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Early Infant Attention as a Predictor of Social and Communicative Behavior in Childhood

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Abstract

Background: The objective was to determine whether infant neurobehavior measured at five post-gestational weeks could predict social and communicative behavior (SCB) through five and eight years.

Methods: Infant neurobehavior was assessed using the Neonatal Intensive Care Unit Network Neurobehavioral Scale, and SCB was measured using the Social Responsiveness Scale (SRS). Adjusted linear regression with generalized estimating equations were employed to estimate the association between infant neurobehavior and SCB. Interaction terms and stratification were used to identify potential effect modification by autism spectrum disorder risk factors.

Results: The analyses include $n = 214$ and $n = 227$ participants who were examined at 5 weeks and followed to 4/5 and 8 years, respectively. Adjusting for maternal age, race, parity, and education as well as gestational age, only the Neonatal Intensive Care Unit Network Neurobehavioral Scale summary score of "attention" (measured at mean 43.9 gestational weeks) was inversely associated with total SRS T-score through 5 years. However, in analyses stratified by maternal age, the inverse association between "attention" and SCB was significant, but only among offspring of women of advanced maternal age (≥35 y); in addition, higher scores of "excitability," "lethargy," and "arousal" were associated with increased total SRS T scores among women of advanced maternal age. The associations were no longer statistically significant at 8 years.

Conclusions: Newborns with lower scores on the attention subscale (determined by an ability to localize and track animate and inanimate objects) were more likely to demonstrate deficits in SCB. In addition, infants with increased excitability, lethargy, or increased arousal were more likely

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to have impaired SCB that persisted through 5 years, but not at 8 years of age. Further work is necessary to identify specific aspects of infant neurobehavior that may affect childhood SCBs.

Keywords

Infant neurobehavior; social and communicative behavior; longitudinal

Introduction

Developmental delays and disabilities affect around 13–15% of children in the United States (Boyle et al., 2011; Centers for Disease Control and Prevention, 2014; Rosenberg, Zhang, & Robinson, 2008). Autism spectrum disorder (ASD) alone is now estimated to affect around 1 in 68 children in the United States, and the number of diagnosed cases continues to rise (Centers for Disease Control and Prevention, 2014). Capturing impairments early in development is crucial for initiation of behavioral interventions. Although having a developmental disability may present life-long challenges in social interaction and eventual independence, evidence suggests that early and intensive intervention can lead to substantially better developmental outcomes (Barnett, 2011; Myers & Johnson, 2007; Spittle, Orton, Doyle, & Boyd, 2007). Due to the timing of neural development and brain plasticity, early intervention provides the greatest possibility for optimal social skill development (Dawson & Zanolli, 2003), and early detection of infants at risk for ASD and other developmental disabilities may offer opportunities to intervene and alter the course of early brain development (Dawson, 2008).

The importance of stability and prediction of infant characteristics to later child development has been reviewed extensively by Bornstein (2014). Although development is often described by maturation and other forms of change, certain characteristics may be stable over time. Heterotypic stability (also referred to as "predictive validity") exists when two related, but not identical characteristics sustain a rank order between two time points. If heterotypic stability exists between two constructs, measurements taken in infancy can be used to predict later related traits. Also reviewed is the vast literature that exists describing infant factors associated with later development of communication and social development; however, few studies assess infant behavior less than three months of age (Bornstein, 2014). Although a broad literature describing autistic symptoms among high risk siblings (children of parents who have one or more children previously diagnosed with ASD) (Rogers, 2009) also exists, it is unclear whether these findings are generalizable to normal risk infants and children. Several studies have evaluated the association between Apgar score and association with later autism. A recent systematic review of the literature identified suboptimal 5-min Apgar scores (<7) as a risk factor for autism (Guinchat et al., 2012). However, the Apgar score is a measure of tolerance to the birthing process as well as adjustment outside the womb and was not developed to make predictions of later child development. Therefore, prediction may be limited to select ASD etiologies or more severe cases. Other work has evaluated the predictive ability of comprehensive neonatal assessments on later cognitive outcomes (Canals, Hernández-Martínez, Esparó, & Fernández-Ballart, 2011; Domsch, Lohaus, & Thomas, 2009); however, associations with neonatal assessments and later social and communicative behaviors (SCBs) is limited. Our goal was to determine whether newborn neurobehavioral assessments can identify children who are at risk for social and communicative neurodevelopmental outcomes in an unselected (low-risk) population. The objective of the present study was to determine whether a direct measure of infant neurobehavior, which includes measurements of individual domains of neurobehavior and has been associated with later developmental outcomes, may predict later SCB. To capture SCB in a low-risk population, we employed the Social Responsiveness Scale (SRS) (Constantino & Todd, 2003). The SRS is an instrument that was developed to measure the social aspects of ASD. SCB is best conceptualized as a spectrum of language and social dysfunction, rather than a "present" or "absent" diagnosis. Therefore, a quantitative scale, such as the SRS, appropriately captures the continuum of social and communicative impairment. The SRS is a valid and reliable instrument, and it provides a quantitative measure of severity of SCB. Of particular relevance to the present analyses is the capability of detecting symptoms below the threshold for diagnoses of an ASD (Constantino & Todd, 2003). Although it would also be of interest to associate infant neurobehavior to a diagnosis of ASD, due to the low prevalence of ASD, the efficiency would be greatly reduced in a longitudinal analysis.

The Neonatal Intensive Care Unit (NICU) Network Neurobehavioral Scale (NNNS) was designed to assess multiple aspects of neurobehavior in normal and at-risk infants (Lester, Tronick, & Brazelton, 2004). Prior studies identified statistically significant associations between NNNS profiles and developmental outcomes measured at 1, 3 (Sucharew, Khoury, Xu, Succop, & Yolton, 2012), and 4.5 years (Liu et al., 2010); however, questions remain regarding the relationship between NNNS performance and later development of certain autistic features, specifically the core social deficits that distinguish ASD.

Our hypothesis was that neurobehavior in 4–5-week-old infants, measured using the NNNS, can predict interpersonal behavior, communication, and repetitive behaviors at ages 4, 5, and 8 years. In addition, prediction may be stronger among women who have risk factors for social impairment. Both maternal depression (Daniels et al., 2008) and advanced maternal age at conception are risk factors for having a child with ASD (Shelton, Tancredi, & Hertz-Picciotto, 2010). We therefore determined whether the association between infant behavior and SCB was stronger among mothers who were ≥35 years of age or those who had experienced depression in pregnancy.

Methods

Study Participants

Analyses were conducted within the Health Outcomes and Measures of the Environment (HOME) Study, a prospective birth cohort from the greater Cincinnati, Ohio metropolitan area. Details of HOME Study enrollment and study procedures have been described in detail previously (Braun et al., 2016). Briefly, the study was designed to determine the contribution of low-level environmental chemical exposures to child health and development (Dietrich et al., 2005). Healthy women were enrolled during pregnancy (16–19 weeks) between March 2003 and January 2006. Of the 468 enrolled women, 389 remained in the study and delivered live singleton infants. Medical records were obtained in the delivery hospital to complete chart reviews for both mother and infant. Home visits were conducted at approximately five weeks and annually through age three. Standard questionnaires were used to assess exposure to environmental chemicals, nutritional intake, medical history, respiratory health, development, behavior, supervision practices, and residential injuries. Clinic visits were completed annually through age five and again at age eight to administer developmental assessments and to collect anthropometrics, biologic specimens, and parent surveys. Institutional review boards of all the research institutions, hospitals, and laboratories that were involved approved the study protocol. Written informed consent was obtained from each participant.

Infant Neurobehavior

Infant neurobehavior was measured using the NNNS (Lester et al., 2004). The NNNS measures three primary components of neurobehavior:

- CNS integrity and neurological functions, such as active and passive tone and primitive reflexes;
- Infant behavior to assess neurologic states as well as sensory and interactive responses; and
- Signs of stress that can manifest as overt or subtle signals during the course of the examination.

The exam draws on previous validated infant examinations (in particular, the Neonatal Behavioral Assessment Scale; Brazelton, Nugent, & Lester, 1987), but has had a standardized administrative format developed to minimize the effect of the examiner from the assessment, providing a greater focus on the infant, rather than the infant-examiner relationship (Lester et al., 2004). There are 115 individual test items. Summary scores were developed using a combined conceptual and statistical approach to aggregate scores from the individual NNNS items to describe 13 dimensions of neurobehavior: habituation, attention, arousal, self-regulation, special handling required to acquire orientation items (from this point on referred to as "handling"), movement quality, excitability, lethargy, non-optimal reflexes, asymmetrical reflexes, hypertonicity, hypotonicity, and signs of stress. For all subscales, higher scores reflect a greater tendency toward that dimension regardless of whether it is a positive or negative trait. Although the exam was developed for high-risk infants, it is appropriate for all infants regardless of risk for neurobehavioral deficits (Lester et al., 2004). The NNNS exam can be administered to infants at 32–48-weeks gestational age. In the HOME Study, the NNNS was administered during a home visit at 4–5 weeks after delivery. The approximately 30-min exams were completed by examiners trained and certified to a reliable standard. Eighty-nine percent of the time, the exams were performed in a room separated from the mother. In all instances, examiners insured distractions were minimized (Yolton et al., 2011).

Autistic Behaviors

Autistic behaviors were measured with the SRS completed by mothers during the 4, 5-, and 8-year–study clinic visits. The 65-item Likert scale is completed in 10–15 min. Raw scores are summarized and transformed into a standardized T score (with a mean of 50, SD of 10). A higher score indicates more ASD symptomology. In addition to the total measure of social deficits, subscales and the associated T scores are provided to describe social awareness, social cognition, social communication, social motivation and restricted interests, and repetitive behavior.

Statistical Analysis

Baseline characteristics and NNNS summary scores were summarized, using means and SDs of continuous variables and the number and percent for categorical variables, and were presented for three groups:

- All participants who had received the NNNS assessment,
- Participants who had had the NNNS assessment plus those who had had the SRS at ages 4 or 5 years (grouped together given the close temporal proximity), and
- Those participants who had had the NNNS and SRS measures at 4, 5, or 8 years.

Means and SDs were used to summarize total and domain-specific SRS raw scores at 4, 5, and 8 years. Associations between NNNS summary scores and total and subscale SRS standardized T scores were estimated with generalized linear regression models with generalized estimating equations to address correlation of the repeated measures of the SRS outcomes. We considered the following potential confounding variables: birth weight (grams), race category (black, white, other), parity (nulliparous, 1 prior birth, >1 prior birth), maternal education (>, < = high school education), and maternal age at infant delivery (years). The models additionally adjusted for the gestational age at the time of NNNS assessment (weeks) to account for both gestational age at birth and actual age at exam. As a secondary analysis, we examined the association between NNNS scores and an SRS total T score ≥ 60 (a T score of 60–75 is interpreted as representing mild to moderate autistic symptoms). We explored potential effect modification with known risk factors for ASD, in particular maternal depression (Beck depression inventory of ≥19; moderate or severe depression) or <19; mild or minimal depression), and advanced maternal age (≥35 or <35 years), using interaction terms and stratification.

Results

Among the 355 mothers whose singleton infants had the NNNS completed at 4–5 weeks, 214 also completed the SRS at 4 or 5 years, and 227 completed the SRS at 8 years. The results of the SRS across years were significantly (p value < 0.001) correlated (between years 4 and 5 r = 0.69, between years 4 and 8 r = 0.66 and between years 5 and 8 r = 0.72). Nine of the 13 NNNS summary scales were available for the present analysis. The habituation scale must be completed when the infant is sleeping and was omitted from our analysis as in previously published analyses (Sucharew et al., 2012; Yolton et al., 2009). Low variability of scores for scales measuring asymmetrical reflexes, hypertonicity, and hypotonicity resulted in their omission from the analysis. Baseline characteristics and mean NNNS summary scores with SDs are shown in Table 1 for the infants who completed the NNNS (n = 355) and for the two analytic populations (4 or 5 years, n = 214; 4, 5, or 8 years, n = 227). All characteristics and scores were comparable between groups. In addition, means and SDs were very comparable to an independent study of healthy newborns assessed using the NNNS (Fink, Tronick, Olson, & Lester, 2012). Note that normative data have not been published for healthy infants at age 4–5 weeks, even though this is the typical time period for application of the assessment in the literature. Means and SDs of raw SRS scores are presented in Table 2.

Results through Year 5

Following adjustment for maternal age at delivery, birth weight, race category (black, white, other), parity, gestational age at NNNS exam, and maternal education (≥ or < a high school education), we found that lower scores for NNNS attention were associated (borderline significance) with higher (more autistic) total SRS T scores at 4 or 5 years $\beta = -0.75$ (p value = 0.06; Table 3). Lower attention was also significantly associated with higher SRS scores on social awareness, social communication, and mannerisms subscales. The mean (SD) attention scores for individuals with a SRS total T score ≥ 60 and <60 were lower than the attention scores for children with total T scores <60, 5.1 (1.4) vs. 5.4 (1.4), data not shown. In addition, the odds ratio (OR) describing the association between "attention" and total SRS T score ≥60 was $OR = 0.69$ (95% CI: 0.54, 0.89), suggesting higher odds of a high SRS T score (≥60) with decreasing scores on the "attention" subscale of the NNNS.

The associations between the NNNS summary scores and SRS total T scores at 4 or 5 years did not differ by moderate to severe maternal depression (≥19 vs. <19 on baseline Beck Depression Inventory), but did vary by maternal age at delivery (Table 4). For the subset of children who were born to women that were 35 years and older at the time of delivery (n = 31), the association between the lower attention summary score and higher SRS total T scores was stronger and statistically significant ($\beta = -2.1$ (p value = 0.02) for older mothers versus for mothers <35 years at delivery ($\beta = -0.23$ (p value = 0.63). Additional significant associations were observed only among older women for the summary scales describing excitability, lethargy, and arousal (borderline, $p = 0.05$), all positively associated with SRS total T score and regulation which was negatively associated. Finally, lower regulation scores were associated with higher SRS total T scores, although with borderline statistical significance.

Results through Year 8

In analyses that additionally included SRS scores measured at 8 years, the association between infant attention and SRS Total T score was attenuated, though the direction of the association remained consistent ($\beta = -0.60$ (p value = 0.12). No other NNNS subscales were significantly associated with SRS total T scores through 8 years in the adjusted models. As with the main effects, although a similar pattern remained at 8 years, the associations were no longer statistically significant.

Discussion

In this study of early infant neurobehavior and the association with SCB at 4, 5, and 8 years of age, we identified an inverse association between a measure of infant attention and overall SCB as well as specific subscales of social awareness, communication, and mannerisms at 4 or 5 years among women of advanced maternal age; however, the associations were no longer statistically significant through 8 years. We observed a stronger, and statistically significant inverse association at 4 or 5 years among children born to women who were of advanced age at the time of delivery (≥35 years). In addition, among this subset of children, three additional aspects of infant neurobehavior—excitability, lethargy, and arousal—were significantly associated with later SCB. As with the main effects, the effect modification by maternal age was no longer significant through 8 years.

The NNNS attention summary scale is a measure of the ability to localize and track animate and inanimate objects (Liu et al., 2010). Impairment in attention is widely recognized among children who have ASD, beginning with the original report by Kanner describing symptoms of inattention and hyperactivity (Kanner, 1943). The exact nature of the relationship between attention and ASD is unclear. A lack of joint attention has been recognized as a feature of young children who are diagnosed with or develop ASD. On attention tasks, such as orienting to auditory stimuli, children with ASD perform poorer when the stimuli are social in nature (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998). These associations have also been observed in infants one year of age and younger. In a study comparing first-birthday-party videos of children who were typically developing and those later diagnosed with ASD, impairment in joint attention was one of the three general areas that differed between groups (Osterling & Dawson, 1994). A similar study determined that children with ASD less frequently orient (attend) to their name (Werner, Dawson, Osterling, & Dinno, 2000). Similarly, toddlers and young children with ASD show preferences for attending to geometric objects versus social scenes during eye-tracking studies. For example, Shic et al. observed that toddlers with ASD, when shown videos with social interaction scenes, focused more on objects in the background and gave less attention to the social interaction compared with typically developing children and children with non-ASD developmental delays (Shic, Bradshaw, Klin, Scassellati, & Chawarska, 2011). These observations are somewhat consistent with our overall observation that decreased attention is associated with higher SRS scores. Contrary to our findings, some studies have reported superior attentive skills among individuals with ASD (Grant & Davis, 2009). Because this was a normal risk population and did not specifically include children with ASD, we were limited in our ability to observe more subtle associations or any differences between orientations to animate versus inanimate stimuli.

Although no other associations between NNNS and SRS at 4 or 5 years reached statistical significance in this sample, the directions of the non-significant associations were most often consistent with our a priori beliefs. For example, increased NNNS excitability and handling (special handling required to acquire orientation items) were positively associated with higher total SRS T scores, whereas increased regulation was associated with lower total SRS T scores.

When modeled through year 8, the modest association between infant attention at 5 weeks and SRS total scores at 4 or 5 years did not remain. We are unsure what might explain this attenuation in the association. It is important to note that these analyses were conducted within a low risk population in which behaviors may be less overt and exhibit more plasticity across time. One future direction for this work is to determine whether neurobehavior among high risk infants may be more strongly associated with later SCB and whether that association may sustain over time.

Among children born to women of advanced maternal age (≥35 years), we observed an association between attention and SRS total scores at 4 or 5 years that was not statistically significant among women < 35 years. We also observed a significant association between both lethargy and arousal during infancy and later developing SCB. Although together these findings seem counter-intuitive, as lethargy and arousal seem to be contradictory responses, one explanation is that they represent a general mode of inappropriate reaction to stimuli. The response to stimuli may manifest as an over- or under-reaction. In fact, this finding is concordant with a prior study that evaluated infant home movies of children later diagnosed with autism (Adrien et al., 1991). In this study, the authors observed either elevated excitability or greater passivity among children who would later develop autism. As with the association between attention and SRS scores, these associations did not remain statistically associated with SRS T scores through 8 years.

Although we found no additional statistically significant results, the majority of associations were observed in the direction that we hypothesized a priori. For example, greater excitability, higher stress response, more lethargy, and greater need for handling to complete the exam were all positivity associated with more SCB impairment at 4, 5, and through 8 years, whereas lower attention, poorer quality movements and reflexes, and poorer regulation were also non-statistically significantly associated with higher SCB. Again, it is likely that because this was not a sample with ASD, and because the sample size was relatively small, we were unable to observe statistically significant associations because the effects were subtle. Similar analyses within a high risk population (for example, infant siblings of children with ASD) may provide additional insight.

Limitations to the present study should be acknowledged. The results are presented without any correction for multiple testing. There were a large number of statistical tests conducted and the results would not have remained significant if they were adjusted for multiple testing. These analyses were exploratory in nature, and replication in an independent sample would provide the best evidence that the observed associations were not the result of type-I error. Further, the sample size was quite small, especially for stratified analyses; this may have hindered our ability to identify additional effect modification by ASD risk factors. In addition, though the association between attention and total SRS T scores was significant among mothers of advanced maternal age and not mothers <35 years, the interaction term was not significant. Recent findings suggest that SRS scores may not be specific only to autistic traits and may be influenced by behavioral problems and levels of expressive language and cognition (Hus, Bishop, Gotham, Huerta, & Lord, 2013), which were not considered in the analyses. Finally, the SRS is a parent-reported assessment and children have not received a clinician-directed assessment, such as the Autism Diagnostic Observation Schedule. Regardless, these results are highly suggestive of an effect that should be examined more closely. There are some noteworthy strengths of the study as well. The analyses were conducted within a prospective birth cohort, and therefore, infant neurobehavior was assessed with no knowledge of later developmental outcomes. An additional strength was the repeated assessment with the SRS for a majority of the participants. Although the correlation between the years 4 and 5 total T scores was quite high, we were able to capture the variability by incorporating the repeated outcomes.

Conclusion

In summary, an early measure of infant attention at five post-gestational weeks was significantly associated with the later development of SCBs through 5 years, but not through 8 years. Among women of advanced maternal age, the association was stronger and statistically significant, and additional associations representing an inappropriate response to stimuli manifested as excitability and lethargy were also associated with SCBs through 5 years. These results are preliminary in nature, particularly given the lack of correction for multiple testing. Although these results should be replicated in independent samples, they provide evidence that the impairment that underlies ASD may be evident in very early infancy.

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Table 1.

Demographic characteristics and NNNS summary cores for participants with completed SRS measures through 5 and through 8 years.

	Participants with NNNS (*n* = 355)	Follow-up through 5 years (*n* = 214)	Follow-up through 8 years[b] (*n* = 227)
Maternal characteristics at baseline [a]			
Maternal age at delivery (years)	29.7 (5.7)	29.6 (5.6)	29.3 (5.9)
Race (African American)	107 (30.1)	64 (29.9)	74 (32.6)
Married	237 (66.8)	148 (69.2)	147 (64.7)
Household Income, midpoint ($K)	59.5 (41.8)	59.5 (40.5)	57.4 (41.8)
Employed during pregnancy	293 (82.5)	183 (85.5)	192 (84.6)
Baseline Beck Depression Inventory	9.6 (6.8)	9.4 (6.4)	9.8 (6.3)
Never drank alcohol during pregnancy	196 (55.2)	125 (58.4)	124 (54.6)
Daily cigarettes smoked in pregnancy	0.5 (2.2)	0.4 (2.2)	0.5 (2.4)
Maternal max serum cotinine delivery (ng/mL)	6.6 (32.3)	4.7 (28.1)	6.2 (30.5)
Infant characteristics			
Male	166 (46.8)	95 (44.4)	98 (44.8)
Birth weight (grams)	3388.4 (611.7)	3380.8 (621.8)	3314.5 (637.2)
Ponderal index	2.5 (0.3)	2.5 (0.3)	2.5 (0.3)
Gestational age (weeks)	39.0 (1.7)	39.1 (1.7)	38.9 (1.9)
Gestational age <37 weeks	31 (8.7)	17 (7.9)	23 (10.1)
Gestational age at exam (weeks)	43.9 (2.0)	43.9 (2.0)	43.8 (2.1)
Nulliparous	155 (43.7)	103 (48.1)	104 (45.8)
NICU stay (yes)	17 (4.8)	11 (5.1)	15 (6.6)
NNNS summary scale scores			
Attention	5.4 (1.4)	5.4 (1.4)	5.3 (1.4)
Regulation	5.5 (0.8)	5.5 (0.8)	5.5 (0.81)
Quality of movement	4.8 (0.6)	4.8 (0.6)	4.8 (0.6)
Habituation[c]	6.3 (2.0)	6.2 (2.1)	6.1 (2.0)
Lethargy	4.2 (1.7)	4.1 (1.8)	4.2 (1.7)
Asymmetric reflexes	1.3 (1.1)	1.2 (1.1)	1.2 (1.1)
Excitability	2.4 (2.0)	2.4 (2.0)	2.4 (2.0)
Handling	0.4 (0.3)	0.45 (0.31)	0.45 (0.31)

	Participants with NNNS (n = 355)	**Follow-up through 5 years (n = 214)**	**Follow-up through 8 years[b] (n = 227)**
Non-optimal reflexes	3.9 (1.7)	4.0 (1.6)	3.9 (1.6)
Hypertonia	0.04 (0.20)	0.04 (0.21)	0.04 (0.2)
Hypotonia	0.27 (0.52)	0.28 (0.55)	0.26 (0.52)
Stress abstinence	0.1 (0.05)	0.13 (0.05)	0.13 (0.06)
Arousal	4.2 (0.7)	4.2 (0.7)	4.1 (0.7)

Note. NNNS Domains Scale range: Attention, Regulation, Quality of Movement, Habituation, Arousal = 1–9; Hypertonia, Hypotonia 0–10; Lethargy, Excitability, Non-optimal Reflexes = 0–15; Asymmetric Reflexes = 0–16; Handling, Stress Abstinence = 0–1.

[a] Values presented are means (SDs) for continuous variables and numbers (percent) for categorical variables.

[b] Attended 8-year visit regardless of attendance at 4- or 5-year visit.

[c] Infants must be asleep for this task, reducing the number of available results (n = 20 at through 5 y; n = 16 at 8 y).

NNNS: Neonatal Intensive Care Unit Network Neurobehavioral Scale; NICU: Neonatal Intensive Care Unit; SRS: Social Responsiveness Scale; *n*: number; y: years; ng/mL: nanograms per milliliter; $K: US dollars in thousands; SDs: standard deviations.

Table 2.

Means and SDs of raw total and domain-specific SRS scores at years 4, 5, and 8 as well as the number and percent of participants scoring above cut-points.

	4 years	5 years	8 years
n	186	206	227
Total	30.7 (15.3)	30.6 (20.0)	31.3 (21.9)
>65	9 (4.8)	21 (10.2)	25 (11.0)
≥76	3 (1.6)	4 (1.9)	6 (2.6)
Awareness	6.7 (2.8)	6.3 (2.7)	6.4 (3.0)
Cognition	5.9 (3.9)	6.3 (4.4)	5.9 (4.7)
Communication	9.3 (5.7)	9.5 (7.3)	9.6 (8.0)
Motivation	5.3 (3.5)	5.0 (4.2)	5.4 (4.4)
Mannerisms	3.3 (3.0)	3.5 (4.2)	3.9 (4.5)

Note. SRS range raw scores: Total score = 0–195, Awareness = 0–24, Cognition = 0–36, Communication = 0–66, Motivation = 0–33, Mannerisms = 0–36. Sample sizes by year: 4 years, *n* = 214; 5 years, *n* = 227.

SDs: standard deviations; SRS: Social Responsiveness Scale.

Table 3.

Beta-coefficient (p value) describing the association between NNNS summary at 4–5 weeks and SRS total and subscale T scores through 5 and through 8 years.

	Through 5 years				Through 8 years			
	Total SRS *T* score							
NNNS summary scale	***n***	**Median (quartile range)**	**β (*p* value)**	**Confidence Interval**	***n***	**Median (quartile range)**	**β (*p* value)**	**Confidence interval**
Attention	203	5.3 (2.1)			213	5.3 (1.9)		
Unadjusted			−0.55 (0.21)	−1.42, 0.32			−0.55 (0.19)	−1.36, 0.27
Adjusted[a]			−0.75 (0.06)	−1.54, 0.04			−0.60 (0.12)	−1.34, 0.15
Excitability	214	2.0 (3.0)			227	2.0 (3.0)		
Unadjusted			0.51 (0.08)	−0.06, 1.09			0.56 (0.05)	−0.01, 1.13
Adjusted			0.44 (0.11)	−0.11, 0.98			0.37 (0.18)	−0.18, 0.93
Handling	210	0.38 (0.63)			222	0.44 (0.63)		
Unadjusted			−0.22 (0.91)	−4.16, 3.74			0.07 (0.97)	−3.74, 3.89
Adjusted			0.72 (0.69)	−2.86, 4.32			0.57 (0.76)	−3.06, 4.20
Lethargy	214	4.0 (2.0)			227	4.0 (0.63)		
Unadjusted			0.33 (0.34)	−0.35, 0.99			0.27 (0.40)	−0.37, 0.91
Adjusted			0.41 (0.18)	−0.20, 1.02			0.31 (0.29)	−0.26, 0.89
Quality of movement	214	4.8 (0.67)			227	4.8 (0.77)		
Unadjusted			−2.1 (0.04)	−4.09, −0.04			−2.33 (0.02)	−4.35, −0.32
Adjusted			−0.73 (0.45)	−2.62, 1.16			−0.99 (0.30)	−2.86, 0.87
Regulation	211	5.6 (1.1)			226	5.5 (1.1)		
Unadjusted			−1.22 (0.09)	−2.65, 0.21			−1.19 (0.12)	−2.68, 0.31
Adjusted			−0.95 (0.18)	−2.33, 0.43			−0.74 (0.31)	−2.16, 0.68
Non-optimal reflexes	214	4.0 (2.0)			227	4.0 (2.0)		
Unadjusted			−0.60 (0.09)	−1.28, 0.09			−0.67 (0.05)	−1.35, 0.01
Adjusted			−0.43 (0.20)	−1.08, 0.23			−0.52 (0.13)	−1.18, 0.15
Stress abstinence	214	0.1 (0.06)			227	0.12 (0.06)		
Unadjusted			12.2 (0.38)	−14.8, 39.15			23.2 (0.04)	0.94, 45.50
Adjusted			8.9 (0.349)	−16.7, 34.6			13.2 (0.22)	−8.02, 34.5
Arousal	214	4.0 (1.0)			227	4.0 (1.0)		

	Through 5 years				Through 8 years			
	Total SRS *T* score							
NNNS summary scale	*n*	Median (quartile range)	β (*p* value)	Confidence Interval	*n*	Median (quartile range)	β (*p* value)	Confidence interval
Unadjusted			0.53 (0.53)	−1.11, 2.16			0.93 (0.30)	−0.82, 2.68
Adjusted			0.47 (0.55)	−1.06, 2.01			0.64 (0.46)	−1.06, 2.33

[a]Models adjusted for: maternal age at delivery (year), birth weight (grams), race category (black, white, other), parity (nulliparous, 1 prior birth, >1 prior birth), gestational age at NNNS exam (days), education (greater than high school education).

NNNS: Neonatal Intensive Care Unit Network Neurobehavioral Scale; SRS: Social Responsiveness Scale; *n* = number.

Table 4.

Adjusted association between NNNS summary at 4–5 weeks and Total SRS *T* Score through 5 years and though 8 years stratified by maternal age (<35 years and ≥35 years).

NNNS summary scale	Through 5 years				Through 8 years			
	Mothers < 35 years, *n* = 183 *β*(*p* value)	Confidence interval	Mothers ≥ 35 years, *n* = 31 *β*(*p* value)	Confidence interval	Mothers < 35 years, *n* = 193 *β*(*p* value)	Confidence interval	Mothers ≥ 35 years, *n* = 34 *β*(*p* value)	Confidence interval
Attention	−0.23 (0.63)	−1.16, 0.70	−2.14 (0.02)	−4.00, −0.31	−0.34 (0.40)	−1.1, 0.45	−1.88 (0.11)	−4.16, 0.40
Excitability	0.30 (0.31)	−0.28, 0.89	1.30 (0.04)	0.06, 2.542	0.29 (0.33)	−0.29, 0.86	1.45 (0.10)	−0.25, 3.16
Handling	0.34 (0.86)	−3.58, 4.27	2.79 (0.57)	−6.86, 12.44	0.83 (0.65)	−2.80, 4.45	−0.32 (0.96)	−13.64, 13.00
Lethargy	0.06 (0.86)	−0.60, 0.72	2.03 (0.02)	0.26, 3.79	−0.001 (0.99)	−0.60, 0.60	2.45 (0.03)	0.30, 4.61
Quality of movement	−1.59 (0.13)	−3.64, 0.45	−0.13 (0.97)	−6.90, 6.63	−1.58 (0.10)	−3.45, 0.29	1.72 (0.65)	−5.70, 9.15
Regulation	−0.75 (0.28)	−2.13, 0.62	−5.16 (0.04)	−10.15, −0.18	−0.55 (0.42)	−1.88, 0.78	−4.72 (0.11)	−10.42, 0.99
Non-optimal reflexes	−0.48 (0.20)	−1.22, 0.26	0.17 (0.86)	−1.81, 2.16	−0.71 (0.05)	−1.41, −0.01	0.98 (0.41)	−1.35, 3.30
Stress abstinence	−0.18 (0.99)	−24.21, 23.84	70.66 (0.14)	−23.84, 165.16	9.52 (0.36)	−11.13, 30.19	70.4 (0.14)	−21.95, 162.71
Arousal	−0.22 (0.78)	−1.80, 1.35	4.23 (0.05)	−0.10, 8.56	0.10 (0.89)	−1.41, 1.62	4.41 (0.17)	−1.90, 10.71

Note. Models adjusted for: birth weight (grams), race category (black, white, other), parity (nulliparous, 1 prior birth, >1 prior birth), maternal education, gestational age at NNNS exam.

NNNS: Neonatal Intensive Care Unit Network Neurobehavioral Scale; SRS: Social Responsiveness Scale.