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Neurobehavior of very preterm infants at term equivalent age is related to early childhood outcomes

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Abstract

Aims: To describe neurodevelopmental outcomes during early childhood among infants born very preterm and define the relationships between neurobehavior of very preterm infants and neurodevelopmental outcomes at 4 years.

Methods: Forty-eight infants born ≤32 weeks gestation had neurobehavior assessed at term equivalent age using the NICU Network Neurobehavioral Scale (NNNS). Outcomes at 4 years were assessed with the Ages and Stages Questionnaire (ASQ-3), the Sensory Profile – Short Form (SF), and the Behavior Rating Inventory of Executive Function – Preschool version (BRIEF-P).

Results: At 4 years, 23 (48%) children had at least one below average score on the ASQ-3, 15 (31%) had a below average total score on the Sensory Profile-SF, and 3 (6%) had an abnormal total score on the BRIEF-P. Children with lower fine motor scores at 4 years had poorer orientation (p=.03) and self-regulation (p=.03), hypertonia (p=.01), and more sub-optimal reflexes (p=.02) as neonates. Children with lower gross motor scores at 4 years of age had more sub-optimal reflexes (p=.03) and lethargy (p=.046) as neonates. Children with tactile sensitivity at 4 years of age had poorer orientation (p=.01) and tolerance of handling (p=.03) as neonates. Children with decreased responsiveness at 4 years of age had low arousal (p=.02) as neonates, and those with poor auditory filtering at age 4 years had hypotonia (p=.03) as neonates.

Conclusion: Early neurobehavior is related to neurodevelopmental outcome in early childhood.

Keywords

development; neonatal intensive care unit; NICU Network Neurobehavioral Scale; preterm birth

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Introduction:

Preterm infants have an increased risk of neurodevelopmental impairment that is evident at term equivalent age [1]. This could be explained by smaller brain size and immature development of gyral folding and myelination of the posterior limb of the internal capsule [2]. These differences in brain structure can be early signs of an altered developmental trajectory [2]. While magnetic resonance imaging (MRI) can identify early alterations [3], brain structural variances can give the impression of permanency, rather than providing information that aids in targeting therapeutic interventions. Early neurobehavioral assessments can be an option for identification of developmental alterations among high-risk infants, especially in hospitals where MRIs can be difficult to access due to limited resources [3].

There are several neurobehavioral assessments that can be used during the neonatal period [4–7]. They can be conducted at the infant's bedside, carry little to no risk to the infant [4–8], and can isolate functional deficits so that targeted interventions can be implemented to improve outcomes. One of these assessments, the NICU Network Neurobehavioral Scale (NNNS), is a comprehensive neurobehavioral assessment that can be used with premature infants starting at approximately 34 weeks postmenstrual age (PMA), up until 6-8 weeks corrected age [4, 9]. Alterations in function have been identified in preterm infants by term equivalent age using the NNNS, meaning variations in performance are already present prior to neonatal intensive care unit (NICU) discharge [10].

There are several ways to interpret the NNNS scores. Outcome on the NNNS can be defined by using its 13 summary scores [12]. Specific NNNS summary scores, such as poorer quality of movement, more excitability, and more lethargy, have been related to a higher risk of poor developmental outcomes at age 2 years, such as cerebral palsy, cognitive challenges, motor impairment, language deficits, and global developmental delay [3, 13]. The NNNS summary scores can be clustered to form discreet profiles. Three discreet NNNS profiles have been identified in a low-risk population: social/easy-going infants, high arousal/difficult infants, and hypotonic infants [11, 12]. Infants who are social/easy-going have high mean scores for attention, self-regulation and quality of movement, and have a higher probability of optimal psychomotor outcome in early childhood. Infants profiled as high arousal/difficult demonstrate high scores for handling, arousal, excitability, and stress, and demonstrate slightly worse behavioral and adaptive skills in childhood, as well as more externalizing behaviors. Hypotonic infants are more likely to have poor psychomotor development and externalizing behaviors and have the worst outcome compared to the other two profiles [11]. Other profiles using the NNNS have also been described following latent profile analysis which considers how each summary score is in relation to the others. In a high-risk population, five distinct profiles were identified. A cluster of children categorized under profile 5 presented with decreased quality of movement, attention and self-regulation; asymmetric reflexes; and increased arousal, excitability, and hypertonicity; with average hypotonicity and lethargy. The infants categorized into profile 5 were more likely to have been born preterm and were at risk for poor behavioral and cognitive outcomes at 4.5 years [14].

While the predictive validity of the NNNS is promising, it is not well understood how individual summary scores of the NNNS at term equivalent age relate to motor or sensory outcomes or executive functioning beyond age 2 years. Although alterations in neurobehavior are evident by term age [10], several studies have shown that approximately 50% of very preterm infants will develop long-term deficits that may not be identified until later in childhood [15, 16]. Therefore, a better understanding of how early neurobehavior relates to developmental outcome is important. When alterations in function can be identified early, there is an opportunity to impact outcomes through therapeutic interventions. The objectives of this study were to 1) describe neurodevelopmental outcomes during early childhood among infants born very preterm, and 2) define the relationships between neurobehavior of very preterm infants at term equivalent age and neurodevelopmental outcomes at 4 years of age.

Methods:

This study was approved by the Washington University Human Research Protection Office, and parents signed informed consent.

In 2011, one hundred infants were enrolled as part of an overarching study that investigated the effects of different neonatal positioning devices [17]. Participants were born ≤32 weeks estimated gestational age (EGA) and were prospectively enrolled within the first week of life. The study site was the 75-bed Level III (now classified as a Level IV) NICU at St. Louis Children's Hospital. Infants were excluded if they had a suspected or identified congenital anomaly. All infants received standard of care, with one group of infants randomized to receive alternative positioning aids, rather than the standard positioning aids in use at the time [17]. All infants received standardized neurobehavioral testing at term equivalent age, between 35-41 weeks PMA, prior to NICU discharge. In 2015-16, at 4 years of age (range 3 years 11 months to 5 years 11 months chronological age), parents completed a comprehensive questionnaire, which included reliable and valid parent-report measures of developmental outcome, sensory function, and executive function. It also contained standardized and unstandardized assessments of home life, socio-demographics, and feeding.

Neurobehavior at Term Equivalent Age:

The NNNS is a 115-item comprehensive assessment appropriate for preterm infants who can tolerate handling, and it can be used until 6-8 weeks corrected age. The NNNS yields 13 summary scores: Habituation, Arousal, Self-Regulation, Orientation, Hypertonia, Hypotonia, Stress, Excitability, Lethargy, Asymmetry, Handling, Sub-Optimal Reflexes, and Quality of Movement [4]. The NNNS has been used extensively with preterm infants, and predictive validity, as well as internal consistency, have been established [4].

Neurobehavior was assessed at term equivalent age by a single examiner, who was trained and certified in the NNNS, prior to NICU discharge. The NNNS was conducted at the infant's bedside approximately 20-30 minutes before a scheduled feeding. Infants were assessed at 35 weeks PMA, when possible, and later (up until 41 weeks PMA) based on medical status, tolerance, and availability of the tester and infant. For the purpose of this study, habituation measures were not administered due to procedures of the overarching study, and therefore, only 12 summary scores were recorded [17].

Developmental Outcomes at 4 Years:

Parent-Reported Child Diagnosis/Diagnoses: The child's diagnosis/diagnoses at 4 years old was defined by the parent questionnaire. Parents identified if their child had anxiety, attention deficit hyperactivity disorder, autism spectrum disorder (ASD)/Asperger's, behavioral problems, depression, developmental delay, learning problems, obsessive compulsive disorder, social problems, asthma, cerebral palsy, failure to thrive, hearing loss/ deafness, Tourette's, vision deficits, other, or none. Parents had the option to write in their child's diagnosis, if not listed.

Developmental Outcome: The Ages and Stages Questionnaire (ASQ-3) is a 30-item parent-report measure for ages 1 month to 5 ½ years that provides information on communication, gross motor skills, fine motor skills, problem-solving, and personal-social interactions [18]. The ASQ-3 scores can be converted to percentiles, and then the child's performance is categorized as below average, average, or above average. Lower raw scores indicate poorer performance [18]. For this study, performance on each ASQ-3 domain (communication, gross motor, fine motor, problem-solving and personal-social) was dichotomized into typical (average or above average) or below average.

Sensory Processing: The Sensory Profile – Short Form (SF) is a 38-item questionnaire, for children birth to 14 years, used to assess a child's sensory processing pattern in the context of everyday life, and was completed by the child's caregiver [19]. The Sensory Profile – SF evaluates how sensory processing may be contributing to or interfering with the child's participation and can be used to inform interventions to support children in their natural environment. Summary scores (categorized as typical performance, probable difference, and definite difference compared to same-age peers) can be obtained for Tactile Sensitivity, Taste/Smell Sensitivity, Movement Sensitivity, Under Responsiveness/Seeks Sensation, Auditory Filtering, Low Energy/Weak, and Visual/Auditory Sensitivity. Lower raw scores indicate poorer performance [19]. For the purposes of this study, each summary score was dichotomized into abnormal (probable or definite differences) or typical performance.

Executive Function: The Behavior Rating Inventory of Executive Function – Preschool version (BRIEF – P) is a 63-item parent-report questionnaire used from ages 2 to 5 years 11 months to determine a child's executive functioning in the context of his or her everyday environment [20]. The BRIEF – P has 3 broad indexes: Inhibitory Self-Control (ISC) index, Flexibility index (FI), and Emergent Metacognition (EMC) index. It also has one composite score: the Global Executive Composite (GEC) [20]. *T* scores for each of the indexes and the global score can be used to interpret a child's level of executive functioning relative to the scores of children in a standardization sample. *T* scores at or above 65 are considered clinically elevated. Higher raw scores indicate worse performance. BRIEF – P indices were dichotomized as typical or clinically elevated.

Medical and Socio-demographics of the Cohort:

Baseline infant medical factors that were collected from the electronic medical record during NICU hospitalization included EGA at birth, sex, Apgar scores at one minute and five minutes, days to first and full feeding by mouth, days of oxygen therapy (which included days of ventilation, days of continuous positive airway pressure (CPAP), and delivery of oxygen via nasal cannula), presence of brain injury (defined as having either a grade III or IV intraventricular hemorrhage and/or cystic periventricular leukomalacia via routine cranial ultrasound or MRI when available), presence of necrotizing enterocolitis (NEC, all stages), confirmed sepsis, PMA at discharge, and length of stay in weeks.

Socio-demographic factors that were collected from the electronic medical record included maternal age and child's race (Black or non-Black). Additionally, caregiver employment status (full-time, part-time, not working), household income (less than $25,000 or more than $25,000), insurance type, number of siblings, the child's family living situation (child living with mother and father, child living with mother only, child living with father only, parents separated/divorced but both have custody rights, other), and maternal education level were documented at 4 years with the parent questionnaire.

Statistical Analyses

Descriptive statistics were used to define the characteristics of the cohort in addition to incidence of different diagnoses and abnormal scores on outcome measures at age 4 years. Logistic regression models were used to define the relationships between NNNS scores at term equivalent age and ASQ-3, Sensory Profile – SF, and BRIEF – P scores at 4 years of age. The 12 summary scores on the NNNS were independently evaluated for relationships to each domain score of the childhood outcome measures, as well as parent reported early childhood diagnoses. Analyses were run controlling for PMA at time of neurobehavioral testing, as PMA can impact testing outcome [10]. This was an exploratory study, and significance was defined as a p value of <0.05. Analyses were re-run controlling for randomization group (from the original study treatment allocation) to ensure there was no impact of the overarching study treatment assignment.

Results:

One hundred infants were enrolled in the overarching study. Ninety-two infants remained in the cohort at discharge after 4 withdrew and 4 expired. Of the 92 families, 48 (52% of those eligible) completed the follow-up questionnaire. In the 48 infants, neurobehavior was assessed between 35 and 41 weeks PMA (average PMA of 38.8 ± 3.5 weeks), and follow-up evaluation completed from 3 years and 11 months to 5 years 11 months (average age of 4.0 ± 0.48 years).

Table I identifies the medical and socio-demographic characteristics of the participants.

Table II describes the prevalence of abnormal NNNS summary scores in infants at term equivalent age, as well as abnormal scores on the assessments during early childhood, and describes the incidence of diagnoses in early childhood.

Table III demonstrates the relationship between NNNS scores at term equivalent age and diagnosis at age 4 years.

Table IV shows the relationships between neurobehavioral scores on the NNNS and developmental outcome measures on the ASQ-3 and Sensory Profile – SF.

Discussion:

Our findings at term equivalent age are consistent with other studies that have shown preterm infants demonstrate alterations across many neurobehavioral domains of function prior to NICU discharge [3, 10]. It validates that evidence of future developmental delays in preterm infants are present in the NICU and not something that emerges later in childhood. Signs of neurobehavioral impairment start early and can be detected with standardized assessments in the neonatal period and need not go unnoticed until the child reaches school age [22].

Although parent-reported, our finding of 49% of children born very preterm having a neurodevelopmental diagnosis (all diagnoses, excluding asthma) at age 4 years is consistent with other reports [17, 23]. Several studies have shown that approximately 50% of very preterm infants have long-term deficits that begin in infancy and become problematic in childhood [16, 17]. Neurodevelopmental delays are common in the premature population, with deficits such as severe cognitive delay, severe psychomotor delay, cerebral palsy, and neurosensory impairment being the most prevalent [23]. Our findings of 31% of preterm children having a sensory processing problem are similar to another study, which found that 37% of their sample of very preterm infants had an atypical sensory profile at ages 1 to 4 years [24]. Our study is the first study, that we know of, to investigate executive functioning in very preterm infants at age 4 years, with 6% identified as having executive function problems in this sample.

Our findings are consistent with other research that has identified relationships between early neurobehavior and developmental outcome in early childhood [15]. Research has identified the relationship between neurobehavior at term equivalent age and outcomes in toddlerhood (1 to 3 years old) [3]. Poorer quality of movement and more excitability and lethargy have been related to a higher risk of cerebral palsy, cognitive delay, motor delay, language delay, and global developmental delay at age 2 years [3, 15]. Poorer performance on behaviorally-focused scales on the NNNS, including attention, self-regulation, and lethargy, have been shown to be associated with poorer cognitive development at 2 years of age, with high excitability and poor self-regulation scores increasing the odds of cognitive delay threefold [3]. This study extends our understanding of how early neurobehavioral alterations relate to outcome in later childhood.

Our findings are consistent with other studies that have identified relationships with early neurobehavior and sensory processing disorder at age 4-6 years [25]. However, previous work identified that infants with sensory processing disorder were more likely to have suboptimal reflexes and more signs of stress [25]. We found that infants with poorer tolerance of handling and orientation demonstrated more tactile sensitivity in childhood, and infants with poorer arousal during the neonatal period later demonstrated under-responsiveness. Infants with early hypotonia had poor auditory filtering in childhood. Children with hypotonia are understood to have decreased responsiveness and require more sensory input to perceive and respond to stimuli [26]; it is possible that this additional need for sensory exposure reflects in a lower score for auditory filtering.

Our study was unable to isolate a relationship between neurobehavioral scores and executive functioning at 4 years of age. Executive functioning is considered to be a general, overarching construct that includes all supervisory or self-regulatory functions. It comprises related, yet distinct, abilities that enable intentional, goal-directed, problem solving. It organizes and directs cognitive activity, emotional responses, and overt behavior [27]. Previous literature has demonstrated the relationship between social and medical characteristics and executive functioning in early childhood at age 4 years [28], but to our knowledge, none have attempted to define its relationship to early neurobehavior in a very preterm population. Executive functioning skills begin developing shortly after birth, with a window of opportunity for dramatic growth during ages 3 to 5 [29]. However, children develop the ability to perform complex cognitive processes at varying rates, based on age and experience-related circumstances [29]. Therefore, it may be that these skills were still emerging when this cohort had executive function measures at age 4 years, making it challenging to isolate these skills and relate them to early behaviors. Additionally, novel and increasingly complex social, physical, and cognitive demands are placed on an individual throughout adolescence and adulthood [30] – therefore, the trajectory of abnormal behaviors throughout these stages would also benefit from further investigation.

There were limitations to this study. There was variability in the timing of neurobehavioral testing with infants being assessed between 35-41 weeks PMA. Performance at term equivalent age could have been confounded by the PMA and maturity of the infant at the time of assessment, as crucial developmental changes occur in the final weeks prior to term equivalent age [10]. In order to mitigate this, we controlled for PMA when performing analyses involving NNNS scores. The sample size was small, and findings from the study may not be generalized to the preterm population as a whole, as this study took place in an urban setting with 40% of the sample considered lower socioeconomic status. Additionally, participant retention rates diminished from original enrollment, with a return rate of 52%. This study used parent-report questionnaires for early childhood assessment and reported diagnoses, which is susceptible to parental bias [30]. We did not control for early therapy services, medical and sociodemographic variables, which could have influenced severity or incidence of abnormal behaviors. The timing of assessment for executive function may have limited our findings. This study relied on multiple comparisons of outcome measures, which increases the risk of type 1 error.

Conclusion:

Alterations in neurobehavior can be detected prior to NICU discharge. Early alterations in neurobehavior at term equivalent age (specifically poor orientation, tolerance of handling, and self-regulation; sub-optimal reflexes, hypertonia, hypotonia, lethargy; and low arousal) is related to poorer developmental outcomes at age 4 years. This elucidates the need for early, skilled assessment that can inform interventions to optimize outcomes of preterm infants.

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Abbreviations:

MRI	magnetic resonance imaging
NNNS	NICU Network Neurobehavioral Scale
PMA	postmenstrual age
NICU	neonatal intensive care unit
EGA	estimated gestational age
ASD	autism spectrum disorder
ASQ-3	Ages and Stages Questionnaire
SF	Short Form
BRIEF-P	Behavior Rating Inventory of Executive Function – Preschool version

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Keynotes:

- Neurobehavioral alterations can be detected in preterm infants at term equivalent age.
- Preterm infants have a high risk of neurodevelopmental impairment in childhood.
- Early neurobehavior during the neonatal period is related to poorer neurodevelopmental outcome in childhood.

Table I.

Medical and Socio-demographic Characteristics of Participants.

Child Factors (n=48)	N (%) or Mean (SD) or Median (IQ Range)
Medical Factors	
Estimated gestational age, weeks	28 (2.7)
Sex (female)	28 (58%)
Apgar scores at 1 minute	4.3 (2.6)
Apgar scores at 5 minutes	6.3 (2.1)
Number of days to 1st feed by mouth	39.8 (25.6)
Number of days to full feed by mouth	56.5 (31.3)
Number of days on oxygen	13.5 (6-69)
Mechanical ventilation, days	1 (0-2.75)
Continuous positive airway pressure, days	1 (0-2.75)
Brain injury *	7 (14%)
Necrotizing enterocolitis	1 (2%)
Sepsis	14 (29%)
Postmenstrual age at discharge, weeks	39.0 (3.5)
NICU length of stay, weeks	10.0 (6.0)
Socio-Demographic Factors	
Maternal age	25.9 (6.7)
Race (Black)	29 (60%)
Maternal education: Some college or higher **	27 (56%)
Parent employed (full-time) **	23 (48%)
Parent income **	
Less than $25,000	19 (40%)
More than $25,000	22 (45%)
Insurance type	
Private	15 (31%)
Public	30 (63%)
Family living situation **	
Number of siblings	1.2 (1.2)
Child living with mother and father	25 (52%)

* Brain injury: grade III or IV intraventricular hemorrhage and/or cystic periventricular leukomalacia.

** Collected in 4 year follow-up questionnaire.

Table II.

Prevalence of Abnormal Assessment Scores and Diagnoses.

Assessment	Mean (SD)	Infants with abnormal summary score*, N (%)
NNNS		
Orientation	3.5 (1.2)	16 (33%)
Handling	0.7 (0.3)	4 (8%)
Quality of Movement	3.2 (0.8)	5 (10%)
Excitability	5.6 (2.9)	6 (13%)
Self-Regulation	4.2 (1.0)	10 (21%)
Sub-optimal Reflexes	7.1 (2.6)	20 (42%)
Asymmetry	2.8 (2.1)	12 (25%)
Arousal	3.6 (1.1)	6 (13%)
Hypertonia	1.4 (1.2)	35 (73%)
Hypotonia	1.0 (1.1)	3 (6%)
Lethargy	7.4 (3.2)	3 (6%)
Stress	0.5 (0.5)	44 (92%)
ASQ-3		
Global Impairment Estimate		23 (48%)
Communication	49.9 (15.3)	4 (8%)
Gross Motor	47.8 (12.8)	5 (10%)
Fine Motor	39.7 (17.5)	6 (12%)
Problem-Solving	48.7 (17.9)	6 (12%)
Personal-Social	51.3 (14.1)	2 (4%)
Sensory Profile-SF		
Total Score	139.7 (52.1)	15 (31%)
Tactile Sensitivity	26.9 (10.6)	14 (29%)
Taste/Smell Sensitivity	16.4 (5.7)	3 (6%)
Movement Sensitivity	11.7 (4.7)	11 (23%)
Under Responsiveness	23.4 (10.1)	23 (48%)
Auditory Filtering	22.3 (8.4)	12 (25%)
Low Energy/Weak	22.2 (8.9)	9 (19%)
Visual/Auditory Sensitivity	17.6 (6.6)	20 (42%)
BRIEF-P		
Global Executive Composite	83.0 (26.1)	3 (6%)
Inhibit	22.5 (7.0)	5 (10%)
Shift	12.6 (4.4)	3 (6%)
Emotional Control	12.7 (3.9)	1 (2%)
Working Memory	23.2 (6.9)	7 (15%)
Planning/Organizing	14.2 (4.0)	3 (6%)
Inhibitory Self Control Index	35.3 (10.6)	4 (8%)
Flexibility Index	25.6 (7.4)	3 (6%)

Assessment	Mean (SD)	Infants with abnormal summary score*, N (%)
Emergent Metacognition Index	37.4 (10.4)	5 (10%)
Diagnoses at 4 Years		**N (%)**
Anxiety		1 (2%)
Attention Deficit Hyperactivity Disorder		2 (4%)
Autism Spectrum Disorder/Asperger's		1 (2%)
Behavioral problems		2 (4%)
Depression		0 (0%)
Developmental delay		5 (10%)
Learning problems		5 (10%)
Obsessive Compulsive Disorder		0 (0%)
Social problems		1 (2%)
Asthma		7 (14%)
Cerebral Palsy		1 (2%)
Failure to thrive		0 (0%)
Hearing loss/deafness		1 (2%)
Tourette's		0 (0%)
Vision deficits		2 (4%)
Other**		4 (8%)
None		18 (37%)
Reported more than one diagnosis		7 (15%)

The NNNS was completed at an average age of 39.0 weeks PMA

At follow-up, the children were aged from 3 years and 11 months to 5 years 11 months (average age of 4.0 ± 0.48 years).

*Abnormal scores on the NNNS are defined as those that are 2 standard deviations below the normative score of a full-term cohort (4); Abnormal scores on the early childhood assessments are defined as ≥1 SD from the mean of normative data (17-19).

**Other diagnoses included: 1 (2%) bronchitis, 1 (2%) sensory processing disorder, and 2 (4%) speech deficits.

NNNS: NICU Network Neurobehavioral Scale; ASQ-3: Ages and Stages Questionnaire; BRIEF-P: Behavior Rating Inventory of Executive Function — Preschool version.

Table III.

Relationship Between NNNS Scores and Diagnoses at 4 Years of Age.

	Diagnoses at 4 Years of Age P Value*			
NNNS	Cerebral Palsy	ASD/Asperger's	Anxiety	Social Problems
Stress		0.03 *	0.03 *	0.03 *
Handling	0.01 *			
Sub-optimal Reflexes	0.046 *			
Hypertonia	0.049 *			

At follow up the children were aged from 3 years and 11 months to 5 years 11 months (average age of 4.0 ± 0.48 years).

* P value is from investigating relationships between NNNS summary scores and diagnoses using logistic regression analyses (p<.05). There were no other significant relationships between NNNS summary scores and diagnoses.

NNNS: NICU Network Neurobehavioral Scale.

Table IV.

Relationships Between Neurobehavioral Scores and Developmental Outcome.

	ASQ-3 P Value* β, 95% CI			Sensory Profile P value* β, 95% CI		
NNNS	Gross Motor	Fine Motor	Problem Solving	Tactile Sensitivity	Under Responsiveness	Auditory Filtering
Orientation	.06	.03* (β=3.6) [.99, 13.2]	.048* (β=3.1) [.92, 10.4]	.01* (β=.36) [.14, .88]	.55	.53
Handling	.29	.96	.79	.03* (β=.48) [.13, .83]	.52	.56
Self-Regulation	.45	.03* (β=2.6) [.73, 9.2]	.39	.58	.94	.86
Sub-optimal Reflexes	.03* (β=.45) [.22, .90]	.02* (β=.47) [.25, .87]	.10	.53	.98	.61
Arousal	.11	.35	.37	.48	.02* (β=.50) [.25, .97]	.13
Hypertonia	.44	.01* (β=.55) [.26, 1.2]	.10	.35	.58	.29
Hypotonia	.31	.59	.34	.99	.18	.03* (β=2.4) [1.0, 5.5]
Lethargy	.046* (β=.66) [.44, .99]	.51	.23	.07	.35	.81

*p value is from investigating relationships between NNNS summary scores and outcome assessment scores while controlling for PMA at the time of assessment using logistic regression analyses ($p<.05$).

NNNS: NICU Network Neurobehavioral Scale; ASQ-3: Ages and Stages Questionnaire.