

Quantifying Neonatal Sucking Performance: Promise of New Methods

Gilson J. Capilouto, Ph.D.

Professor

Department of Rehabilitation Sciences

University of Kentucky

Lexington, Kentucky

Tommy J. Cunningham, Ph.D.

Adjunct Assistant Professor University of Kentucky

Co-Founder & Chief Operating Officer

NFANT Labs, LLC

Atlanta, Georgia

David R. Mullineaux, Ph.D.

Professor in Sports Science

School of Sport and Exercise Science

University of Lincoln

Lincoln, England

Eleonora Tamilia, Ph.D.

Postdoctoral Research Fellow in Pediatrics

Department of Medicine

Boston Children's Hospital, Harvard Medical School

Boston, Massachusetts

Christos Papadelis, Ph.D.

Assistant Professor

Department of Pediatrics

Boston Children's Hospital, Harvard Medical School

Boston, Massachusetts

Peter J. Giannone, M.D.

Chief of Neonatology, Vice Chair Pediatric Research

Department of Pediatrics

University of Kentucky College of Medicine

Lexington, Kentucky

Correspondence:

Gilson J. Capilouto, Ph.D.

900 S. Limestone, CTW 124G

Lexington, KY 40536-0200

E-mail: gilson.capilouto@uky.edu

Phone: 859-218-0555

Fax: 859-327-8957

ABSTRACT

Neonatal feeding has been traditionally understudied so guidelines and evidence-based support for common feeding practices are limited. A major contributing factor to the paucity of evidence-based practice in this area has been the lack of simple-to-use, low cost tools for monitoring sucking performance. We describe new methods for quantifying neonatal sucking performance that hold significant clinical and research promise. We present early stage results from an ongoing study investigating neonatal sucking as a marker of risk for adverse neurodevelopmental outcomes. We include quantitative measures of sucking performance to better understand how movement variability evolves during skill acquisition. Results showed the coefficient of variation of suck duration (COV_D) was significantly different between preterm infants at high risk for developmental concerns (high risk preterm; HRPT) and preterm infants at low risk for developmental concerns (low risk preterm; LRPT). For HRPT, results indicated the coefficient of variation of suck smoothness (COV_{SM}) increased from initial feeding to discharge and remained significantly greater than term infants (healthy full term; FT) at discharge. There was no significant difference in our measures between FT and LRPT at discharge. Our findings highlight the necessity of early sucking evaluation as part of the routine clinical evaluation of early sucking to capture the relative risk of adverse neurodevelopmental outcomes at discharge.

KEYWORDS

Premature infant; suck behavior; nutritive sucking patterns, oral feeding, feeding skills

DISCLOSURES

Gilson J. Capilouto receives a salary from the University of Kentucky (UK) where the work was carried out. She has a financial interest in NFANT Labs, LLC. Dr. Capilouto is serving as the

Guest Editor for the 20th Anniversary Issue on “Pediatric Feeding and Swallowing” for Thieme's *Seminars in Speech and Language*.

Tommy J. Cunningham receives a salary from NFANT Labs, LLC, serves as a Board Member and has a financial interest in the company. He is an adjunct assistant professor at the University of Kentucky (UK) where the work was carried out.

David R. Mullineaux receives a salary from the University of Lincoln, UK.

Eleonora Tamilia receives a salary as a Postdoctoral Research Fellow of Boston Children's Hospital, the primary pediatric teaching hospital of Harvard Medical School.

Christos Papadelis receives a salary as Assistant Professor of Pediatrics from the Division of Newborn Medicine at Harvard Medical School, Boston Children's Hospital.

Peter J. Giannone receives a salary from the University of Kentucky (UK) where the work was carried out.

Neonatal feeding has been described as the most precocious and complex behavior of the newborn¹ and requires integration of physiologic function and neurobehavioral ability.^{2,3} Safe and efficient feeding is necessary to provide essential nutrients for neonatal brain development; the importance of which is underscored by the fact that independent oral feeding is a final criteria of hospital discharge for preterm and sick terms infants.⁴ At the same time, neonatal feeding has been traditionally understudied so guidelines and evidence-based support for common feeding practices are limited.⁵ A major contributing factor to the paucity of evidence-based practice in this area has been the lack of simple-to-use, low cost tools for monitoring sucking performance.⁶

In this paper, we describe new methods for quantifying neonatal sucking performance that have the potential to support crib side visual assessment of sucking, help caregivers interpret their infants' feeding cues, and serve as valuable resource for studying a myriad of important research questions surrounding neonatal feeding. The approach we describe leverages a number of significant technological advances to inform and advance neonatal feeding practice. To illustrate the utility of this approach, we present early-stage results from our ongoing study investigating early sucking as a marker for later neurodevelopmental outcomes.

The survival of preterm infants has increased markedly in the last decade due to advances in technology and neonatal care.⁷ Despite these medical advances, the risk of poor neurobehavioral functioning is common.⁸ Consequently, early identification of neonates at risk for adverse neurodevelopmental outcomes is crucial⁹ to enable prevention or treatment during infancy, when neuroplasticity mechanisms are thought to be greatest.¹⁰ Scientists studying the maturational sequence of infant feeding have theorized that early nutritive sucking skills may be an early marker of overall central nervous system integrity¹ and as such, a potential predictor of neurodevelopmental outcomes.¹¹⁻¹³

Indeed, the literature suggests a strong relationship between early nutritive sucking and neurodevelopmental outcomes early on. For example, Medoff-Cooper et al. investigated the relationship between early nutritive sucking patterns of preterm infants and neurodevelopmental outcomes in the first year of life. The study population included early and moderate preterm infants. Infants received a five-minute sucking test at 34 and 40 weeks post menstrual age (PMA) and developmental outcomes were measured at 6- and 12- months corrected age using the Bayley Scales of Infant Development (BSID).¹³ Sucking performance was quantified using a prototype sucking apparatus fitted with an adapted nipple. Results indicated that sucking parameters (number of sucks, sucks per burst, mean sucking pressure peaks, and suck maturity index) at 40 weeks PMA were significant predictors of developmental status at 1 year.

Observational scale data also suggest a relationship between early sucking and relative risk of developmental concerns. In a study by Tsai, Chen, and Lin the Neonatal Oral Motor Assessment Scale (NOMAS), a 28 items observational scale, was used to characterize sucking patterns in preterm infants.¹⁴ Participants included early preterm, moderate preterm and late preterm infants. The first 2 minutes of nutritive sucking were video recorded weekly from initiation of oral feeding until discharge and then the videos were reviewed by NOMAS certified assessors. Based on those results, the infants were assigned to one of two groups: normal sucking pattern (by 37 weeks) or persistent disorganized sucking pattern (after 37 weeks). At 6- and 12- months corrected age, the BSID was administered to determine developmental status. Results suggested that the risk for developmental delay was significantly greater in those infants classified as having a persistent disorganized sucking pattern. A similar trend was noted at 12 months; however, the results were not statistically significant.

Early sucking has also been shown to relate to neurodevelopmental outcomes at later ages. For example, Mizuno and Ueda investigated whether neonatal feeding performance would predict neurodevelopmental outcomes at 18 months.¹ Subjects included a mix of later preterm and term infants. Nipples were modified to measure the suction and expression components of nutritive sucking. Adverse events during feeding were noted; however, feedings were not stopped following a desaturation or bradycardic event. Visual inspection of compression-expression waveforms was used to classify feeding performance from immature to mature. Neurodevelopmental status at 18 months was determined using the BSID. Results indicated a significant correlation between feeding pattern and neurodevelopmental outcomes; more mature feeding patterns at 2 weeks post initial oral feeding were associated with better neurodevelopmental outcomes.

Wolthuis-Stigter and colleagues reported evidence that the status of sucking behavior as late as six weeks after birth is associated with developmental concerns at 2 years of age. The researchers investigated the association between specific elements of sucking and neurodevelopmental outcomes. The study population included very early, early, moderate and late preterm infants. Nutritive sucking behavior was assessed using the NOMAS. NOMAS scores were collected at two time points: weekly between 37 and 40 weeks PMA and every 2 weeks between 40 and 50 weeks PMA.¹⁵ The Dutch version of the BSID was completed at 27 months corrected age. Results showed that atypical sucking performance at 4-6 weeks post term was positively correlated with poor neurodevelopmental outcomes in preterm infants at 2 years of age.

The relationship between early sucking and neurodevelopment has also been documented in children as old as three years. In a study reported by Hiramoto and colleagues, a questionnaire

focused on sucking behavior was administered to mothers of children during routine 18-month and/or 3-year-old child health check-ups. No demographic data detailing the characteristics of the sample were provided. Public health nurses completed an assessment of age-appropriate developmental milestones adapted from the Enjoji Scale of Infant Analytical Development.¹⁶ Based on screening results, subjects were categorized as either typically developing (pass) or possible developmental delay (fail). Odds ratios were used to calculate the likelihood for questionnaire items to associate with developmental delay. Results indicated that the lack of a ‘smooth suck and rest pattern’ during feeding, as reported by parents, was associated with significantly higher likelihood of being labelled developmental delayed at both 18- months and at 3 years.

Taken together, these studies provide strong evidence that early sucking is a reflection of the overall integrity of the central nervous system, and as such, may be a behavioral marker for risk of poor neurodevelopment outcomes from as early as six months to three years. However, the methods reported have some important limitations. First, the use of the NOMAS as the sole measures of sucking integrity^{14,15} is limiting, as it requires specialty certification, is subjective, and the inter-rater reliability has been shown to vary significantly from rater to rater.¹⁷ The use of modified nipples to quantify sucking characteristics¹ is also considered a limitation. Modifying a nipple could in fact alter critical sensory aspects of sucking for infants and potentially confound findings. Also of importance is the fact that a number of reported studies have analyzed sucking performance using a specific time point in the feeding (e.g. first five minutes). Yet, the feeding experience of premature infants varies from moment to moment so summary statistics from a limited time in the feeding could potentially miss important clinical and predictive information.¹⁸ Moreover, in most cases, studies did not include healthy full term infants as a comparison

population which we believe is clinically valuable to provide context for results and interpretation of findings. Lastly, multiple observations of sucking performance are necessary to consider the ways in which movement changes as a function of maturation and experience.

The purpose of the current study was twofold: (1) compare metrics of sucking performance between preterm infants and healthy term infants at initiation of feeding and at discharge; and, (2) investigate changes in sucking performance longitudinally among preterm infants from initiation of oral feeding through post discharge. Our methods for collecting sucking data address the limitations of previous approaches. Here, we relied on automated analyses of elements of sucking to provide a set of summary statistics. Moreover, our present methodology uses a scalable and noninvasive tool to measure important sucking parameters throughout the course of a feeding so no modification of nipples was required and the moment to moment variability characterizing neonatal sucking was captured.

METHODS

Participants. Two groups of infants were recruited for participation: healthy term infants (FT) (N = 15) defined as >37 weeks gestational age (GA), with appropriate weight for gestational age, and healthy preterm infants (PT) (N = 40) with appropriate weight for gestational age (Table 1). Infants in the FT group met the inclusion criteria for no anomalies or diseases known to interfere with feeding (e.g. cleft lip and/or palate). PT infants met the following inclusion criteria: no anomalies or diseases known to interfere with feeding, no congenital disorders, chromosomal abnormalities, or major congenital anomalies, no disorders secondary to known perinatal exposure to toxic substances and no history of intraventricular hemorrhage greater than Grade II. Preterm infants could have a diagnosis of respiratory distress syndrome, but could not be ventilated for a prolonged period of time. Participants were recruited

from Kentucky Children's Hospital, a 70-bed level IV NICU. The study was approved by the Institutional Review Board of the University of Kentucky where the study was carried out.

Insert Table 1 about here

Measures. nfant® Feeding Solution (NFANT Labs, Atlanta GA) was used to collect nutritive sucking data and determine our sucking variables of interest (Figure 1). nfant Feeding Solution consists of a disposable nfant Coupling that connects a bottle to a standard nipple or pacifier. The nfant SSB Sensor connects to the coupling and non-invasively measures nipple movement. Data are streamed from the sensor to a mobile tablet and nipple movement is displayed in real time on the nfant Mobile App. Following a feeding, data were stored in the nfant Cloud Database for later analyses. Signal processing of nipple movement included a one second rolling minimum baseline shift and outlier suck peak removal to account for any movement artifact. Amplitudes were then normalized to the maximum peak observed (0 to 100%).

Recently, Tamilya and colleagues described the importance of including analyses of quantitative measures of sucking performance more characteristic of sucking in the context of dynamical systems theory.^{19,20} For example, previous researchers have limited findings to sucking parameters such as number of sucks, sucks per burst, and mean sucking pressure peaks, among others.¹³ In contrast, Tamilya and colleagues introduced variables calculated across *each* sucking burst to reflect sucking stability vs. variability. Because variability contains important information about human movement in general²¹, a shift in focus to metrics of coordinated movement could be particularly important in investigations of early sucking as a potential

marker of later neurodevelopment. Therefore, for this study, algorithms to identify key features and metrics describing the suck pattern, consistent with Tamilia et al.,²⁰ were developed, and all analyses were performed using custom software (Matlab 2013a, Mathworks, Natick MA).

Insert Figure 1 about here

Our primary measures of interest focused on movement variability of the nipple during sucking (Figure 2). Variability was assessed using the Coefficient of Variation (COV, i.e. standard deviation divided by the mean) for four distinct suck metrics: suck peak amplitude (COV_{PKA}), duration (COV_D), frequency (COV_F , i.e. 1/suck period) and smoothness (COV_{SM}). Summarized here but best described in previous literature,^{19,22} smoothness is a measure of motor performance which is derived from the speed profile of the movement signal and indicates the amount of oscillations within a suck where the fewer the oscillations, the “smoother” the movement.

Insert Figure 2 about here

Procedures. Once subjects were declared medically stable and ready to begin oral feeding, nurse researchers checked daily notes to determine readiness to begin data collection. Data collection for FT infants took place within 2 weeks of birth. PT infants entered the protocol when they showed evidence of sustained bottle feeding (1-2 feedings per day). Measures of interest were collected at three time points during the hospital stay: when infants were taking 1-2 feedings per day (evidence of sustained bottle feeding), when they were taking 4-6 oral feedings

per day (established bottle feeding) and at discharge when they were taking all feedings orally.²³ Measures were collected within 24-36 hours of being notified that an infant had met the respective criteria for each time period. Specific feeding instructions as ordered by the attending physician were maintained and recorded. Infant cue-based feeding procedures²⁴ were followed so that the feeding was stopped according to the cues of the infant and/or after 30 minutes. In all cases, data collection was scheduled so as not to interfere with breastfeeding. Each session began with one minute of nonnutritive sucking followed by nutritive sucking in their typical feeding position (held by caregiver). Data were collected for the entire feeding. For the purposes of this paper, only the nutritive sucking results are reported and used in analyses.

To meet the aims of the study, infants were stratified into three groups (Table 2). Infants in Group 1 were preterm, but were not considered high risk for developmental concerns and so were released to their primary care physician and/or pediatrician after discharge (low risk preterm; LRPT). Infants in Group 2 were also preterm but considered at risk for developmental concerns (high risk preterm; HRPT) based on criteria established by our outpatient follow-up clinic, including but not limited to gestational age and birth weight. These infants were released to a multidisciplinary follow-up team with expertise in preterm infant care. Group 3 was comprised of healthy, full term (healthy full term; FT) infants. HRPT infants were seen at critical developmental time points including one month, 3 months, and 6 months corrected age. The BSID is administered at 1 and 2 years corrected age and then again at 3-years chronological age. (Note: At the time of this reporting, only 5 of our study infants had reached the age for administration of their 1 year BSID so these data are not reported).

Statistical Analyses. Sample population characteristics were analyzed using univariate analyses of variance. A least squares difference post-hoc analysis was performed for metrics with

alpha <0.05. Measures of interest were calculated for the initial exam (IE) and discharge exam (DE) for HRPT and LRPT. Additionally, for the HRPT, measures were calculated for their follow-up exams (FE). For FT subjects, only the DE was used in analyses since there was only one feeding session for term babies prior to discharge. A mixed ANOVA was performed between groups comparing exam time points. Paired t-tests were used within HRPT and LRPT to determine changes in metrics within each group between exam time points and unpaired t-tests between groups. Significance for all analyses was set a priori at $p < .05$. One FT subject was removed from analysis due to low quality signal, leaving 14 FT, 28 HRPT and 12 LRPT subjects for analysis (Table 2).

Insert Table 2 about here

RESULTS

Results from analyses of sample population characteristics were as expected. Preliminary analyses indicated significant differences in mean gestational age, birthweight, age at first feeding, age at discharge feeding and feeding related length of stay between the three groups (Table 2). Probably the most interesting finding was the fact that, for our study population, there was no significant difference in age at discharge feeding between our LRPT babies and FT. Yet, the time from initial feeding to discharge feeding (FRLOS) was significantly greater for LRPT babies as compared to FT; reinforcing the notion that even in ‘healthy’ preterm babies, gestational age may not be the best predictor of readiness to feed or expectations relative to feeding. Moreover, these results reinforce the suggestion that moderate and late preterm infants

may be at higher risk for subtle feeding problems than previously reported,^{25,26} and so warrant more careful observation by feeding specialists and healthcare teams.

COV measures for HRPT, LRPT and FT groups for all respective exam time points are shown in Figure 3. Significant differences in mean values for each exam in comparison to FT are indicated by (*), between PT groups by (+), and changes in exams values within groups by (#). These results suggest that low risk premature infants have comparable variability in suck amplitudes, frequencies, durations and smoothness values from the time they begin oral feeding (IE) to the time they are discharged from the hospital (DE). Moreover, only smoothness variability at IE was statistically distinguishable between our population of low risk premature infants and healthy full terms infants (FT). Findings suggest that the nature of sucking behavior for these two groups is, at least initially, very similar. These findings are in contrast to those with our high risk infants. In comparison to full term babies, high risk premature babies actually start out with comparable variability in suck frequencies, durations and smoothness values from the time they begin oral feeding (IE) to the time they are discharged from the hospital (DE). However, as the HRPT infants matured (FE), the value for these metrics, with the exception of suck amplitude and duration variability, were statistically different compared to FT at hospital discharge (DE). When comparing our variability measures between high risk and low risk premature infants, results showed that only the variability of suck duration at discharge feeding (DE) was statistically different between these two groups; the low risk groups had lower variability relative to suck duration as compared to the high risk group.

Insert Figure 3 about here

To examine changes in variability over time, we conducted within group comparisons for the high risk preterm infants in the study. Variability in amplitude, duration and frequency decreased significantly from initiation of feeding (IE), to feeding at hospital discharge (DE) and then again, for suck frequency, to post discharge final feeding (FE). In contrast, variability of smoothness actually increased significantly from the time of the initial exam to the time of the discharge exam (DE). Variability of smoothness of the suck did not change substantially from values obtained at hospital discharge and those collected at the final exam (FE). What follows is an interpretation of these results in the context of what is known about movement variability in general, and the complexity of nutritive sucking.

DISCUSSION

Variability is an intrinsic property of human movement and it has been suggested that there may be a degree of ‘healthy’ movement variability associated with the optimal state for producing a given movement.²¹ In an attempt to capture that optimal state, we collected metrics of movement variability longitudinally for a group of preterm infants who were determined a priori to be at risk for poor developmental outcomes. The duration, amplitude and frequency of a suck are fundamental characteristics that infants must learn to control as they master the complex skill of nutritive sucking. Variations in these suck parameters, as described by COV metrics, may be an indication of an infant’s skill at any point in time. Therefore, the aims of the current study were to: (1) compare metrics of sucking performance between preterm infants and healthy term infants at initiation of feeding and at discharge; and, (2) investigate changes in sucking performance longitudinally among preterm infants at high risk for adverse outcomes from initiation of oral feeding through post discharge.

Our results indicated that variability in suck duration (COV_D) was a distinguishing feature when comparing inpatient suck performance; values were similar for LRPT and FT infants as compared to HRPT, suggesting that LRPT and FT babies had greater control of this suck feature at discharge. At the same time, the mean COV_D for our high risk babies at the final exam indicated advancement to a more stable state, comparable to that of FT infants, even while all other COV features remained significantly different between the two groups.

Variation in suck duration cannot however be contextualized independently from other suck features or from maturation. The noted decrease in $COV_{P_{kA}}$ and trend toward decreasing COV_F for the HRPT group and the simultaneous stabilization of COV_D (i.e. comparable to FT) at FE, could reflect greater adaptability of the infant to control sucking characteristics from suck duration to peak amplitude and frequency with experience and maturation. From a dynamical systems perspective, these measures could be a reflection of the infant's ability to decrease the number of degrees of freedom of one suck characteristic in favor of others in response to a shift in attractor states, resulting from maturity level or underlying pathology. It is hard to know the causative nature of the differences observed across these measures considering that nutritive sucking comes under volitional control during the period covered by the FE. It should be mentioned that a major limitation in this comparison is that we do not know how these metrics change for FT in response to experience and maturation, since we did not follow them after discharge. However, these results add support to the idea that a decrease in variability over time is consistent with skill acquisition (motor learning)²¹ and *how* human movement in general evolves over time is important²¹ and should be explored longitudinally for all of these populations.

A surprising finding of this study was the amount and direction of variation in smoothness between HRPT and FT. Mastery of a skill is typically associated with improved smoothness (decrease in value/oscillations) and a concomitant decrease in movement variability. Our results show COV_{SM} *increasing* for the HRPT group over time. There are two main factors that could influence the suck characteristic of smoothness and thus COV_{SM} for a population: (1) perturbations within a suck indicative of neuromuscular instability; or (2) increased oscillations due to the move toward a more complex, coordinated sucking pattern. It is our thinking that the latter contributed to the increased amount of COV_{SM} observed for the HRPT group.

Theoretically, we would expect variability in smoothness to decrease in response to maturation and skill acquisition. Consistent with Lau,⁷ we observed several types of sucking patterns seemingly influenced by maturation. For example, our HRPT infants started with a “simple” suck pattern during the initial stages of data collection (inpatient) characterized by small peak amplitudes of short duration. We would have expected that by the FE, HRPT infants would have progressed to a more complex, coordinated sucking pattern with defined oscillations characterized by larger amplitudes, even shorter durations and greater frequencies; all of which suggest greater control and coordination of these suck characteristics.

The natural tendency for smoothness values to become larger with an increased amount of oscillations within the suck, coupled with the possibility of the infant’s control pattern switching between simple suck patterns and more coordinated patterns in response to experience and learning, could have led to the increased COV_{SM} values noted for HRPT. To explore this idea, we conducted a post hoc analysis of mean smoothness values and results supported this notion. Smoothness values for HRPT infants decreased from initial exam to discharge exam and values at discharge exam remained consistent through to the final exam. However, the final exam

values remained substantially less as compared to term babies. The fact that mean smoothness values at final exam did not increase to the level of term infants at hospital discharge could be an indication that this group continues to shift between simple and complex sucking patterns even after discharge and that HRPT infants are challenged in their ability to develop rhythmic, successive sucks *across* an entire feeding.²⁷ With more data, we may find that relative smoothness may be indicative of neurological dysfunction and a response variable similar to that observed by Nieuwenhuis and colleagues who equated “fidgety” movements to dysfunctional or disorganized sucking patterns using the NOMAS.²⁸

Lastly, the procedures described for collecting these data take into account the suggestions of researchers who have previously reported on neonatal sucking. For example, as suggested by Medoff-Cooper et al,¹³ we have collected data beyond the more common ‘single 5-minute sucking test’ to capture the natural variability in sucking performance as a function of arousal, temperament etc. We collected data consecutively for our population of preterm infants, completing feedings on average once a week from initiation of feeding to discharge for an average of three feedings. As a result, we were able to distinguish the HRPT and the LRPT groups, validating the potential use of the variable as an early marker for infants at risk for adverse neurodevelopmental outcomes.

LIMITATIONS AND FUTURE DIRECTIONS

Early identification of infants at risk for adverse neurodevelopmental outcomes is necessary if we are to positively impact the rates of disability and poor neurodevelopmental sequelae in this population. This is especially the case for infants that survive preterm birth and whose long-term outcomes have remained a challenge despite the significant advances in medicine over the past decade. The noninvasive technology used here to capture and report

sucking metrics enables greater insight into what researchers have postulated for quite some time: that sucking behavior is a manifestation of the overall integrity of the neuromuscular system in this fragile, developing population. However, given the complexity of feeding and the dynamical systems that may drive sucking skill development, there are important feeding parameters we need to capture and investigate beyond those reported here.

For the current study, we focused solely on capturing nipple movement and COV metrics as descriptors. Capturing additional sucking metrics (e.g. sucks per burst, intersuck interval, etc.), feeding parameters (e.g. negative intra-oral pressure), and measures influenced by feeding would allow us to use more advanced non-linear statistical analyses to better estimate the coordinative structure of sucking dynamics. Such an approach might yield additional distinguishing suck characteristics among high risk population cohorts. Moreover, factors that influence the infant's feeding environment (e.g. nipple type/flow rate, position during feeding, time of day, etc.) were captured but not analyzed in this study. Such information, combined with traditional comorbidity indicators (GA, birth weight) and measures of physiological stability during feeding (i.e. oxygen saturation, respiration rate, etc.) will allow us to gain full insight into the overall neonatal feeding construct and the ability of the infant to adapt to conditions that could vary across feedings.

Simultaneous capture of all of these variables may seem difficult, but in reality, it is not. The technology and algorithms described here easily capture all of the feeding parameters and metrics mentioned. The single limiting factor is simultaneous *noninvasive* integration of additional physiological signals into everyday NICU workflow. We believe that technology and the enhancement of predictive algorithms coupled with near real-time statistical modeling techniques are no longer a limiting factor to fully understanding the end effect of the complex

dynamical system of feeding. Our methods and results are a critically important addition to the emerging body of evidence that neonatal sucking is a measurable behavior that has the potential to alert us to the risk of poor neurodevelopmental outcomes.

The next important step, which has not yet been reported, is to assess the complex brain network that controls feeding and sucking in neonates via advanced neuroimaging technologies, and to correlate deficits in the feeding brain network with early abnormalities identified in patterns of sucking performance during bottle feeding. Such an approach is a necessary way to provide clear evidence of the association between early abnormalities in feeding performance and underlying brain injury. Combining anatomical or dysfunctional neurological features with sucking parameters and other physiological signals, will allow us to definitively categorize HRPT infants and develop predictive algorithms to help guide clinicians in the assessment and treatment of neurological disorders.

ACKNOWLEDGEMENTS

Collection of data were made possible with a grant from the University of Kentucky NIH Center for Clinical and Translational Science (NIH CTSA UL1TR000117) and the University of Kentucky College of Health Sciences Office of Research (Grant 1012003440). Grantors had no role in study design, collection, analyses and/or interpretation of data, writing of the manuscript or the decision to submit the manuscript. The authors thank Dr. Lu Dong and Mr. Jeff Rowberg for their technical expertise in development of instrumentation and signal analyses. The authors are also grateful to nurse researchers Deb Grider, Vicki Whitehead, Holly Nieves and Kimberly Walker for their assistance with recruitment and inpatient data collection and graduate student Christina Eimers for her help with data input. Finally, we thank the participants and their families for taking part in this research.

REFERENCES

1. Mizuno K, Ueda A. Neonatal feeding performance as a predictor of neurodevelopmental outcome at 18 months. *Dev Med Child Neurol.* 2005;47(5):299-304
2. Holloway EM. The dynamic process of assessing infant feeding readiness. *Newborn Infant Nurs Rev.* 2014;14(3):119-123
3. Browne JV, Ross ES. Eating as a neurodevelopmental process for high-risk newborns. *Clin Perinatol.* 2011;38(4):731-743
4. Bertocelli N, Cuomo G, Cattani S, et al. Oral feeding competences of healthy preterm infants: a review. *Int J Pediatr.* 2012;2012:896257

5. Lau C. Interventions to improve oral feeding performance of preterm infants. *Perspectives on Swallowing and Swallowing Disorders*. 2014;23(2):23-45
6. Tamilia E, Taffoni F, Formica D, et al. Technological solutions and main indices for the assessment of newborns' nutritive sucking: a review. *Sensors (Basel)*. 2014;14(1):634-658
7. Lau C. Development of Suck and Swallow Mechanisms in Infants. *Ann Nutr Metab*. 2015;66 Suppl 5:7-14
8. Silberstein D, Geva R, Feldman R, et al. The transition to oral feeding in low-risk premature infants: relation to infant neurobehavioral functioning and mother-infant feeding interaction. *Early Hum Dev*. 2009;85(3):157-162
9. Martinez-Biarge M, Diez-Sebastian J, Rutherford MA, Cowan FM. Outcomes after central grey matter injury in term perinatal hypoxic-ischaemic encephalopathy. *Early Hum Dev*. 2010;86(11):675-682
10. Fiori S, Guzzetta A. Plasticity following early-life brain injury: Insights from quantitative MRI. *Semin Perinatol*. 2015;39(2):141-146

11. Gewolb IH, Vice FL. Maturation changes in the rhythms, patterning, and coordination of respiration and swallow during feeding in preterm and term infants. *Dev Med Child Neurol.* 2006;48(7):589-594
12. Gewolb IH, Vice FL, Schweitzer-Kenney RL, Taciak VL, Bosma JF. Developmental patterns of rhythmic suck and swallow in preterm infants. *Dev Med Child Neurol.* 2001;43:22-27
13. Medoff-Cooper B, Shults J, Kaplan J. Sucking behavior of preterm neonates as a predictor of developmental outcomes. *J Dev Behav Pediatr.* 2009;30(1):16-22
14. Tsai SW, Chen CH, Lin MC. Prediction for developmental delay on Neonatal Oral Motor Assessment Scale in preterm infants without brain lesion. *Pediatr Int.* 2010;52(1):65-68
15. Wolthuis-Stigter MI, Luinge MR, da Costa SP, et al. The association between sucking behavior in preterm infants and neurodevelopmental outcomes at 2 years of age. *J Pediatr.* 2015;166(1):26-30
16. Hiramoto A, Takagai S, Tsuchiya K, et al. Abnormal sucking behavior in infants as a predictor of developmental delay in 18-month or 3-year of age. *Journal of Brain Science.* 2014;43:5-23

17. da Costa SP, van der Schans CP. The reliability of the Neonatal Oral-Motor Assessment Scale. *Acta Paediatr.* 2008;97(1):21-26
18. Shaker C. Cue-based co-regulated feeding in the Neonatal Intensive Care Unit: Supporting parents in learning to feed their preterm infant. *Newborn Infant Nurs Rev.* 2013;13:51-55
19. Tamilia E, Delafield J, Fiore S, Taffoni F. An automatized system for the assessment of nutritive sucking behavior in infants: a preliminary analysis on term neonates. *Conf Proc IEEE Eng Med Biol Soc.* 2014;2014:5752-5755
20. Tamilia E, Formica D, Scaini A, Taffoni F. An automated system for the analysis of newborns' oral-motor behavior. *IEEE Trans Neural Syst Rehabil Eng.* 2015
21. Stergiou N, Decker LM. Human movement variability, nonlinear dynamics, and pathology: is there a connection? *Hum Mov Sci.* 2011;30(5):869-888
22. Rohrer B, Fasoli S, Krebs HI, et al. Movement smoothness changes during stroke recovery. *J Neurosci.* 2002;22(18):8297-8304
23. Scheel CE, Schanler RJ, Lau C. Does the choice of bottle nipple affect the oral feeding performance of very low-birthweight (VLBW) infants? *Acta Paediatrica.* 2005;94:1266-1272

24. Shaker CS. Cue-based feeding in the NICU: using the infant's communication as a guide. Neonatal Netw. 2013;32(6):404-408
25. Natarajan G, Shankaran S. Short- and long-term outcomes of moderate and late preterm infants. Am J Perinatol. 2016;33(3):305-317
26. Horgan MJ. Management of the late preterm infant: Not quite ready for prime time. Pediatr Clin North Am. 2015;62(2):439-451
27. Pandit AS, Robinson E, Aljabar P, et al. Whole-brain mapping of structural connectivity in infants reveals altered connection strength associated with growth and preterm birth. Cereb Cortex. 2014;24(9):2324-2333
28. Nieuwenhuis T, da Costa SP, Bilderbeek E, et al. Uncoordinated sucking patterns in preterm infants are associated with abnormal general movements. J Pediatr. 2012;161(5):792-798

Table 1. Mean (Standard Deviation) Of Variables Of Interest For The Full Study

Population

Study Population		
Variable	Preterm (N = 40)	Full Term (N = 15)
F:M ¹	24:16	4:11
Gestational Age (weeks)	30.7 (2.8)	38.6 (1.0)
Birthweight (grams)	1496 (575)	3158 (343)
FRLOS ² (days)	25.6 (11)	2.5 (2)

¹ Female to male ratio; ²Feeding-related length of stay calculated from date of initial oral feeding to discharge

Table 2. Mean (Standard Deviation) Of Variables Of Interest For Our Study Population Subcategories, Outlier Removed

Variable	Study Population			<i>Post hoc</i> <i>p values</i> ^d
	LRPT ^a (N = 12)	HRPT ^b (N = 28)	FT ^c (N = 14)	
F:M ¹	4:8	20:8	4:10	NA
GA ²	34.1 (1.3)	29.2 (2)	39.1 (1)	FT>LR>HR
BW ³	2139 (610)	1220 (253)	3203 (309)	FT>LR>HR
GA at Initial Exam	35.6 (1.5)	34.2 (1.3)	39.3 (1.3)	FT>LR>HR
GA at Discharge Exam	36.4 (1.4)	37 (1.6)	39 (1)	HR> FT, LR
FRLOS ⁴	16 (4)	30 (10)	2 (2)	FT>LR>HR

^a Preterm infants considered low risk for developmental concerns

^b Preterm infants considered high risk for developmental concerns

^c Full term infants

^d all ANOVAs were significant at $p < .000$; post hoc direction of significant findings

¹ Female to male ratio; ²Gestational age in weeks; ³Birthweight in grams;

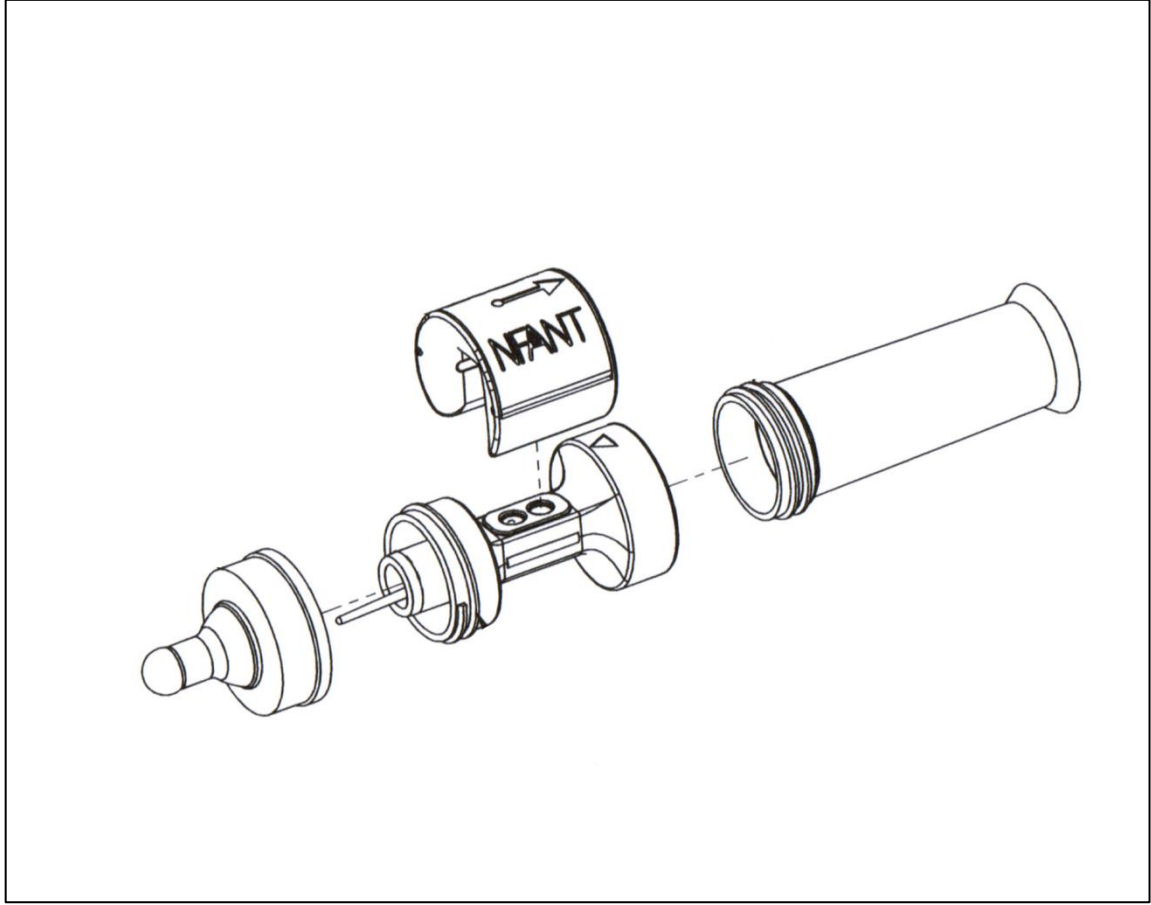
⁴Feeding-related length of stay in days

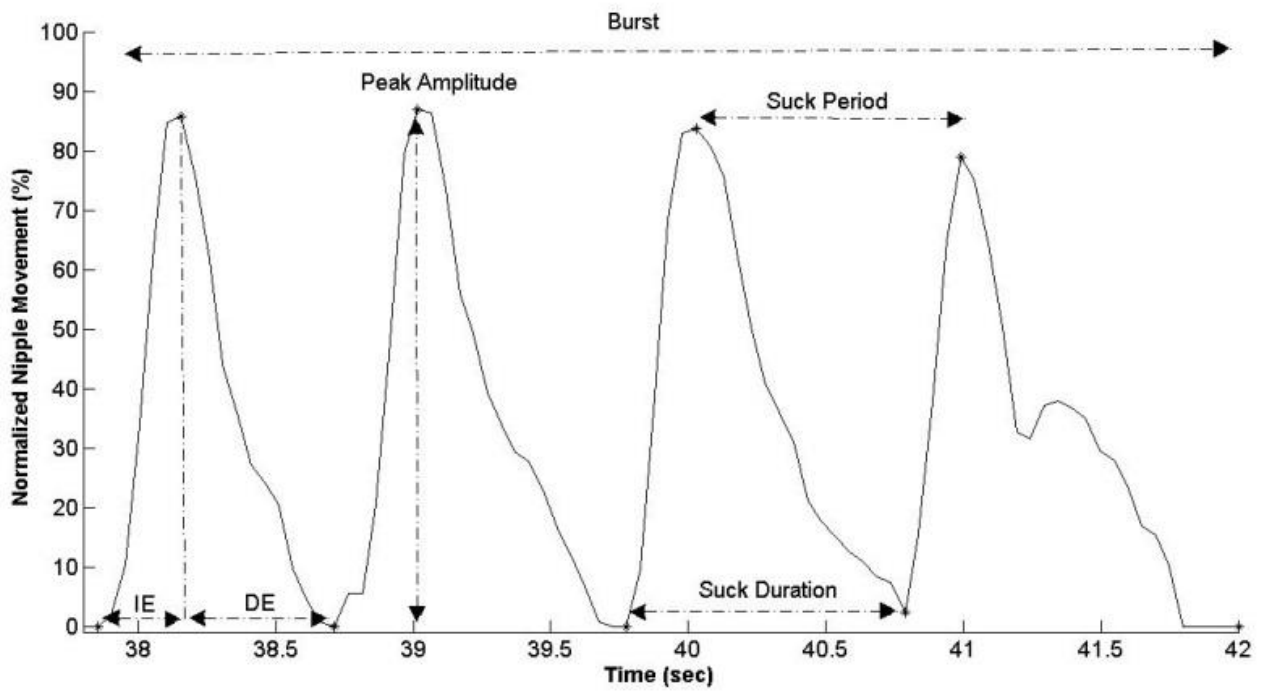
FIGURE LEGENDS

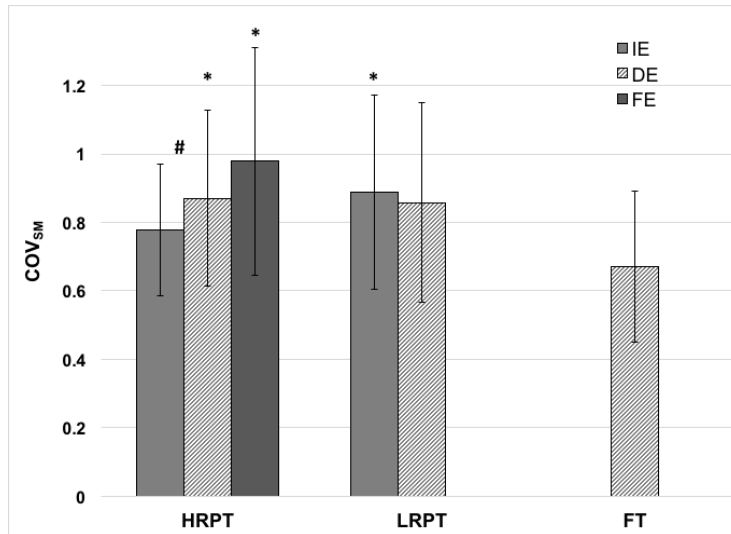
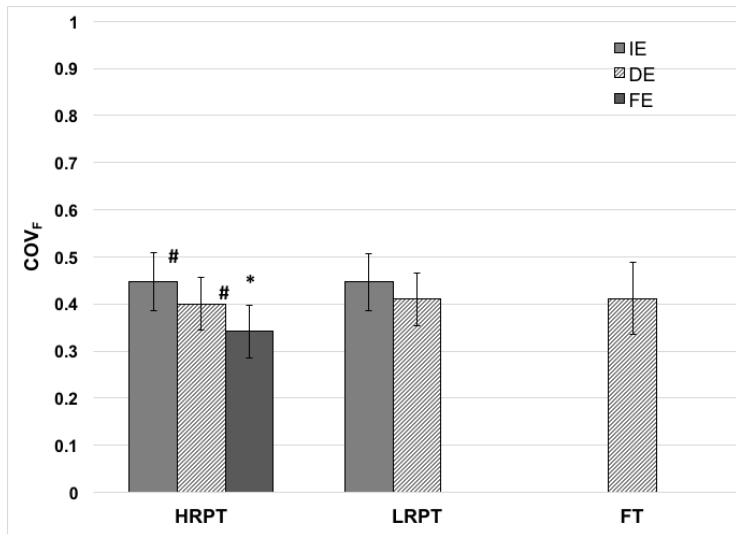
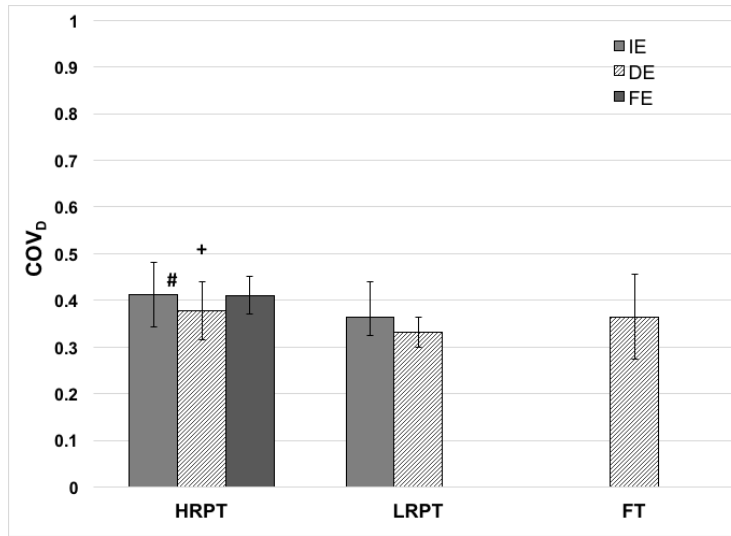
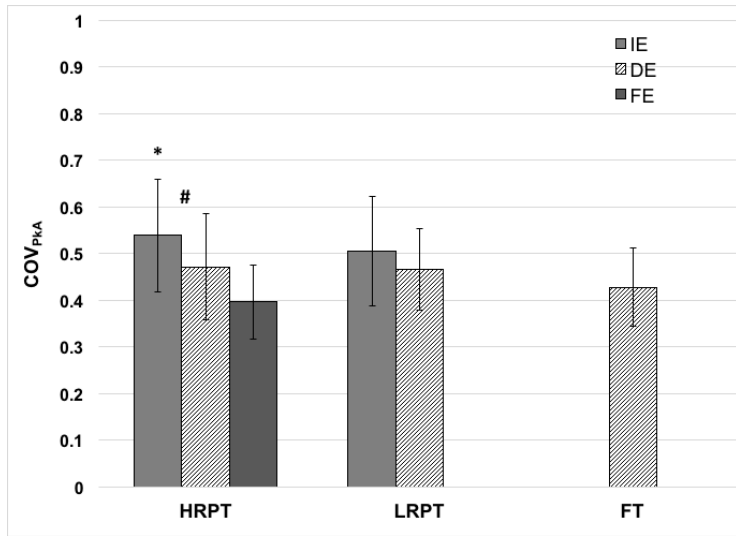
Figure 1 Diagram of nfan[®] Feeding Solution.

Figure 2 Suck pattern excerpt from a representative full term subject. Points indicate the start, end and peak of the suck events, generated from the custom suck algorithm employed in this study. Indicated suck features are used to generate metrics for analyses.

Figure 3 Comparison of Coefficient of Variation (COV) for peak amplitude (COV_{PKA}), duration (COV_D), frequency (COV_F) and smoothness (COV_{SM}) at initial exam (IE) and discharge exam (DE) for the high risk preterm group vs. full term (FT). Significant differences in mean values for each exam in comparison to FT are indicated by (*), between PT groups by (+), and changes in exams values within groups by (#).







CONTINUING EDUCATION QUESTIONS

1. Early identification of neonates at risk for poor neurobehavioral functioning:
 - a. Is available through a number of commercially available tools
 - b. Has become a part of routine screening in the NICU
 - c. Takes advantage of neuroplasticity mechanisms**
 - d. Is not necessary for prevention and/or treatment during infancy
2. Research correlating early sucking and later neurodevelopmental outcomes is limited by the fact that:
 - a. Methods used may alter sensory feedback during feeding
 - b. Appraisal of sucking performance is based largely on subjective data
 - c. Only a snapshot of sucking performance is analyzed
 - d. All of the above**
3. To provide clear evidence of the association between early sucking and later neurodevelopment we must:
 - a. Complete a randomized clinical control trial
 - b. Correlate brain imaging with early patterns of sucking during bottle feeding**
 - c. Identify an observational tool of early sucking with high inter-rater reliability
 - d. Screen all preterm infants at discharge
4. Dynamical systems theory:
 - a. Emphasizes the importance of variability in any human movement**
 - b. Describes sucking in the context of three phases
 - c. Fails to account for the coordination of sucking, swallowing, and breathing for safe, efficient sucking

- d. Fails to take into account the gestational age of infants
5. The variables of interest reported here:
- a. Focus on movement variability of the nipple during sucking
 - b. Are calculated taking the standard deviation of the mean, and dividing by the mean
 - c. Emphasize the motor learning and coordination aspects of neonatal sucking
 - d. Are calculated across each sucking burst
 - e. **All of the above**

LEARNING OBJECTIVES

As a result of this activity, the reader will be able to:

1. Summarize the literature suggesting early sucking as a predictor of neurodevelopmental outcomes in preterm infants.
2. Discuss the limitations of previous findings and how they are overcome in the current study.
3. Explain neonatal sucking in the context of dynamical systems theory.

BIOGRAPHIES

Gilson Capilouto Ph.D. CCC-SLP is professor in the Department of Rehabilitation Sciences at the University of Kentucky and a certified and licensed speech-language pathologist. She has more than 30 years of experience in assessment and treatment of pediatric feeding and swallowing disorders and has presented extensively in this clinical area. Dr. Capilouto has focused her clinical research on neonatal feeding for the last 10 years and has received extramural funding to study neonatal feeding from multiple sources. She is co-inventor of an FDA cleared medical device to study issues related to neonatal sucking in preterm infants.

Tommy J. Cunningham, Ph.D. is co-founder and chief operating officer for NFANT Labs, LLC. He is an adjunct assistant professor in the Department of Rehabilitation at the University of Kentucky. His career goal is to develop and commercialize evidence-based medical technologies that will provide patients access to the best possible care without prohibitive costs. Experiences and formal training include both private sector and academic settings in mechanical engineering, biomechanics, medical device design, clinical testing and IP development. He holds a Ph.D. and M.S. in Biomechanics from the University of Kentucky as well as a B.S. in Mechanical Engineering. Prior to NFANT Labs, he founded an engineering firm to consult with clinicians and conceptualize, design, build, and test custom research tools for their various projects. He has presented his work at local, national, and international conferences. He currently holds 6 US and several international patents in various technologies to measure human movement and rehabilitate the musculoskeletal system.

David R. Mullineaux Ph.D. is a professor in Sport and Exercise Science at the University of Lincoln, England. His primary research interests are in biomechanics, research methods and data analysis techniques. This includes analyzing coordinated movements and functional-variability, which relate to exploring movements from a dynamical systems theory perspective. He has worked in industry and academia in both the UK and USA, and has managed clinical trials units, research centers and the research activity of academic departments. His research has been published in areas including Medicine, Biomedical Engineering, Sports Medicine, Orthopedics, Athletic Training and Physical Therapy.

Eleonora Tamilia Ph.D. is a postdoctoral research fellow in pediatrics at the Fetal-Neonatal Neuroimaging & Developmental Science Center (FNNDSC) of Boston Children's Hospital (BCH) and Harvard Medical School (HMS). She received her M.Sc. (2010) and PhD (2015) in Biomedical Engineering, respectively, from University of Tor Vergata and University Campus Bio-medico of Rome (Italy). Her research activities are focused on the analysis of electroencephalography (EEG) and magnetoencephalography (MEG) data from pediatric patients with major neurological problems, such as epilepsy, or at high-risk for neurodevelopmental delays, such as preterm or very low birth weight infants. Her main research interest is the development of innovative tools and methods to investigate children's development and disorders starting from the neonatal age.

Christos Papadelis Ph.D. is Assistant Professor at Boston Children's Hospital (BCH) / Harvard Medical School (HMS). He leads a research group that is dedicated to pediatric brain research using multimodal neuroimaging. He has a broad background in neuroimaging, clinical

neurophysiology, and biomedical engineering. He received first-rate training in magnetoencephalography (MEG) and electroencephalography (EEG) from three laboratories in Japan, Italy, and USA. He has more than ten years of experience with neuroimaging experiments for multiple human studies using MEG and EEG technology with both adults and children. He has a demonstrated record of accomplished and productive research projects leading to >40 peer-reviewed articles (on 18 of them he is either first or senior author) and numerous articles in conference proceedings. His work has so far been cited >1100 times. He is ad-hoc reviewer in 38 journals, as well as guest editor in special issues of his field.

Peter J. Giannone, M.D. is the Chief of the Division of Neonatology and Vice Chair of Pediatric Research at Kentucky Children's Hospital, University of Kentucky. He received his medical degree from SUNY Health Science Center at Syracuse College of Medicine in Syracuse, New York. He completed his pediatrics residency at Eastern Virginia Medical School in Norfolk, Virginia at Children's Hospital of the King's Daughters. Dr. Giannone completed his neonatology fellowship at Brown University in Providence, Rhode Island with a concentration in neonatology in the Women and Infants Hospital of Rhode Island. He is board certified in pediatrics and neonatology.