

Prevalence of Early Feeding Alterations Among Preterm Infants and Their Relationship to Early Neurobehavior

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Importance: Feeding difficulties are common among preterm infants during neonatal intensive care unit (NICU) hospitalization. Although most preterm infants achieve full oral feeding by term-equivalent age, whether feeding difficulties persist despite the infant taking full volume and whether these difficulties may relate to other neurobehavioral challenges remain unclear.

Objective: To identify the prevalence of feeding problems among preterm infants and the relationships between infant feeding behaviors and neurobehavior at term-equivalent age.

Design: Cohort study.

Setting: Level 4 NICU with 85 beds.

Participants: Thirty-nine very preterm infants born ≤ 32 wk gestation (range = 22–32 wk). Exclusion criteria were congenital anomalies, >32 wk gestation at birth, and lack of feeding or neurobehavioral assessment at term-equivalent age.

Outcomes and Measures: Standardized feeding assessments using the Neonatal Eating Outcome Assessment and standardized neurobehavioral evaluation using the NICU Network Neurobehavioral Scale.

Results: Thirty-nine infants (21 female) were included in the final analysis. The mean Neonatal Eating Outcome Assessment score was 66.6 ($SD = 13.3$). At term-equivalent age, 10 infants (26%) demonstrated feeding challenges, 21 (54%) demonstrated questionable feeding issues, and 8 (21%) demonstrated normal feeding performance. Lower Neonatal Eating Outcome Assessment scores (poorer feeding performance) at term-equivalent age were associated with more suboptimal reflexes ($p = .04$) and hypotonia ($p < .01$).

Conclusions and Relevance: Feeding challenges and questionable feeding performance were prevalent among preterm infants at term-equivalent age and appeared in conjunction with suboptimal reflexes and hypotonia. Understanding this finding enables therapists to take a holistic approach to addressing feeding difficulties.

What This Article Adds: Elucidating the relationships between feeding performance and neurobehavior during the neonatal period allows for a better understanding of potential contributors to early feeding challenges and identifies targets for intervention.

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Pretermaturity can result in prolonged hospitalization in the neonatal intensive care unit (NICU) and is associated with both immediate and long-term challenges (Allotey et al., 2018; Younge et al., 2017). The sequelae of premature birth have the potential to alter brain development, leading to adverse functional outcomes (Ream & Lehwald, 2018; Thompson et al., 2020; Twilhaar et al., 2018). Alterations in brain structure among preterm infants include abnormalities of gray and white matter, reduced brain volumes, and

immaturity of cortical micro- and macrostructures (Back, 2014, 2017; Bouyssi-Kobar et al., 2016; Dimitrova et al., 2021). Subsequently, many preterm infants demonstrate poor postural control, adverse tone patterns, asymmetrical behaviors, limited exploratory behaviors, and reduced visual motor skills when compared with full-term counterparts (Brown et al., 2006; Pineda et al., 2013). Such neurobehavioral alterations are predictors of feeding impairment at 12 mo (Sanchez et al., 2017).

Although the majority of infants are able to achieve full oral feeding by NICU discharge, up to 40% of preterm infants already display feeding challenges at 40 wk postmenstrual age (PMA; [Hawdon et al., 2000](#)). Rates of feeding impairment in childhood are also high, with 25% to 40% of typically developing children and 70% to 80% of children with developmental delays or chronic medical needs having feeding problems ([Kleiner, 2017](#); [Lefton-Greif & Arvedson, 2007](#)). Therefore, understanding early alterations in feeding performance, including contributing factors, can aid in early identification and trigger early therapy interventions to prevent or minimize long-term sequelae.

Feeding skills may be markers for neonatal brain injury and adverse developmental outcome. Early nutritive sucking performance of infants near term age has been shown to be an independent predictor of neurodevelopmental status at 6 to 18 mo corrected age ([Medoff-Cooper et al., 2009](#); [Mizuno & Ueda, 2005](#)). Cerebral palsy and other cognitive impairments are important risk factors for developing severe feeding disorders ([Schädler et al., 2007](#)), and research has demonstrated associations between developmental delay and feeding impairment at 12 to 30 mo corrected age ([Crapnell et al., 2013](#); [Sanchez et al., 2017](#)). Although an alteration in feeding could be a marker for underlying neurodevelopmental problems, feeding performance is likely affected by alterations in early neurobehavior. A better understanding of these relationships is important for identifying interventions to optimize feeding outcomes.

Oral feeding represents one of the most critical and complex skills in infancy ([Jadcherla, 2016](#)) and is a major criterion for discharge from the NICU ([American Academy of Pediatrics Committee on Fetus and Newborn, 2008](#)). Before term-equivalent age, preterm infants demonstrate immature feeding responses that can include inadequate suction, poor suck–swallow–breathe synchrony, and poor oral–motor coordination ([Viswanathan & Jadcherla, 2020](#)). As preterm infants approach their due date, challenges associated with immaturity often resolve, and most preterm infants achieve full oral feeding by 40 wk PMA ([Amaizu et al., 2008](#); [Jackson et al., 2016](#); [Van Nostrand et al., 2015](#)). However, despite taking in full volume, oral–motor and feeding problems may persist.

To engage in feeding, various neural mechanisms—including multiple cranial nerves, afferent and efferent neural networks, inhibitory and excitatory neurons, and central pattern generators—must work together ([Jadcherla, 2016](#)). Moreover, for effective feeding, infants must perceive and integrate a variety of sensory stimuli; coordinate sucking, swallowing, and breathing; maintain appropriate alertness and postural control; and sustain adequate body and oral–motor tone ([Bauer et al., 2008](#); [Browne & Ross, 2011](#); [Griffith et al., 2017](#)). Infants' oral feeding skills are also reflective of their ability to organize and coordinate oral–motor functions ([Thoyre et al., 2005](#)). However,

aside from factors related to feeding an immature infant, it remains unclear how factors related to early neurobehavior may relate to early feeding performance during the neonatal period. By better understanding these relationships, a comprehensive therapeutic approach could be developed and implemented earlier in the developmental trajectory.

The aims of this study were to identify (1) the prevalence of feeding problems among preterm infants at term-equivalent age and (2) relationships between preterm infant feeding behaviors and neurobehavior at term-equivalent age.

Method

Participants

This study was approved by the Human Research Protection Office at Washington University in St. Louis with a ceded approval from the University of Southern California. Parents provided informed consent for the study, which included assessments of their infant's feeding and neurobehavior.

Fifty very preterm infants born ≤ 32 wk estimated gestational age (EGA) were enrolled within 1 wk of birth from January 2014 to June 2015. EGA was determined on the basis of the mother's last menstrual period in addition to Ballard exam. Participants were from an overarching study investigating the trajectory of feeding behaviors across hospitalization ([Pineda et al., 2018](#)). Infants were excluded if they had a congenital anomaly or were >32 wk EGA at birth. All infants who were admitted to an 85-bed Level 4 NICU (the highest acuity NICU) in St. Louis, Missouri, and who met inclusion criteria during the study period were recruited. Participants received standard of care, which often included feeding-related therapies, such as occupational therapy and speech-language pathology services.

Procedures

At term-equivalent age (i.e., for the purposes of this study, between 36 and 42 wk PMA), an oral feeding session was video recorded after the infant had achieved full oral feeding and discharge from the NICU was planned. Infants were fed by a parent or family member when present, and the mode of feeding (breast or bottle) was chosen at the parent's discretion. Feeders were instructed to feed the infant in the manner they typically would. When a parent was unavailable, a bottle feeding was conducted by therapists or nurses in accordance with standard of care. Video recordings included a close-up lateral view of the neck, jaw, and mouth as well as a clear view of the lips in contact with the nipple. Video recording commenced before placement of the nipple in the infant's mouth and was stopped after 20 min of oral feeding.

Neurobehavioral assessment, with the NICU Network Neurobehavioral Scale (NNS; [Lester et al., 2004](#)), was conducted at the infant's bedside within 20 to 30 min of a hands-on care time at term-equivalent

age. The neurobehavioral assessment most often occurred on the same day that a feeding was video recorded, but when not possible, it occurred within the same week (which coincided with discharge being imminent). The neurobehavioral assessment was scored by a certified evaluator, who was different from the person who scored the feeding assessment.

Outcome Measures

Neonatal Eating Outcome Assessment

Feeding videos were scored with the Neonatal Eating Outcome Assessment, a comprehensive assessment of infant oral feeding skills. The following three sections of the assessment were scored: prefeeding behaviors, oral feeding, and observations at the end of feeding. Each of the 18 scored items is added for a total raw score that ranges from 18 to 90, with higher scores indicating better performance. Scores can then be categorized as normal (77–90), questionable (58–76), or feeding challenge (18–57). Normal feeding categorization indicates that the infant performed as expected for oral–motor and feeding skills on the basis of their PMA. A questionable result indicates that some challenges were observed that are not in line with the infant’s PMA, although it remains unclear whether the feeding skills are still emerging or whether there is a feeding challenge. Feeding challenge indicates an abnormal result, with the infant demonstrating poor feeding performance and feeding skills that are not appropriate for their PMA (Pineda, 2016). The Neonatal Eating Outcome Assessment has established content validity, good to excellent interrater reliability, and concurrent and predictive validity (Kwon et al., 2020; Pineda et al., 2018, 2020). A single trained evaluator who had achieved reliability of scoring (80% accuracy after a training program) scored the feeding on the basis of video analysis using the Neonatal Eating Outcome Assessment (Pineda, 2016). The evaluator was blinded to neurobehavioral performance.

NICU Network Neurobehavioral Scale

At term-equivalent age (36–42 wk PMA), infant neurobehavior was assessed with the NNNS, a comprehensive assessment of neurobehavioral function that has 13 summary scores: habituation, orientation, handling, quality of movement, self-regulation, suboptimal reflexes, stress, arousal, hypertonia, hypotonia, asymmetry, excitability, and lethargy (Lester et al., 2014). Habituation items were not conducted on the infants because of variations in environmental auditory exposures during testing, which can affect results. Predictive validity and internal consistency have been established for the NNNS (El-Dib et al., 2012; Liu et al., 2010; Stephens et al., 2010; Tronick & Lester, 2013). Reliability is achieved through training and certification. Administration and scoring of the NNNS were conducted by a certified evaluator who was blinded to feeding performance.

Infant Medical and Sociodemographic Factors

Infant information collected from the electronic medical record included EGA, sex, race (White or non-White), birth weight, mode of delivery, multiple or singleton birth, Apgar score at 5 min, PMA at discharge, and length of NICU stay. Medical information included number of days on endotracheal ventilation, nasal cannula, noninvasive mechanical ventilation, and total parenteral nutrition in addition to presence of necrotizing enterocolitis (all stages), retinopathy of prematurity (all stages), intrauterine growth restriction, chronic lung disease (requiring supplemental oxygen at ≥ 36 wk PMA or requiring at least 28 days on $>21\%$ oxygen), patent ductus arteriosus (requiring indomethacin or surgical ligation), or cerebral injury. Cranial ultrasound and MRI tests, when available, identified the presence of cerebral injury, which was defined as having either a Grade III or IV intraventricular hemorrhage or cystic periventricular leukomalacia. Maternal demographic factors—including maternal age, marital status (married or single), and insurance type (private or public, as a proxy for socioeconomic status)—were also collected.

Statistical Analyses

Statistical analyses were run with IBM SPSS Statistics (Version 28; $p < .05$). Descriptives were used to identify the prevalence of feeding challenges in the sample. Relationships between medical and sociodemographic factors and feeding performance were investigated, and collinearity of significant variables ($p < .05$) were defined to determine which variables to include in the statistical model. Because the timing of assessment could affect outcomes, and because variability in timing of assessment occurred because of differences in timing of discharge, it was decided to include PMA at time of assessment in the model (Amaizu et al., 2008; Bingham et al., 2010; Pineda et al., 2013). Univariate and multivariate linear regression analyses were used to investigate relationships between feeding performance (with the total Neonatal Eating Outcome Assessment score) and neurobehavior (with 12 summary scores of the NNNS) while controlling for factors related to feeding performance. Analyses were also run with analysis of variance to investigate differences in neurobehavior among infants who were categorized as feeding challenged, questionable, or normal.

Results

Fifty preterm infants were enrolled in the overarching study. Thirty-nine (78%) infants had feeding and neurobehavioral assessments at term-equivalent age and thus were included in the final analysis. Reasons for not having assessments included death ($n = 1$), transferring or discharge before 35 wk PMA ($n = 5$), and medical and social reasons preventing the research team from doing the assessments ($n = 5$).

Sample descriptives are shown in Table 1. Feeding problems identified in the sample are described in Table 2.

On the basis of regression models, it was determined that EGA, birth weight, chronic lung disease, days on total parenteral nutrition, days of endotracheal intubation, days of noninvasive mechanical ventilation, PMA at discharge, and length of NICU stay were related to feeding outcome (total score on the Neonatal Eating Outcome Assessment) and were investigated for collinearity. All aforementioned variables were determined to be collinear ($r > .30$, $p < .05$), and EGA was selected to include in the multivariate statistical model along with PMA at the time of testing. EGA was selected because it related to all the other variables that

were associated with feeding outcome (Gilbert et al., 2003; Jadcherla et al., 2010).

Table 3 includes relationships between Neonatal Eating Outcome Assessment raw scores and each of the 12 NNNS summary scores (see Figure 1 for NNNS summary score distributions based on Neonatal Eating Outcome Assessment categorical scores: normal, questionable, or feeding challenge).

Discussion

The key findings of this study are that feeding problems, including categories of questionable and feeding challenge, among very preterm infants are common at term-equivalent age and that neurobehavior, specifically tone and reflexes, is related to neonatal feeding performance. Alterations in early feeding performance and neurobehavioral outcomes are interrelated and evident by term-equivalent age.

The rate of feeding problems (80%) among very preterm infants in this sample, defined as questionable or feeding challenge on the Neonatal Eating Outcome Assessment, is higher than those reported in other studies, which range from 40% to 42% (Crapnell et al., 2013; Hawdon et al., 2000; Mizuno & Ueda, 2005). This discrepancy in findings could be related to the use of different feeding assessments, as some assessments are more detailed in evaluation of feeding skills compared with others. The high rate of feeding problems in this cohort could also be because of the large number of infants with extremely low birth weight represented in this study: 3 infants who were born at 23 wk were included in this small sample, and the average EGA was 27 wk. However, the high prevalence of feeding problems found in this study highlights that although infants may be orally feeding by term-equivalent age, they may also be showing problematic feeding behaviors that may warrant intervention. Therefore, assessment tools that isolate specific constructs related to feeding performance may aid in improving the understanding of such feeding alterations.

Previous studies have shown that preterm infants have poorer rooting, sucking, and esophageal reflexes compared with their full-term counterparts, which can have direct implications on feeding performance (Ince et al., 2015; Jadcherla et al., 2015). It is well understood that early infant reflexes and muscle tone are vital for oral feeding competence (Bauer et al., 2008;

Table 1. Sample Characteristics (N = 39)

| Factor | n (%) |
|--|-----------------|
| Infant Medical Factors | |
| EGA, wk, <i>M (SD)</i> | 27.4 (2.7) |
| Female sex | 21 (54) |
| White | 22 (56) |
| Birth weight, g, <i>M (SD)</i> | 1,081.0 (401.9) |
| Cesarean section delivery | 27 (69) |
| Multiple birth | 10 (26) |
| Apgar at 5 min, <i>M (SD)</i> | 5.7 (2.2) |
| Days of endotracheal intubation, <i>Mdn (IQR)</i> | 2 (1–16) |
| Days on nasal cannula, <i>Mdn (IQR)</i> | 33 (9–58) |
| NIMV days, <i>Mdn (IQR)</i> | 7 (0–16) |
| Days on TPN, <i>Mdn (IQR)</i> | 11 (7–16) |
| NEC | 3 (8) |
| ROP | 11 (28) |
| IUGR | 3 (8) |
| CLD | 33 (85) |
| PDA | 12 (31) |
| Cerebral injury | 6 (15) |
| PMA at discharge, wk (<i>n</i> = 38), <i>M (SD)</i> | 40.0 (3.4) |
| Length of stay, days (<i>n</i> = 38), <i>M (SD)</i> | 88.5 (39.4) |
| Maternal Demographic Factors | |
| Maternal age, <i>M (SD)</i> | 28.3 (6.9) |
| Marital status: Married | 16 (41) |
| Insurance type: Public | 27 (69) |

Note. CLD = chronic lung disease; EGA = estimated gestational age; IQR = interquartile range; IUGR = intrauterine growth restriction; NEC = necrotizing enterocolitis; NIMV = noninvasive mechanical ventilation; PDA = patent ductus arteriosus; PMA = postmenstrual age; ROP = retinopathy of prematurity; TPN = total parenteral nutrition. Cerebral injury is defined as having a Grade III or IV intraventricular hemorrhage or cystic periventricular leukomalacia from routine cranial ultrasound or MRI.

Table 2. Feeding Problems in the Sample (N = 39)

| Variable | n (%) |
|---|-------------|
| Neonatal Eating Outcome Assessment raw score, <i>M (SD)</i> | 66.6 (13.3) |
| Neonatal Eating Outcome Assessment categorical scores | |
| Normal | 8 (21) |
| Questionable | 21 (54) |
| Feeding challenge | 10 (26) |

Table 3. Relationships Between Feeding Performance and Neurobehavior

| Variable | Univariate Regression | | | Multivariate Regression | | |
|------------------------------|-----------------------|-------------|-----------------------|-------------------------|-------------|-----------------------|
| | <i>R</i> ² | β | <i>p</i> ^a | <i>R</i> ² | β | <i>p</i> ^b |
| Orientation (<i>n</i> = 35) | .01 | .12 | .50 | | | |
| Handling (<i>n</i> = 37) | <.01 | .09 | .60 | | | |
| Quality of movement | <.01 | −.02 | .90 | | | |
| Self-regulation | <.01 | .06 | .70 | | | |
| Suboptimal reflexes | .18 | −.43 | <.01 | .19 | −.39 | .04 |
| Stress | −.38 | −.19 | .24 | | | |
| Arousal | .09 | .30 | .07 | | | |
| Hypertonia | <.01 | −.07 | .65 | | | |
| Hypotonia | .26 | −.51 | <.01 | .26 | −.54 | <.01 |
| Asymmetry | .04 | −.19 | .25 | | | |
| Excitability | .02 | .12 | .45 | | | |
| Lethargy | .03 | −.18 | .26 | | | |

Note. Boldface indicates relationships found to be significant ($p < .05$).

^aThe *p* value signifies the relationship between Neonatal Eating Outcome Assessment raw scores and NICU Network Neurobehavioral Scale (NNNS) summary scores evaluated with univariate linear regression models.

^bThe *p* value signifies the relationship between Neonatal Eating Outcome Assessment raw scores and NNNS summary scores evaluated with multivariate linear regression models, controlling for estimated gestational age and postmenstrual age at the time of assessment; significant at $p < .05$.

Browne & Ross, 2011; Crapnell et al., 2013). Relationships between neurodevelopment and feeding outcomes later in infancy and childhood have also been reported (Medoff-Cooper et al., 2009; Rinat et al., 2022; Sanchez et al., 2017) as well as a relationship between oral feeding and attention scores on the NNNS among infants with congenital heart disease (Gakenheimer-Smith et al., 2019). However, this is the first study, to our knowledge, that has isolated early neurobehavioral alterations among preterm infants that are related to feeding performance during the neonatal period.

We have found that reflexes and tone may be important contributors to neonatal feeding because of their relationships with feeding outcomes at term-equivalent age. Our findings are consistent with research that indicates hypotonia may impair oral-motor development among preterm infants (Peredo & Hannibal, 2009) and that hypotonia at term-equivalent age may be a risk factor for adverse feeding outcomes in early childhood (Crapnell et al., 2013). Interventions such as therapeutic handling, joint approximation, and infant stimulation within the preterm period have been identified in the NICU (Ross et al., 2017), and these interventions may be used to optimize feeding performance.

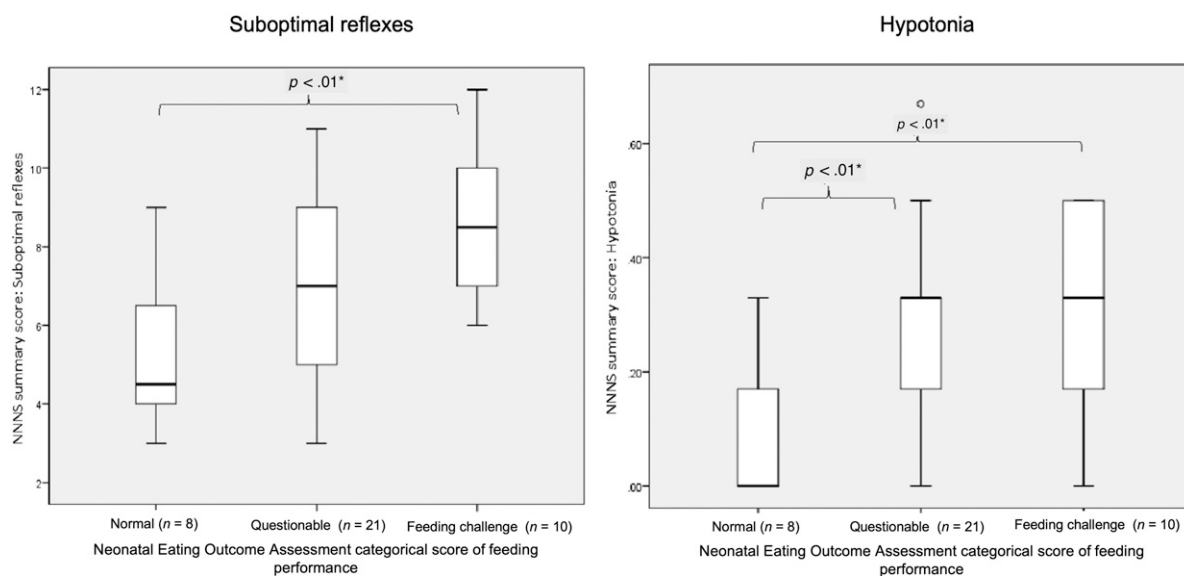
Although most preterm infants achieve full oral feeding by term-equivalent age (Amaizu et al., 2008; Jackson et al., 2016; Van Nostrand et al., 2015), the continued prevalence of feeding challenges in association with poor neurobehavior, as identified in this study, indicates the need for early intervention focused on more than just oral-motor skills. This finding is

consistent with reports recommending a comprehensive neurodevelopmental approach to feeding that considers the infant's physiology, arousal, motor function, and sensory input (Browne & Ross, 2011). Oral feeding is an important skill related to the neonatal period and is an important criterion for NICU discharge; therefore, understanding and addressing the complexities related to oral feeding with an approach that supports immediate oral feeding performance, in addition to neurobehavioral performance and long-term neurodevelopmental outcomes, is crucial. A multidisciplinary team that can provide a comprehensive approach to address feeding, as well as infant reflexes and tonal patterns that affect feeding performance, may make the largest impact. Occupational therapy, physical therapy, and speech-language pathology services are now standard of care in many NICUs to aid in this approach being a reality (Pineda et al., 2021; Ross et al., 2017).

Limitations

This study was limited by a small sample size from an overarching study that was not powered to address the research question. Moreover, some infants who were initially enrolled did not complete study procedures, which could limit the findings. Although relationships were found, additional research with a properly powered sample is important. This study may have been limited by a single feeding evaluator, which could have introduced personal bias across all measurements; however, the evaluator underwent reliability training and testing. In addition, variability across measurements

Figure 1. Relationships between NICU Network Neurobehavioral Scale (NNNS) hypotonia and suboptimal reflexes scores of infants with normal, questionable, and feeding challenge on the Neonatal Eating Outcome Assessment at term-equivalent age.



Note. Significant differences between groups are reported ($p < .05$). The high and low bars represent the highest and lowest scores with the box in the middle representing 25th–75th percentiles. The circle in the Questionable column of the Hypotonia figure indicates an outlier.

*The p values are from investigations of Neonatal Eating Outcome Assessment categorical scores with NNNS summary scores using analysis of variance.

could have been avoided because of a single evaluator, strengthening the results. This study is also limited by a single assessment of feeding and neurobehavior, which may or may not have been representative of the infant’s typical performance.

In this study, feedings were administered by nurses, parents, and therapists of varying levels of feeding experience and knowledge of intervention techniques, which was not controlled and could have affected the infant’s feeding performance. It is unknown whether and how often infants received therapy services as part of standard care, which could have affected their performance on either the feeding or neurobehavioral assessments. Additionally, multiple analyses were used to determine relationships between neurobehavior and feeding performance, which increases the risk of a Type I error. The impact of social and medical factors could not be untangled in this study, further limiting the generalizability of these results to only a portion of the preterm infant population. This study could also be limited by feeding assessment scoring occurring by video analysis, which could have provided a limited view of the infant and context.

Future Directions

Further investigation is warranted to elucidate relationships among medical factors, neurobehavior, and feeding performance; examine the impact of higher medical acuity on feeding outcome; identify environmental and other modifiable factors that affect feeding

performance; outline the progression of feeding over the first several years of life among preterm and normally developing children; and elucidate how different early intervention programs and therapy can affect long-term outcomes related to neurobehavior and feeding outcomes. However, this study contributes to current knowledge by identifying the important relationship of neurobehavioral performance with feeding behaviors, which warrants further attention.


Implications for Occupational Therapy Practice

This article extends the understanding of feeding among preterm infants by reporting on the relationships between early feeding alterations and neurobehavioral performance. The implications for occupational therapy practice include the following:

- The findings further support occupational therapy practitioners’ critical role in optimizing feeding in the NICU as a discipline that uses a holistic approach.
- Understanding the relationships between neurobehavior and feeding can aid in designing targeted interventions to improve outcomes.
- Expanding the understanding of neurobehavioral contributors to oral feeding can lead to comprehensive interventions.

Conclusion

The prevalence of feeding problems in an extremely low birth weight sample was high (80%). Those with

poorer feeding performance at term-equivalent age were more likely to have hypotonia and suboptimal reflexes. This information can aid clinicians in understanding neurobehavioral contributions to feeding performance and identifying targeted interventions. 

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