NUTRIENT INTAKE IN THE FIRST 2 WEEKS OF LIFE PREDICTS BRAIN GROWTH IN PRETERM NEONATES

Juliane Schneider[1,2], Lydie Beauport[1], Emma G. Duerden[1], Ting Guo[1], Justin Foong[1], Patric Hagmann[3], M. Mallar Chakravarty[4,5], Petra S Hüppi[6], Céline J. Fischer Fumeaux[2], Anita C. Truttmann[2*]/ Steven P. Miller[1*]

[1]Paediatrics, University of Toronto and the Hospital for Sick Children, Toronto, Canada, [2]Paediatrics and [3] Radiology, University Hospital Center and University of Lausanne, Switzerland, [4]Douglas Mental Health University Institute, Montreal, [5]Department of Psychiatry and Biological and Biomedical Engineering, McGill University, Montreal, Canada, [6]Paediatrics, University Hospital of Geneva, Switzerland. ***last 2 co-authors**

Background

- Optimizing early nutritional intake might promote brain health and neurodevelopmental outcomes through enhanced brain maturation.
- The relationship of energy and nutrient intake in the first weeks of life with brain growth during neonatal intensive care needs to be determined.

Objective

To determine the association of energy and nutrient intake during the two first weeks of life with brain regional and total brain growth, and white matter maturation, assessed by serial magnetic resonance imaging (MRI) in very preterm neonates.

Methods

Participants:

- 49 very preterm neonates: 21 males, median[IQR] gestational age (GA): 27.6[2.3] weeks
- 3 serial scans between birth and term-equivalent age (TEA) at median postmenstrual weeks (PMA): (i) 29.4, (ii) 31.7 and (iii) 41.0 weeks

MRI analysis:

- **Volume segmentation:** Basal nuclei (thalamus and basal ganglia), cerebellum and total brain semi-automatically segmented in the T1-weighted images using MAGeT brain segmentation pipeline (Figure 1)
- **TBSS:** Fractional anisotropy (FA) in main white matter tracts extracted from the diffusion-tensor imaging (DTI) data using tract-based spatial statistics (TBSS)

Nutrition:

- Collection of cumulative nutritional intake from days of life 1 to 14 (enteral and parenteral)

Statistical analysis:

- Multivariate linear regression and generalized estimating equations (GEE) for repeated measures used to assess the association between nutrient intake and volumes, and FA values in separate models, adjusting for PMA at MRI.

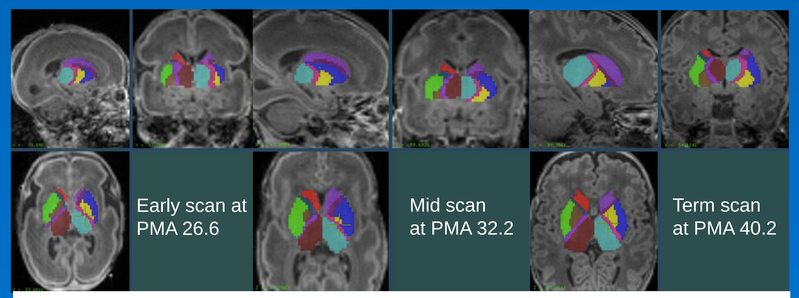
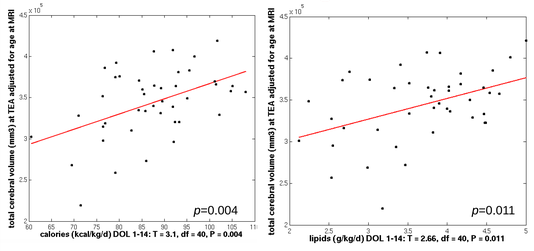


Figure 1: Segmentation templates on T1-weighted images from the same patient born at GA 27.3

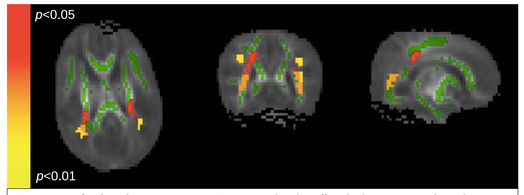
Results

Greater early energy and nutrient intake predicts more robust regional and total brain growth



- Greater energy [kcal/kg/d] and lipid [g/kg/d] intake predicted increased basal nuclei (β=839.8, p=0.021 and β=13425.5, p=0.019, respectively), and total brain (β=37.6, p=0.019 and β=616.8, p=0.017, respectively) growth over the course of neonatal intensive care to term age.
- Examining volumes at each scan, the associations of energy and lipid intake with basal nuclei, cerebellar and total brain volumes became increasingly robust on the second and third scans.

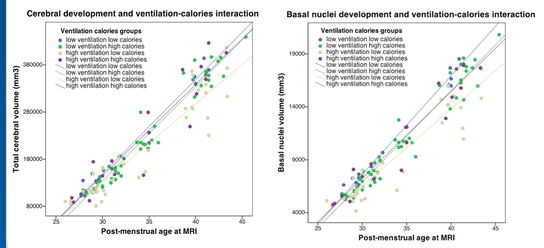
Greater early energy and nutrient intake predicts accelerated microstructural maturation of white matter tracts



TBSS analysis of term scans. FA map (red-yellow) demonstrating the significant positive linear association between lipid intake and FA in the posterior WM tracts and cortico-spinal tract. The mean FA skeleton is shown in green.

- Maturation of WM tracts was positively associated with energy and lipid intake in posterior corona radiata, posterior thalamic radiation, and superior longitudinal fasciculus.
- Lipid intake also predicted maturation of superior corona radiata and cortico-spinal tract (all p<0.05).

Optimized early nutrition might mitigate the negative effect of respiratory morbidity on brain development



- The interaction of energy intake by duration of ventilation positively predicted total brain (β=150.4, p=0.048), cerebellum (β=15.4, p=0.044) and basal nuclei (β=5.7, p=0.032) growth.
- Preterm neonates exposed to longer duration of ventilation and with low energy intake have slower growth of their regional and total brain volumes over the course of the intensive care.

Conclusions

- In very preterm neonates, greater energy and lipid intake during the first two weeks of life predicted more robust brain growth particularly in subcortical structures and cerebellum, and accelerated white matter maturation.
- Although respiratory morbidity is a strong predictor of adverse outcome, improved nutrition appeared to mitigate its negative impact on brain development.
- Optimizing early nutrition in very preterm neonates warrants further attention as a potential avenue to improve brain health outcomes.

Acknowledgements: Swiss National Science Foundation (number 33CM30 –124101) / SICPA Foundation / Société Académique Vaudoise / CIHR / NeuroDevNet