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Behavioral problems are associated with cognitive and language scores in toddlers born extremely preterm

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Abstract

Objective: To evaluate the relationship of parent-reported child behaviors on the Child Behavior Checklist (CBCL) to cognition, language, and motor skills on the Bayley Scales of Infant and Toddler Development – III (Bayley-III) in toddlers born extremely preterm.

Study Design: Toddlers born extremely preterm (gestational ages 22 0/7 to 26 6/7 weeks) were tested at 22 – 26 months corrected age with Bayley-III while parents completed the CBCL. Socio-demographic variables and medical history were recorded. Linear regression models were used to assess the relationship of Bayley-III cognitive, motor, and language scores with CBCL scores, adjusting for medical and socio-demographic factors.

Results: Internalizing, affective, and pervasive development problem behavior scores on the CBCL correlated significantly with lower Bayley-III cognitive, language, and motor scores on unadjusted and adjusted analyses. Although externalizing and anxiety problems were significantly associated with cognitive and language scores on unadjusted analysis, the relationships were not

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

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significant after adjusting for socio-economic factors. CBCL scores were similar for boys and girls, with the exception of the pervasive developmental problem scale; boys had significantly more problems than girls ($p=0.02$).

Conclusions: This study showed that parent reported behavior problems were related to lower cognitive, language, and motor development in toddlers born extremely preterm. Early findings of behavioral problems in toddlers born extremely premature may help identify children at greater risk for later learning difficulties. Adding a measure of behavior to the evaluation of these children may help better understand factors that can contribute to delays, especially in cognition and language.

Keywords

development; CBCL; Bayley-III; extremely low birth weight

1. INTRODUCTION

Children born extremely preterm are at risk for a variety of developmental problems, including cognitive delay [1], language disorders [2], and behavioral problems [3]. Early developmental difficulties continue into school age, where children born extremely preterm have higher risks of learning disabilities and behavioral disorders [4]. Specific medical and socio-demographic factors have been associated with developmental outcomes [5]. However, the relationship of behavioral problems to developmental outcomes in young children is not well understood. A better understanding of these relationships could have implications for both early identification and intervention. For example, anxiety, attention deficits, internalizing, and externalizing behaviors negatively affect a child's ability to concentrate and attend to tasks, especially as tasks become more difficult and potentially frustrating [6]. Early demonstration of executive function difficulties among extremely preterm born children has been associated with challenges in subsequent academic skills [7].

The additive effect of medical, socio-demographic, and behavioral factors can result in worsening of developmental impairments, especially when the toddler is asked to perform tasks requiring attention and early working memory skills [8,9]. It is important to better understand the interactions of these different skill sets on outcome. Early identification and recognition of behavioral and developmental difficulties, interacting with demographic and medical factors, can help optimally target intervention services to improve the outcomes of extremely preterm children.

We sought to assess the relationship between behavioral difficulties reported in the Child Behavior Checklist [10] with developmental scores of the Bayley Scales of Infant and Toddler Development – 3rd edition [11], at 22-26 months corrected age. We hypothesized that CBCL scores for both externalizing and internalizing behaviors would be inversely related to Bayley-III cognitive, language, and motor scores after adjusting for socio-demographic and medical severity factors.

2. METHODS

2.1. Study Population

Prospectively collected data, as part of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN) Generic Database (GDB) and Follow-Up studies, were analyzed retrospectively. Children born extremely preterm who were seen for follow-up at 22 to 26 months corrected gestational age between August 2014 and August 2016 were eligible for this analysis. All infants 22 0/7 to 26 6/7 weeks gestation, or with a birth weight of 401 to 1000 grams, inborn at participating NRN sites, and who had neurodevelopmental assessment at 22-26 months corrected gestational age were included.

Demographic information included child's birth weight, sex, categorization as small for gestational age (SGA), age at testing, NRN center, maternal medical insurance, and race. Due to 21% of the cohort missing data for maternal education, we decided that maternal medical insurance, which was only missing for 0.2%, was a better proxy for socio-economic status (SES). Medical events recorded included severe intraventricular hemorrhage (grade 3-4 IVH), cystic periventricular leukomalacia (PVL), bronchopulmonary dysplasia (BPD, defined as receiving supplemental oxygen at 36 weeks CGA or at discharge if discharged before 36 weeks), late onset sepsis (LOS, defined as late onset culture positive septicemia/bacteremia >72 hours treated with antibiotics for 5 days or died before treatment was completed), retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), defined as proven NEC ('Modified Bell's staging criteria IIA or greater), and patent ductus arteriosus (PDA).

2.2. Measures

2.2.1. Bayley Scales of Infant and Toddler Development, 3rd edition (Bayley-III)—The Bayley-III is one of the most widely used tests of development for infants and toddlers from 2 to 42 months. The cognitive, language, and motor scales have a standardized composite score with a mean of 100 and standard deviation of 15. The language scale consists of receptive and expressive language subscales and the motor scale consists of gross and fine motor subscales. The reliability coefficients for the Bayley-III scales in premature infants are all greater than 0.94 [12]. Each year, the primary Bayley-III examiner from each NRN Center submitted a video of him/herself performing the exam to one of four NRN gold standard examiners. Then, the primary Bayley-III examiner was responsible for training and certifying additional examiners at their Center. Scoring was completed using the age corrected for gestational age to calculate the standard scores for each scale.

2.2.2. Child Behavior Checklist/1 ½- 5 years(CBCL)—The CBCL is a widely used questionnaire in both research and clinical practice. Parents complete 100 questions from observations of their child's behaviors, using a 3-point scale (this behavior is: "not true", "somewhat true", "very or often true" for my child). The mean and standard deviation is 50 ±10. Higher scores on the scales indicate increased behavioral problems. Summary scores were derived by NRN staff at each center, entering the responses for each item obtained using the hard-copy of the CBCL questionnaire (ages 1.5-5 form) into scoring software

(Assessment Data Manager, Version 9.1, ASEBA). The 100 questions are grouped into Diagnostic and Statistical Manual (DSM) oriented scales (affective, anxiety, pervasive developmental, attention deficit/hyperactivity, and oppositional defiant problems) which have been consistent with DSM-V diagnostic categories. These scales are then grouped into empirically based composite scales measuring internalizing, externalizing, and total problem behavior scores. The scales are normed with t- scores that have a mean of 50 and standard deviation of 10, with higher scores indicating more problems. When calculating the standard scores for each scale, corrected gestational age was used.

2.3. Statistical Analysis

Data from the NICHD NRN are collected by each center on standard forms and are compiled at the data-coordinating center, RTI International, Research Triangle Park, NC, USA. Institutional Review Boards at each center approved the study. RTI personnel assessed data completion and consistency. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Mean standard scores were calculated for the Bayley-III scales and for each CBCL scale of interest: Affective, Anxiety, Pervasive Developmental, Attention Deficit/Hyperactivity, Oppositional Defiant, Internalizing, Externalizing, and Total Problems. Each CBCL measure was tested for correlation with each Bayley-III outcome (cognitive, language, and motor score). Linear regression models were then constructed for each Bayley-III outcome to investigate their relationship with each CBCL measure, adjusting for child's gestational age, sex, SGA status, age at testing, NRN center, maternal medical insurance, race, BPD, IVH/ PVL, LOS, ROP, NEC, and PDA. Betas representing the change in Bayley-III score for every 10-point increase in CBCL score were calculated. Statistical significance was ascribed to p-values less than 0.05, with no adjustment for multiple testing.

For associations that were no longer statistically significant after covariate adjustment, further analyses were conducted to determine which factors led to this change. First, each covariate was individually added to models fitting the Bayley-III score to the CBCL subtest score of interest. Individual covariates that led to insignificance were removed from the full model and verified to cause loss of significance even after adjusting for other characteristics. The amount of variance from these factors was analyzed by comparing full and reduced models.

3. RESULTS

Of the 1,231 toddlers born less than 27 weeks gestational age and eligible for follow-up between August 1, 2014 and August 31, 2016, 114 were lost to follow-up (8.4%). Those lost to follow-up tended to be heavier at birth, had lower maternal education attainment, classified as 'other' for race, and were less likely to have PDA (results not shown). Of the 1,085 that completed follow-up, 1,074 (99%) completed both the CBCL and Bayley-III exams and were included in the study. Demographic characteristics for this population are shown in Table 1.

Descriptive statistics for the CBCL and Bayley-III scales are shown in Figures 1a and 1b. For DSM-oriented scales (Affective, Anxiety, Pervasive Developmental, Attention Deficit/Hyperactivity, and Oppositional Defiant Problems) mean scores ranged from 53.8 (anxiety) to 56.6 (pervasive developmental). Internalizing, externalizing, and total problem standardized mean scores were 49.6, 51.3, and 51.3, respectively.

Higher scores on the internalizing, total, affective, and pervasive development scales correlated significantly with lower cognitive, language, and motor scores on both unadjusted and adjusted analyses (Table 2). For every 10-point increase in the internalizing score, there were 2.24, 3.14, and 2.54 point decreases in the cognitive, language, and motor scores, respectively ($p<0.001$) on adjusted analyses. Similarly, total problem scores saw 1.16, 2.02 and 1.09 point decreases in cognitive, language, and motor scores ($p<0.05$). For every 10-point increase in the affective score, there were 2.57, 3.58, and 3.01 point decreases in cognitive, language, and motor scores ($p<0.01$). The highest association was seen between increased pervasive developmental problems and lower Bayley-III scores: for every 10-point increase, there were 3.62, 5.40, and 4.05 point decreases in cognitive, language, and motor scores, respectively ($p<0.001$) (Table 2).

In contrast, externalizing and anxiety problems were significantly associated with cognitive scores on unadjusted analysis, but were no longer significant after adjusting for socio-economic factors (mother's medical insurance and study center). Similarly, externalizing, anxiety, attention deficit/hyperactivity, and oppositional defiant problem scores showed significant association with decreasing language scores on unadjusted analysis, but were not significant after adjusting for socio-economic factors (Table 2).

In unadjusted analyses, CBCL scores were similar for boys and girls, with the exception of the pervasive developmental problem scale where boys scored significantly higher ($p=0.02$). Among Bayley-III scores, boys scored significantly lower than girls (See Appendix A).

4. DISCUSSION

In this study, we confirmed our hypothesis that internalizing, affective, and pervasive developmental behavioral problem scores reported on the CBCL were significantly associated with lower Bayley-III cognitive, language, and motor scores. Externalizing and anxiety scale scores were associated with lower cognitive scores on unadjusted analyses, however, when the model took into account socio-economic factors (mother's medical insurance and test center) statistical significance was lost, along with substantial attenuation of the effect size. Similarly, externalizing, anxiety, attention deficit/hyperactivity, and oppositional behavior problems were significantly associated with lower language composite scores, however, when the model controlled for socio-economic factors, the association disappeared. These results emphasize the importance of evaluating behavioral problems in toddlers born preterm, and underscore the impact of socio-economic factors on behavior.

Our findings that behavioral problems were associated with lower developmental scores were consistent with those found in the Early Childhood Longitudinal Study, Birth Cohort (ECLS-B) [13] that followed 8,000 children born term and preterm. The ECLS-B study

found that those children with cognitive delay at 9 and 24 months (defined by scores on the Bayley Short Form) had significantly more behavioral problems by 4 and 5 years, with SES associated with worse behavior problems. In general, however, problems in areas of cognition, academics, and behavior are often reported separately in outcome studies of preterm children [14], and the inter-relationships of these problems have not been well studied. For example, a meta-analysis of behavioral indices in infants and preschool-age children [8] showed that preterm children had more problems than term-born children in areas of self-regulation, hyperactivity, distractibility, shyness, and attention; however, the relationship of behavioral problems to development was not reported. In another example, the ELGAN study [3] found that preterm children had more problems with dysregulation, which was associated with maternal socioeconomic risk factors. The preterm children in that study also had more problems related to cognition, language, and executive functioning; however, the relationship of these domains to their behavior problems was not evaluated.

Although usually reported separately, several previous studies do support our findings of an interrelationship of behavioral problems with cognition and language difficulties. Peralta et al recently reported that socio-emotional and behavioral competence problems in very preterm born toddlers were associated with cognitive and language delays on the Bayley-III scales [15]. Additionally, a study in the Netherlands compared a parent questionnaire of development (Ages and Stages Questionnaire) to the CBCL questionnaire in a group of moderately preterm and term 4 year olds [16]. They found that problem-solving skills correlated with externalizing behavioral problem scores while personal-social skills correlated with internalizing behavioral problems. It is not possible to determine from our study if behavior problems resulted in developmental delays, or if developmental delays were attributed to behavioral problems; findings support the importance of incorporating both measures of behavior and cognition/language into studies designed to measure outcomes of children born preterm.

Our finding that boys did significantly worse on the Bayley-III scales of cognitive, language, and motor skills, in addition to the Pervasive Developmental Scale on the CBCL, is consistent with several previous studies. For example, in the ELGAN study, boys consistently had significantly higher levels of cognitive impairment and higher rates of autism spectrum disorder [17]. The finding that boys have cognitive delay compared to girls is consistent with the literature; however, these sex-related differences appear to diminish by school age [18]. While preterm-born children continue to have behavioral problems at school age [19], studies either have not specifically examined the effect of sex on these problems [20], or have not found sex differences in academic or executive function skills [21].

This study has several limitations, one of which is the use of parent report for the measure of child behavior. Though the CBCL is widely used and a well-validated measure, it does require a parent to rate their child's behavior, which could result in either over or under reporting of behavior problems. The CBCL lower limit is 18 months, therefore it may not have been reliable for those children who were below this level. There were also no observational measures of behavior, which could have provided a more objective measure of behavior. Testing of 2-year olds can be challenging, so scores obtained may not be a valid

assessment of child developmental abilities. The strengths of this study included a long-standing research network infrastructure, the use of certified examiners to administer the Bayley-III test, and a large sample size.

4. Conclusion

This study adds to the limited research evaluating the relationship of behavior to development in toddlers born preterm. We showed that parent reported behavior problems were related to lower cognitive, language, and motor development in toddlers born extremely preterm. Early findings of behavioral problems in toddlers born extremely premature may help identify children at greater risk for later learning difficulties. Adding a measure of behavior to the evaluation of these children may help to better understand factors that can contribute to delays, especially in cognition and language. Our findings have several implications for evaluation and early intervention for these children. Early intervention programs have been shown to have cognitive benefits and improve the parent-child relationship [22]. Longitudinal research is needed regarding the ability of early intervention programs to improve self-regulation and behavior.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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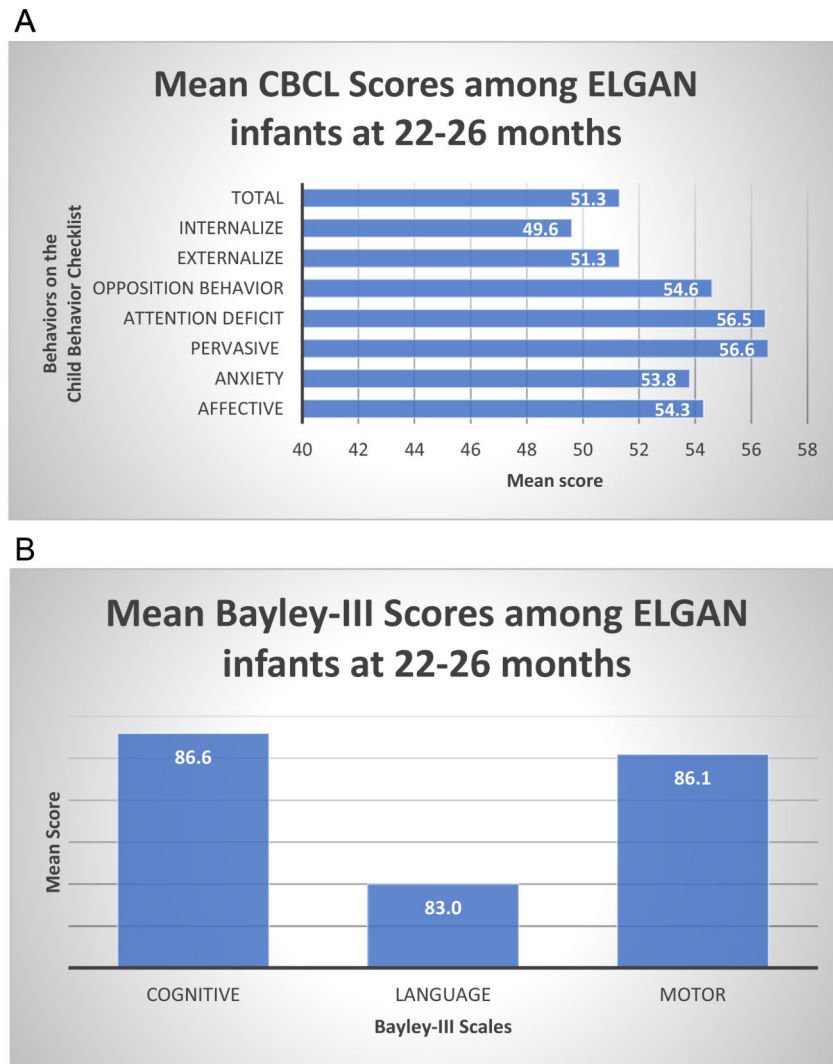
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Highlights

- Internalizing, affective, and pervasive development problem behavior scores on the CBCL correlated significantly with lower Bayley-III cognitive, language, and motor scores on unadjusted and adjusted analyses.
- CBCL scores were similar for boys and girls, with the exception of the pervasive developmental problem scale; boys had significantly more problems than girls ($p=0.02$).
- This study indicated that parent reported behavior problems were related to lower cognitive, language, and motor development in toddlers born extremely preterm.
- Early findings of behavioral problems in toddlers born extremely premature may help identify children at greater risk for later learning difficulties.

**Fig. 1.**

(a) Unadjusted mean Child Behavioral Checklist scores among extremely low birthweight infants at 22-26 months.

(b) Unadjusted mean Bayley-III scores among extremely low birthweight infants at 22-26 months.

Table 1.

Maternal and neonatal characteristics and demographics of toddlers

Characteristics	Subgroup	Statistic*	All study participants N=1,074
Child test age (months)		Mean (SD)	23.6 (1.4)
Sex	Male	n (%)	584 (51%)
	Female		526 (49%)
Birth weight(g)		Mean (SD)	752 (159)
Maternal insurance	Medicaid	n (%)	623 (59)
	Private Insurance		383 (36)
	Self-pay/uninsured		49 (5)
Race	Black	n (%)	455 (44)
	White		538 (52)
	Other		51 (5)
Bronchopulmonary Dysplasia		n (%)	668 (62)
Grade 3-4 IVH/PVL		n (%)	184 (17)
Late onset sepsis		n (%)	269 (25)
Small for Gestational Age		n (%)	65 (6)
Necrotizing Enterocolitis		n (%)	86 (8)
Retinopathy		n (%)	753 (71)
Patent Ductus Arteriosus		n (%)	606 (56)

* Percentages calculated based on number of non-missing responses

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Bayley-III Scales of Infant Development											
Child Behavior Checklist	Cognitive				Language				Motor		
	Unadjusted	Adjusted ^I	Unadjusted	Adjusted ^I	Unadjusted	Adjusted ^I	Unadjusted	Adjusted ^I	Unadjusted	Adjusted ^I	P value
	β (SE) ²	P value	β (SE) ²	P value	β (SE) ²	P value	β (SE) ²	P value	β (SE) ²	P value	P value
Internalizing Problems	-3.73 (0.43)	<0.001	-2.24 (0.44)	<0.001	-4.68 (0.47)	<0.001	-3.14 (0.47)	<0.001	-3.53 (0.48)	<0.001	<0.001
Externalizing Problems	-0.96 (0.42)	0.02	-0.23 (0.42)	0.58	-1.69 (0.46)	<0.001	-0.79 (0.45)	0.08	-0.06 (0.46)	0.90	0.58
Total Problems	-2.24 (0.42)	<0.001	-1.16 (0.43)	0.01	-3.25 (0.46)	<0.001	-2.02 (0.46)	<0.001	-1.65 (0.47)	<0.01	0.02
Affective Problems	-4.74 (0.78)	<0.001	-2.57 (0.77)	<0.01	-5.89 (0.85)	<0.001	-3.58 (0.82)	<0.001	-4.67 (0.87)	<0.001	<0.001
Anxiety Problems	-2.20 (0.78)	<0.01	-0.03 (0.75)	0.97	-2.29 (0.86)	0.01	-0.20 (0.81)	0.81	-1.39 (0.86)	0.11	0.99
Pervasive Developmental Problems	-5.49 (0.57)	<0.001	-3.62 (0.58)	<0.001	-7.20 (0.62)	<0.001	-5.40 (0.62)	<0.001	-5.39 (0.64)	<0.001	<0.001
Attention Deficit/Hyperactivity Problems	-0.97 (0.65)	0.13	0.10 (0.63)	0.88	-1.67 (0.72)	0.02	-0.11 (0.68)	0.88	-0.08 (0.72)	0.91	0.39
Oppositional Defiant Problems	-0.72 (0.71)	0.31	0.41 (0.69)	0.55	-2.02 (0.78)	0.01	-0.56 (0.74)	0.45	0.67 (0.78)	0.39	0.10

² Beta values reflect the mean change in Baylev-III scores for every 10-point increase in CBCL scores.