(16%)

Table 2: Best fitting unconditional model of adaptive behavior change over time with both linear and quadratic estimates.

Parameter	Estimate	Std. Error	t	Sig.	95% CI	
Intercept	94.03	.78	120.54	.000	92.50	95.56
Linear Time	-4.61	.62	-7.45	.000	-5.83	-3.40
Quadratic Time	.63	.10	6.29	.000	.43	.83

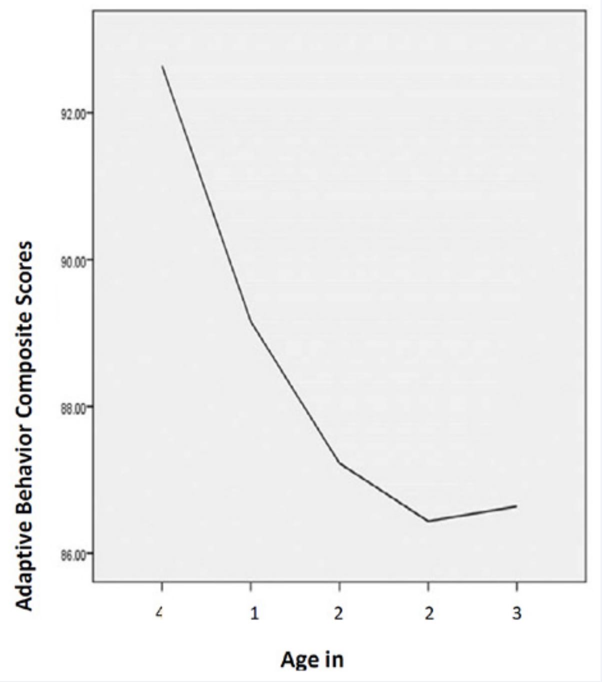

Figure 1 Change in average adaptive behavior composite scores over the first three years of life. Linear and quadratic chronological age mean scores for Vineland Adaptive Behavior Composite decline to the low end of the average range by 28 months before increasing

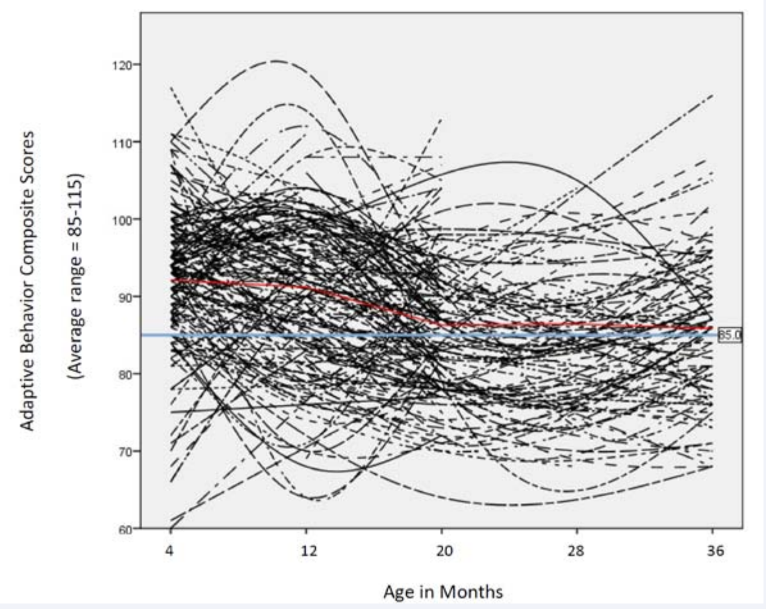

Figure 2 Curvilinear Spaghetti Plot for Individual Varied Trajectories of Adaptive Behavior over the First Three Years of Life. Individual trajectories of linear and quadratic chronological age mean scores for Vineland Adaptive Behavior Composite demonstrates varied rates and patterns of change for individual subjects over the first three years of life. Blue line marks the lower end of the average range.

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Table 3: Effects of Sex, Gestational Age, Illness Severity, Income and Maternal Education on Adaptive Behavior over the First Three Years of Life.

	Estimate	Std. Error	t	Sig.	Confidence Interval	
					Lower	Upper
Intercept	66.14	7.33	9.02	.000	51.69	80.60
Linear Time	-5.76	1.06	-5.46	.000	-7.84	-3.69
Quadratic Time	.89	.24	3.76	.000	.42	1.35
Male sex	-.97	1.20	-.80	.423	-3.34	1.41
Gestational Age	.95	.20	4.68	.000	.55	1.35
Illness Severity	-.05	.48	-.10	.918	-.99	.89
Family Income	2.62	1.55	1.69	.092	-.43	5.68
Maternal Education	-.13	.46	-.29	.771	-1.03	.767
Linear time x Male	1.78	.62	2.88	.005	.56	3.00
Linear time x Income	-1.71	.62	-2.73	.007	-2.94	-.47

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

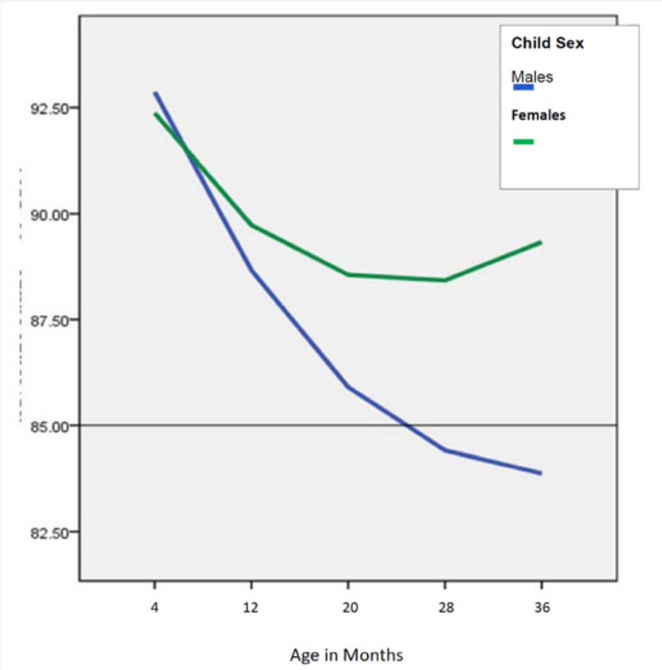

Figure 3 Interaction of linear trajectories for mean chronological age scores for Vineland Adaptive Behavior Composite varies over time for males versus females. The mean score for females plateaus at about 20 months of age, while the mean score for males continues to decline and drop below the lower end of the average range by about 2 years of age.

(4035) and lower level one residual (54.15). Data suggest that adding these predictors resulted in a model that fit the data better than the unconditional model (the model with only the linear and quadratic effects of time of assessment). As in the single predictor model, gestational age had a significant effect at baseline, but not over time. Consistent with the single predictor model, male sex did not have a significant effect at baseline, and the cross-level interaction was significant (Figure 3). As illustrated in the figure, the difference between adaptive behavior 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, severity of neonatal illness and maternal education did not have significant effects in the composite model. Although family annual 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. In the composite model, a dichotomous variable was created for income (< or > $50,000 per year). With all predictors in the model, lower income was also a significant predictor of lower adaptive behavior scores over time. The change in significance of income over time is and differences for infants from families with incomes above and below $50,000 per year is illustrated in (Figure 4).

CONCLUSIONS

Findings from this study highlight the significant variability

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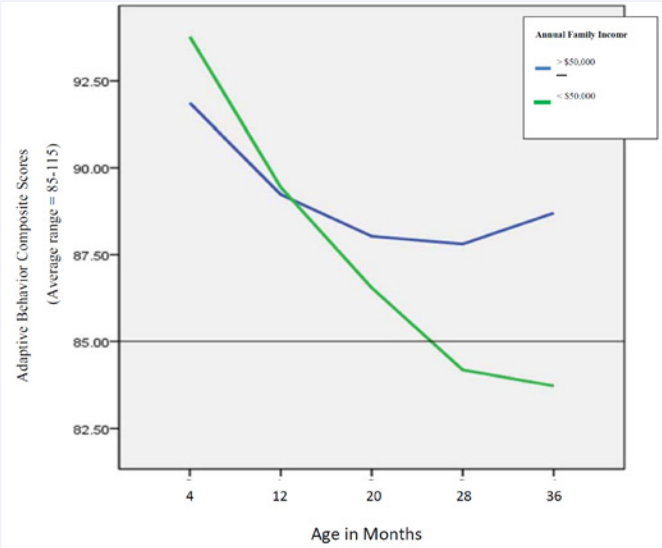

Figure 4 Interaction of Family Annual Income and Linear Mean Adaptive Behavior over the First Three Years of Life. Interaction of linear trajectories for mean chronological age scores for Vineland Adaptive Behavior Composite varies over time by family income level. Scores for children who came from families with income less than $50,000 per year continued to decline and drop below the lower end of the average range at around 2 years of age.

in adaptive behavior trajectories of children born prematurely. Some children started with low adaptive behavior scores and achieved scores in the normative range (above 85) by age 3. This trajectory is consistent with current expectations that preterm children catch-up to term born peers by age 2 or 3 [43], unless they are extremely premature. Other children initially scored in the normative range and their scores dropped below average over time. However, the majority of children had adaptive behavior scores that clustered around the lower end of the average range and trended downward over time. The average trajectory was a negative linear trend down to the lowest end of the average range. This pattern is largely consistent with previous studies in children born prematurely [44]; however, the finding of a small positive trend in the third year of life (i.e., 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.,* [35] found that illness severity predicted fine motor function of preterm children, using a tool specific for motor function at age 4 years. The lack of a significant finding in our study suggests that the Vineland Adaptive Behavior Composite Score may not be sensitive to changes in fine motor skills. It is also possible that the measure of illness severity we used 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, gestational age may have 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 [5,6] 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 of the emergence of these differences. At 28 to 36 months of age, girls experience an upswing in their adaptive behavior skills while boys continue to decline.

Our findings also indicate that the effect of income on adaptive behavior becomes more significant as a child ages. By 24 months of age, children from families with annual incomes less than $50,000 dropped below the average range for adaptive behavior skill. By 36 months of age, this sharp decline slowed but continued. In contrast, children from families with higher annual income experienced a slight positive upswing in their trajectories by 36 months of age. Aylward [6] 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 [11,18,35]. 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, adaptive behavior skills decline until about 28 months of age when the trajectory starts 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 means 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 specific area of daily living skills is not typically evaluated in very young children.

Therefore, inclusion of an additional measure of adaptive behavior would have been useful to support findings from the Vineland Scales. In addition, our sample was from one Western region of the U.S. and 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 third 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 [19-21,45-47]. It may also be important to evaluate factors that influence trajectories of specific areas of adaptive behavior, such as social skills or motor skills.

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 [43]. In light of our findings, it may be time to reconsider the practice 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.

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.

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