## **Comparison of Established Neurobehavioral Profiles for Healthy Infants to Preterm NICU Infants**

**Authors**: Amy D'Agata, PhD, MS, RN<sup>1,2</sup>, Stephen Walsh, ScD<sup>1</sup>, Dorothy Vittner, RN, PhD<sup>1,3</sup>, Jacqueline M. McGrath, PhD, RN, FNAP, FAAN<sup>1,3</sup>

- 1. University of Connecticut, Storrs, CT
- 2. University of South Florida, Tampa, FL
- 3. Connecticut Children's Medical Center, Hartford, CT

**Background:** The burden of stress that the human body endures during critical periods of development is postulated as having implications in the development of later life mental health and physical illnesses.<sup>1-3</sup> Risks from early life developmental adversity are linked to later life illnesses and diseases of the cardiovascular and endocrine systems, as well as mental health illness.<sup>4-8</sup> An early life stress experience that often receives inadequate attention yet may be of considerable later life consequence is the caregiving environment of the neonatal intensive care unit (NICU). While NICU care is often lifesaving, the intensity and chronicity of these experiences are evolutionarily unexpected and occur during a period of developmental vulnerability. Stress exposure from necessary care in the neonatal intensive care unit (NICU) can have profound effects on infant brain development. Interpreting neurodevelopmental effects from adverse early life experiences in the NICU can be challenging.

**Research Objectives:** The purpose of this study was to explore whether established term infant neurobehavioral profiles may be used to characterize a preterm NICU infant cohort. The potential of longitudinal NICU stress exposure to further discriminate profiles was also examined.

**Methods:** A sample of 41 preterm NICU infants were analyzed for stress exposure and neurodevelopmental functioning. The sample of preterm infants analyzed in this study were previously described in the primary study.<sup>10</sup> Briefly, the primary study explored the relationships between neurodevelopmental outcomes at NICU discharge, *FKBP5* genotype and NICU stress exposure. An established algorithm was applied to investigate membership of preterm infants at near term age within 3 neurobehavioral profiles. Total 21-day and weekly average stress were also examined and found to be correlated to infant neurobehavioral profiles.

Descriptive demographic data and stress data were analyzed using IBM© SPSS® Statistics, version 22.0. The NNNS neurobehavioral profiles were analyzed using the algorithm in R statistical software.<sup>11</sup> Finally, multivariate analysis was used to discriminate the probability of NISS stress scores by week (week 1, week 2, week 3) to predict if the preterm profiles were similar to the healthy infant profiles.

**Results:** There were significant differences in the distribution of membership within the developmental profiles between preterm infants and healthy full-term infants. An interaction was found between the membership with the three profiles and time within mean range of stress value. Using Pearson Chi-Square test, there was a statistically significant difference (p = 0.02) in the distribution of neurobehavioral profiles between the sample of preterm NICU infants and the comparison to the healthy full-term infant sample from the Sucharew study<sup>12</sup>.

While statistically significant results were not detected (p = 0.11) for preterm infants in the mean value for 21 days of stress across the three profiles (see Table 3), the mean stress score was lowest for the preterm infants categorized into Profile 1 (social/easy-going) and the highest mean stress scores for infants categorized into Profile 2 (hypotonic). There was a statistically significant interaction (p = 0.03) between the 3 neurobehavioral profiles and the mean value of weekly average stress.

**Conclusions:** Preterm infants neurobehavioral functioning may be classified with these neurodevelopmental profiles to better understand the influence of early life experiences. Interestingly, the comparison of preterm profiles to Sucharew et al. term profiles, demonstrate a reversed yet near exact matched percentage of Profile 1 (easy-going) and Profile 2 (hypotonic), while the Profile 3 (difficult) percentage remains consistent between the two groups. Stress exposure in the NICU has the potential to discriminate NNNS profile membership.

Keywords: NICU; preterm infant; stress; neurodevelopment; NICU Network Neurobehavioral Scale

## References

- 1. Shonkoff JP, Garner AS, Siegel BS, et al. The Lifelong Effects of Early Childhood Adversity and Toxic Stress. *Pediatrics*. 2012;129(1):e232-e246.
- 2. Daskalakis NP, Bagot RC, Parker KJ, Vinkers CH, de Kloet ER. The three-hit concept of vulnerability and resilience: towards understanding adaptation to early-life adversity outcome. *Psychoneuroendocrinology*. 2013;38(9):1858-1873.
- 3. McLaughlin KA, Sheridan MA, Alves S, Mendes WB. Child Maltreatment and Autonomic Nervous System Reactivity: Identifying Dysregulated Stress Reactivity Patterns using the Biopsychosocial Model of Challenge and Threat. *Psychosomatic medicine*. 2014;76(7):538-546.
- 4. Goosby BJ, Cheadle JE, McDade T. Birth weight, early life course BMI, and body size change: Chains of risk to adult inflammation? *Social Science & Medicine*. 2016;148:102-109.
- 5. Kemppainen KM, Ardissone AN, Davis-Richardson AG, et al. Early Childhood Gut Microbiomes Show Strong Geographic Differences Among Subjects at High Risk for Type 1 Diabetes. *Diabetes Care.* 2015;38(2):329-332.
- 6. Johnson S, Wolke D. Behavioural outcomes and psychopathology during adolescence. *Early Human Development*. 2013;89(4):199-207.
- Godfrey KM, Costello PM, Lillycrop KA. The Developmental Environment, Epigenetic Biomarkers and Long-Term Health. *Journal of developmental origins of health and disease*. 2015;6(5):399-406.
- 8. Heindel JJ, Balbus J, Birnbaum L, et al. Developmental Origins of Health and Disease: Integrating Environmental Influences. *Endocrinology*. 2015;156(10):3416-3421.
- 10. D'Agata AL, Walsh, S., Vittner, D., Cong, X., McGrath, J. M., Young, E. E. FKBP5 Genotype and Early Life Stress Exposure Predict Neurobehavioral Outcomes for Preterm Infants. *Developmental Psychobiology*. 2017.
- 11. Team RC. R: A Language and Environment for Statistical Computing. 2015; <u>https://www.R-project.org</u>.
- 12. Sucharew H, Khoury JC, Xu Y, Succop P, Yolton K. NICU Network Neurobehavioral Scale Profiles Predict Developmental Outcomes in a Low-Risk Sample. *Paediatric and Perinatal Epidemiology*. 2012;26(4):344-352.

## **Statement of Financial Support:**

D'Agata, A., Walsh, S., Vittner, D., & McGrath, J., have no financial relationships with commercial entities to disclose.