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Screening for Autism Spectrum Disorders in Extremely Preterm Infants

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Abstract

Background—Extremely preterm (EP) infants screen positive for Autism Spectrum Disorders (ASD) at high rates. However it is not clear whether this is due to high rates of ASD in EPs or to high rates of false positive screens for ASD in children with a high rate of underlying neurodevelopmental impairments. Combining a parent questionnaire designed to distinguish developmental delay from ASD with direct observation of infant behavior may more accurately screen for ASD in EPs.

Objectives—To determine rates of positive screen for ASD at 18–22months(m) in EPs using three screens; to determine factors associated with a positive screen.

Methods—554 infants born <27 weeks were screened at 18–22m using the Pervasive Developmental Disorders Screening Test, 2nd edition, Stage 2 (PDDST-II) and the response to name and response to joint attention items from the Autism Diagnostic Observation Schedule. Infants with severe cerebral palsy, deafness and blindness were excluded. Associations between positive screen and neonatal/infant characteristics were determined.

Results—113/554 (20 %) had ≥1 positive screen. 10% had a positive PDDST-II, 6% response to name, 9% response to joint attention; in only 1% were all 3 screens positive. Positive screen was associated with male gender, more hospital days, white race, lower maternal education, abnormal behavioral scores, and cognitive/language delay.

Conclusions—The use of three screens for ASD in EPs results in higher screen positive rates than use of one screen alone. Diagnostic confirmation is needed before true rates of ASD in EPs are known.

Keywords

Autism; Prematurity; Screening

Background

Autism Spectrum Disorder (ASD) is a group of neurodevelopmental disorders characterized by abnormalities in social interaction, impaired verbal and nonverbal communication, and restricted or repetitive patterns of behavior or interests.[1] Though low birth weight and prematurity may result in a 2–3 fold increase in the risk of ASD,[2, 3] true risk of ASD in very preterm infants is unknown. Several authors have reported high rates of screen positive in very low birth weight (VLBW; ≤1500 grams) on the Modified Checklist for Autism in Toddlers (M-CHAT), ranging from 10–25%. [4–6] The only study to date where diagnosis was confirmed, found that while 16% of extremely preterm (EP) children screened positive for ASD, 8% had been diagnosed with ASD at 11 years.[7]

While the American Academy of Pediatrics recommends screening of all children for ASD at 18 months and referral for ASD assessment for all positive screens,[8] screening for ASD as early as 18 months in EP infants may not be accurate,[9, 10] especially when using a screening tool developed for use in the general population. A valid estimate of the rate of ASD in EP infants may require the use of a screening instrument designed for a population with high rates of neurodevelopmental impairment, to decrease the false positive rate seen as a result of these impairments.

The objectives of this study are to determine the rate of positive screen for ASD in a large cohort of EP infants at 18 months using 3 screens for ASD; one designed for use in a population with high rates of impairment and 2 involving direct infant observation; and to explore the association between positive screen for ASD and maternal, neonatal and infant characteristics including cognitive or language impairment among EP infants.

Methods

Study Population

All infant survivors born <27 weeks at 15 participating centers of the NICHD Neonatal Research Network (NRN) who returned for developmental follow-up at 18 months corrected age over one year were enrolled. Each center began enrollment between 11/1/08 and 4/8/09 and continued for one year. Infants with hearing impairment requiring amplification, blindness, or severe cerebral palsy were excluded due to the anticipated high rate of false positive screen due to their underlying condition.

The Neonatal Research Network cohort consists of all infants admitted to one of 15 academic Neonatal Intensive Care Units, who survived and were administered comprehensive neurologic and developmental and behavioral assessments at 18–22 months corrected age during the year of the study. The NRN has conducted follow-up for over 20 years. Study personnel received training on performance of the ASD Screens. 784 children were eligible for follow-up during the study period.

This study was approved by the Institutional Review Board at each participating center.

Assessment

Interim medical history, family, social and demographic information, and growth parameters were obtained. Infants had a neurologic exam and an assessment of their Gross Motor Function Classification[11] performed by certified examiners. A developmental assessment using the Bayley Scales of Infant and Toddler Development Third edition (Bayley III)[12] was performed by examiners trained to reliability. A behavioral screen, The Brief Infant-Toddler Social and Emotional Assessment (BITSEA),[13] was used. The ASD pilot study was explained and ASD Screens administered.

Neonatal characteristics including gestational age, birth weight, gender, multiple gestation, days in the hospital, days on the ventilator and rates of neonatal morbidities including chronic lung disease (CLD), necrotizing enterocolitis (NEC), periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), and blood culture-positive sepsis were collected. CLD is defined as oxygen dependence at 36 weeks post-conceptional age, NEC defined as greater than Bell's Stage 2,[14] and IVH defined as grade 3 or 4 by Papile's grading system.[15] PVL was defined as cystic PVL identified radiographically prior to discharge. Maternal characteristics including age, parity, education, and insurance were also collected.

Neurodevelopmental impairment (NDI) is typically defined as the presence of one or more of the following: moderate to severe CP, blindness, deafness, and a Bayley III cognitive score <70. As infants with severe CP, blindness and deafness were excluded, for the purposes of this study NDI was moderate CP and a Bayley III cognitive score <70. CP was defined as a nonprogressive central nervous system disorder characterized by abnormal muscle tone in at least 1 extremity and abnormal control of movement and posture. Infants with CP and a Gross Motor Function Classification of 2–3 were classified as moderate CP and 4–5 were classified as severe CP.

More than half of the children screened were already receiving Early Intervention services (n=290; 52%) because they were considered high risk due to their extreme prematurity. For those who were not, a referral was made for Early Intervention.

ASD Screening Tools

Three specific screens for ASD, the Pervasive Developmental Disorders Screening Test, Second edition (PDDST-II) Stage 2,[16] Response to Joint Attention, and Response to Name were administered by psychologists or physicians trained in these screening methods. The latter two are items adapted from items on the Autism Diagnostic Observation Scales (ADOS), a gold standard observational assessment tool for ASD, that allow for objective scoring of direct observation of the infant by the examiner. Each of these items has been used as an individual screen for ASD as early as 12–14 months. [17, 18]

There are no screening tools specifically designed for or validated in a group of extremely preterm infants. The PDDST-II, a screening tool for ASD in children 12–48 months old, includes three parent report measures designed for specific clinical settings; Stage 2 was used in this study because it is the only screen specifically designed for use in developmental clinics (such as neonatal follow-up clinics) and thus comes the closest of any screening tool available to a validated instrument in this population. It consists of 14 parent report questions with yes/no answers and was performed as an interview by the psychologists or physicians in clinic. A score of ≥ 5 was considered a positive screen. This cut point of 5 has a sensitivity of 0.73 and specificity of 0.49 for ASD, [16] similar to that reported for many other screening tools

The Response to Joint Attention item on the ADOS has been used as a screen for ASD as early as 14 and 24 months.[18] For this item the examiner uses gaze/pointing to direct the child's attention to a distant object. The child must follow the examiner's gaze/pointing by turning his/her face or eyes in the direction of the object. The child scores 0 if they follow the examiner's gaze; 1 if they follow the examiner's pointing; 2 if they look at the object when placed in front of them only; and 3 if they demonstrate no interest or awareness in the object. This item has a percent agreement between examiners of 100%, a kappa of 1.00 and an F Value for ASD of 10.71.[19] A positive screen is defined as a score of 2 or 3.

The Response to Name item has been investigated as a screen for ASD as early as 12 months, and found to have a specificity of 0.89 and a sensitivity of 0.50 for a diagnosis of ASD at 24 months.[17] For this item the examiner is positioned 3 to 5 feet from the child so that the child has to turn in order to see the examiner. While the child is engaged in free play the examiner calls the child's name up to 4 times. If the child does not respond in 4 attempts the parent is asked to call the child's name 2 times in an attempt to get his/her attention. The child scores 0 if he/she looks toward the examiner and makes eye contact on one of the first 2 attempts; 1 if the child looks towards and makes eye contact with the examiner on the third or fourth attempt, or looks towards the parent and makes eye contact; 2 if the child shifts gaze only briefly; and 3 if the child never looks towards the examiner or parent.[19] The kappa coefficient for this item is 0.88 at 12 months. [17] A positive screen is defined as a score of 2 or 3.

Statistics

Pilot data were collected on the rate of positive screen for ASD at 18 months using the PDDST-II Stage 2, Response to Joint Attention and Response to Name. Perinatal, demographic, and social factors associated with ASD in this population were compared between those with and without a positive screen. The association between positive screen and BITSEA Score, language impairment or cognitive impairment was examined using chi-

square tests for categorical variables and analyses of variance for continuous variables. Rate of positive screen was compared between English and non-English speakers.

Three logistic regression models were conducted to determine the relative contributions of demographic and medical characteristics and cognitive, language, and behavioral scores to prediction of positive ASD screens. Model 1 included neonatal, infant and maternal characteristics only, Model 2 added infant cognitive and language outcomes, and Model 3 added behavioral scores on the BITSEA. The area under the ROC curve (AUC) is helpful for assessing the explanatory power of a logistic regression model with a value of 0.50 indicating not better than chance and a value of 1.00 being perfect. The AUCs for the models were compared to assess improvement in model fit with the inclusion of the additional variables.

Results

Of the 784 children eligible for follow-up during the study period, 13 (2%) were hearing impaired, 5 (1%) were blind, and 18 (3%) had severe cerebral palsy (CP); 5 children had both severe CP and either blindness or hearing impairment. Among the remaining children, 45 (6%) were seen at follow-up but did not have data on the autism screeners and 153 (20%) were lost to follow-up). The study population consisted of the remaining 554 infants, with a mean gestational age of 25 weeks and mean birth weight of 786 grams, who were seen at 18 months and screened for ASD. Of those, 52% were male; 20% were multiples; 34% were black, 44% white and 18% Hispanic. Rates of neonatal morbidities were similar to those previously reported.[20, 21]

Compared to children who were lost to follow-up, those in the analyses were born at greater gestational age, had fewer ventilation days, were less likely to have BPD or sepsis, and had mothers with lower education ($p < .05$); there were no significant differences between the two groups by gender, multiple birth, birth weight, advanced maternal age, race, Medicaid, NEC, IVH/PVL, or length of hospital stay.

Twenty percent of infants screened positive on one or more ASD screens. (Table 1) English and non-English speakers had similar rates of positive screen ($\chi^2(1)=3.14$, $p = .076$; Table 1). There was little overlap among the 3 screens; 10% had a positive PDDST II, 6% response to name and 9% response to joint attention; 16% had only one positive screen with a rate of 3–8% for each screen; only 3% had 2 positive screens and in 1% all three screens were positive (Table 1).

The most commonly positive items on the PDDST II were: hard to get to “talk” back (31%) and walking on toes (30%) (Table 2). The least common were stopped using gestures he/she had mastered (5%) and cries when you leave but doesn’t notice when you return (6%).

Infants with one positive screen were more likely to be male and have less educated mothers.(Table 3) Infants with one or more positive screens were more likely to be white, non-Hispanic. Smaller, sicker infants were more likely to have two or more positive screens. One or more positive screen was associated with higher rates of other impairments.

Of the 7 infants for whom all 3 screens were positive, the majority (5/7) were white males. Five had elevated BITSEA Problem scores and 6 had low BITSEA Competence scores. Only 2 of these infants were cognitively impaired but all had language impairment.

The regression models are shown in Table 4. While birth weight, male gender and non-white race were associated with a positive ASD screen at 18–22 months, only male gender remained a significant predictor of positive ASD screen when cognitive and language

outcomes were added to the model. Lower cognitive and language scores on the Bayley III, higher BITSEA Problem score and lower BITSEA Competence score were associated with greater odds of a positive ASD screen. The AUCs for the models in Table 4 were: Model 1 (0.77), Model 2 (0.85), and Model 3 (0.88). The AUCs for the three models differed significantly from each other, suggesting the inclusion of the Bayley III and BITSEA scores improved the ability of the model to predict positive ASD screens beyond neonatal and maternal characteristics alone: Model 1 vs. 2 ($p < .001$), Model 1 vs. 3 ($p < .001$), and Model 2 vs. 3 ($p=.022$).

Discussion

This large, multicenter study confirms that infants born EP have high rates of screening positive for ASD. However screen positive rates on each individual screen were lower than previously reported in the literature using other ASD screens.[4–7] In fact, only 1% of infants in this cohort screened positive on all 3 screens used, a number that approximates the rate of ASD in the general population. These findings suggest that previously reported rates of ASD in EP infants may be overestimates and that EP infants may have high false-positive rates on ASD screens due to high rates of other underlying impairments.

This is the first study of EP infants to use a screen for ASD designed for a high risk population, or screening tools that involve direct observation of the child. This may contribute to the lower screen positive rates seen. These screens are quick and easy to administer, and could thus be used in any clinic setting in which EP infants are seen. Which combination of tools should be used to best screen for ASD in EP infants is not known and awaits long term follow-up studies with diagnostic confirmation.

It is interesting that the items most often endorsed on the PDDST (Table 2) are NOT those that address the core symptoms of ASD but rather those that one would expect to see more commonly in EP infants with language or motor delays. This also supports the idea that EP infants may have high rates of false positive ASD screens due to underlying language or motor impairments. However again, this is difficult to interpret without long term surveillance of this population.

The higher rates of cognitive and language impairment in those who screened positive is not surprising. Both cognitive and language impairment are well known co-morbidities of ASD. It is also not surprising that infants with more than one positive screen were more likely to have these impairments than those with only one positive screen. What is not clear is whether these findings are a result of early ASD screening tools simply identifying the wider range of developmental impairments known to exist in EP infants.

The lack of overlap among the 3 screens chosen for this study may impact future work. It is possible that each of these screens has a low sensitivity in this population and that the use of all 3 screens in combination would be necessary to keep from missing individuals with ASD. If in fact ASD is being over identified in the EP population, then it is also possible that each of these screens has a low specificity and that only those infants who screen positive on more than one will have a confirmed diagnosis of ASD. Further diagnostic assessment is needed to evaluate the sensitivity and specificity of these screens and determine the true rates of ASD in EP children.

While Limperopoulos et al[4] reported that 25% of VLBW infants screen positive on the M-CHAT and the ELGAN Study reported a screen positive rate of 21% of extremely low gestational age newborns (<28 weeks) on the M-CHAT at 2 years of age, these results are also difficult to interpret without diagnostic confirmation. After eliminating children with cognitive impairment, only 10% of ELGANs screened positive.[5, 6] But cognitive impairment

is a common co-morbidity in children with ASD. Thus eliminating infants with cognitive impairment will inevitably result in the elimination of not only infants with false positive screens, but infants with true positive screens who have both ASD and cognitive impairment.

The EPICure Study [7] is the only study to date of EP infants where an attempt was made to confirm ASD diagnosis administering a structured parent psychiatric questionnaire which was reviewed by study psychiatrists, no clinical assessment involving direct observation/ assessment of the children by a clinician was performed. Twenty nine EP (15.8%) children screened positive on the Social Communication Questionnaire (SCQ) at 11 years of age while only sixteen (8%) were identified as having ASD using a parent questionnaire.

A potential weakness of this study is the choice of screening tools. While the PDDST-II is the only ASD screening instrument specifically designed for use in developmental clinics such as a neonatal follow-up clinic, the wording is at times confusing with the potential for misinterpretation.[22] Every attempt was made to clarify parental confusion during the interview using suggestions for clarification published in the PDDST-II Manual.[16] In addition, literature supporting the use of the PDDST-II is sparse.

Another weakness is that similar to prior studies, our study lacks diagnostic confirmation. However, it was designed as a pilot to determine the rates of positive ASD screens in the EP population in order to plan for a definitive study with diagnostic confirmation at 6–7 years of age to include examination of the predictive validity of various configurations of screen items in relation to diagnostic outcome.

Conclusion

While it is clear that EP infants have high rates of communicative, social, and behavioral impairments, the long term implications of these findings require additional study. Our findings reinforce that without diagnostic confirmation, it remains unclear whether EP infants screen positive for ASD due to high rates of ASD, or due to high rates of underlying impairments leading to high rates of false positive screens. We speculate that both factors are at play. The relationships between positive ASD screen at 18 months and future diagnosis of ASD or any of the other cognitive, learning or behavioral disabilities known to impact EP infants and result in high rates of special educational needs still needs to be explored. Larger definitive longitudinal studies are needed and until they are completed, caution should be used in interpreting this or any other ASD screening procedure in this population.

Abbreviations

ASD	autism spectrum disorder
EP	extremely preterm
M	months
PDDST-II	Pervasive Developmental Disorders Screening Test, 2nd edition, Stage II
ADOS	Autism Diagnostic Observation Scales
VLBW	very low birth weight
NICHD	National Institute of Child Health and Human Development
NRN	Neonatal Research Network

Bayley III	Bayley Scales of Infant and Toddler Development III
BITSEA	Brief Infant-Toddler Social and Emotional Assessment
CLD	chronic lung disease
NEC	necrotizing Enterocolitis
PVL	periventricular leukomalacia
IVH	intraventricular hemorrhage
CP	cerebral palsy
NDI	Neurodevelopmental impairment
M-CHAT	Modified Checklist for Autism in Toddlers
ELGAN	extremely low gestational age newborns
SCQ	Social Communication Questionnaire
RN	Response to Name
RJA	Response to Joint Attention

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Table 1

Autism PDDST-II and ADOS Item Screening Results by Language Used for Administration of Screeners

Screening Results	All N (%)	English N (%)	Non-English N (%)
All Children (N=554)			
N	554	500	54
No positive screens	441 (80)	403 (81)	38 (70)
One or more positive screens	113 (20)	97 (19)	16 (30)
Positive PDDST-II	57 (10)	51 (10)	6 (11)
Positive Response to Name	34 (6)	25 (5)	9 (17)
Positive Response to Joint Attention	52 (9)	43 (9)	9 (17)
1 Positive Screen			
PDDST-II only	44 (8)	41 (8)	3 (6)
Response to Name only	15 (3)	12 (2)	3 (6)
Response to Joint Attention only	31 (6)	28 (6)	3 (6)
2 Positive Screens			
PDDST-II and Response to Name	2 (<1)	1 (<1)	1 (2)
PDDST-II and Response to Joint Attention	4 (1)	3 (1)	1 (2)
Response to Name and Response to Joint Attention	10 (2)	6 (1)	4 (7)
3 Positive Screens	7 (1)	6 (1)	1 (2)

Note: Participants were placed in the Non-English category if any screen was not administered in English.

Table 2

Percentage of Children Exhibiting Behaviors Measured by the PDDST-II Items

Item	Behavior present	
	N=554	%
Birth to 6 Months		
1. Hard to get baby to “talk” back (cooing, etc)	173	31
6 to 12 Months		
2. Avoided looking at you during feeding	51	9
12 to 18 Months		
3. Not show what he/she wanted	91	16
4. Seemed bored or uninterested in conversation	126	23
5. Interested in feeling different textures	123	22
6. Stare at his/her fingers	130	23
7. Didn’t want to do something until he/she could do it just right	106	19
18 to 24 Months		
8. Enjoys tickling and chasing but not pat-a-cake or peek-a-boo	47	8
9. Doesn’t care if you are there or not	41	7
10. Cries when you leave but doesn’t notice when you return	35	6
11. Hard time getting used to new toys	38	7
12. Walks on his/her toes	164	30
13. Became less interested in toys	53	10
14. Stopped using gestures he/she had mastered	25	5

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Table 3

Neonatal and Maternal Characteristics and 18-Month Neurodevelopmental Outcomes by Autism Screening Results

Variable	All (N=554)	No Positive Screens (N=441)	1 Positive Screen (N=90)	2 or 3 Positive Screens (N=23)	1 vs. 0 Positive Screens p	2 or 3 vs. 0 Positive Screens p	2 or 3 vs. 1 Positive Screens p
Neonatal Characteristics							
Gestational age	25 ± 1	25 ± 1	25 ± 1	25 ± 1	0.560	0.656	0.913
Birth weight	786 ± 157	786 ± 157	775 ± 145	706 ± 123	0.600	**0.017**	**0.034**
Male	287 (52)	212 (48)	61 (68)	14 (61)	< **0.001**	0.235	0.531
Multiple birth	113 (20)	95 (22)	17 (19)	1 (4)	0.567	**0.047**	0.089
BPD	272 (49)	218 (49)	42 (47)	12 (52)	0.601	0.856	0.670
NEC	43 (8)	31 (7)	9 (10)	3 (13)	0.334	0.282	0.672
Sepsis	202 (36)	154 (35)	38 (42)	10 (43)	0.194	0.407	0.913
IVH/PVL	101 (18)	79 (18)	21 (23)	1 (4)	0.231	0.093	**0.040**
Ventilation days	26 ± 24	26 ± 24	26 ± 23	37 ± 28	0.875	**0.034**	0.061
Days in hospital	107 ± 36	105 ± 34	110 ± 34	130 ± 52	0.156	**0.001**	**0.033**
Maternal Characteristics							
Maternal age > 35	89 (16)	71 (16)	14 (16)	4 (17)	0.891	0.874	0.830
Race							
Black, non-Hispanic	186 (34)	143 (32)	37 (41)	6 (26)	0.119	0.517	0.185
White, non-Hispanic	242 (44)	211 (48)	25 (28)	6 (26)	< **0.001**	**0.040**	0.871
Hispanic	102 (18)	74 (17)	21 (23)	7 (30)	0.145	0.095	0.481
Other	22 (4)	11 (2)	7 (8)	4 (17)	**0.012**	< **0.001**	0.165
Education							
Less than high school	88 (16)	61 (14)	22 (24)	5 (22)	**0.012**	0.290	0.786
High school graduate	328 (59)	266 (60)	50 (56)	12 (52)	0.402	0.437	0.771
More than high school	138 (25)	114 (26)	18 (20)	6 (26)	0.242	0.980	0.524
Medicaid	244 (44)	192 (44)	39 (43)	13 (57)	0.972	0.222	0.257
18-Month Outcomes							
Moderate CP	16 (3)	11 (2)	4 (4)	1 (4)	0.309	0.585	0.984
NDI	42 (8)	23 (5)	12 (13)	7 (30)	**0.004**	< **0.001**	0.054
Cognitive impairment (<70)	28 (5)	10 (2)	11 (12)	7 (30)	< **0.001**	< **0.001**	**0.035**

Variable	All (N=554)	No Positive Screens (N=441)	1 Positive Screen (N=90)	2 or 3 Positive Screens (N=23)	1 vs. 0 Positive Screens p	2 or 3 vs. 0 Positive Screens p	2 or 3 vs. 1 Positive Screens p
Language impairment (<70)	72 (13)	30 (7)	26 (29)	16 (70)	**< 0.001**	**< 0.001**	**< 0.001**
BITSEA Scores							
Problem Score	12 ± 7	12 ± 6	16 ± 8	15 ± 9	**< 0.001**	**0.014**	0.704
Competence Score	17 ± 4	17 ± 3	14 ± 4	12 ± 4	**< 0.001**	**< 0.001**	**0.002**
ASD-Specific Items	13 ± 4	12 ± 3	16 ± 4	19 ± 5	**< 0.001**	**< 0.001**	**0.006**

N (%); Mean ± SD

Table 4

Logistic Regression Models of One or More Positive Autism Screens by Neonatal and Maternal Characteristics and 18-Month Bayley and BITSEA Scores

	Model 1: Neonatal/Maternal		Model 2: Neonatal/Maternal + 18-Month Cog/Lang		Model 3: Neonatal/Maternal + 18-Month Cog/Lang + BITSEA	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Neonatal Characteristics						
Birth weight (kg)	**0.09 (0.01, 0.56)**	**0.010**	0.17 (0.02, 1.40)	0.099	0.14 (0.01, 1.29)	0.082
Male	**2.45 (1.48, 4.06)**	**<0.001**	**1.80 (1.01, 3.23)**	**0.047**	1.69 (0.93, 3.10)	0.087
Multiple birth	0.92 (0.49, 1.72)	0.794	0.73 (0.36, 1.48)	0.382	1.00 (0.47, 2.13)	0.994
BPD	0.69 (0.39, 1.21)	0.197	0.78 (0.41, 1.48)	0.449	0.66 (0.33, 1.29)	0.224
NEC	0.93 (0.40, 2.16)	0.873	1.14 (0.44, 2.93)	0.785	1.48 (0.55, 4.03)	0.440
Sepsis	1.05 (0.63, 1.76)	0.843	0.81 (0.46, 1.44)	0.472	0.87 (0.48, 1.59)	0.655
IVH/PVL	0.86 (0.46, 1.62)	0.640	0.70 (0.34, 1.44)	0.334	0.67 (0.32, 1.43)	0.303
Days in hospital	1.00 (1.00, 1.01)	0.158	0.99 (0.99, 1.00)	0.242	0.99 (0.99, 1.00)	0.274
Maternal Characteristics						
Maternal Age > 35	1.07 (0.55, 2.08)	0.837	0.82 (0.39, 1.73)	0.610	1.06 (0.48, 2.31)	0.892
Race						
Black, non-Hispanic	**2.07 (1.09, 3.94)**	**0.027**	1.76 (0.87, 3.55)	0.117	1.65 (0.79, 3.43)	0.183
White, non-Hispanic	ref		ref		ref	
Hispanic	1.90 (0.93, 3.89)	0.079	1.23 (0.54, 2.81)	0.619	1.27 (0.53, 3.05)	0.594
Other	**5.13 (1.64,16.01)**	**0.005**	3.43 (0.94,12.51)	0.061	3.74 (0.94,14.89)	0.061
Education						
Less than high school	ref		ref		ref	
High school graduate	0.67 (0.36, 1.25)	0.210	0.69 (0.35, 1.37)	0.289	0.79 (0.39, 1.62)	0.520
More than high school	0.51 (0.23, 1.13)	0.099	0.72 (0.30, 1.74)	0.470	0.89 (0.35, 2.28)	0.809
Medicaid	0.88 (0.53, 1.48)	0.630	0.87 (0.49, 1.54)	0.627	0.84 (0.46, 1.54)	0.571
18-Month Neurodevelopmental Outcomes						
Bayley Scores						
Cognitive score			**0.94 (0.92, 0.97)**	**<0.001**	**0.94 (0.92, 0.98)**	**0.001**
Language score			**0.95 (0.92, 0.97)**	**<0.001**	**0.96 (0.94, 0.99)**	**0.013**

	Model 1: Neonatal/Maternal		Model 2: Neonatal/Maternal + 18-Month Cog/Lang		Model 3: Neonatal/Maternal + 18-Month Cog/Lang + BITSEA	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
BITSEA Scores						
Problem Score					**1.06 (1.02, 1.11)**	**0.003**
Competence Score					**0.86 (0.78, 0.95)**	**0.002**

Note: Models also control for medical center. AUCs by model are: Model 1 (AUC=0.77), Model 2 (AUC=0.85), and Model 3 (AUC=0.88)