Relationship between cerebral blood flow and oxygen metabolism with neurological status at term-equivalent age in infants born preterm

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Conflict of interest

- None of the authors have a conflict of interest to disclose.

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Introduction

- Infants born 29-36 weeks' gestational age (GA) represent the majority of preterm births and are at increased risk of developmental delay (DD).

- Specialized neurodevelopmental follow-up for all these infants is :
  - Unrealistic due to a lack of resources
  - Most likely unnecessary as more than half will do well

- Early identification of those benefiting the most from specialized follow-up is needed.

- New screening strategies could help in this risk stratification.

- Advanced near infrared spectroscopy (NIRS) is a non-invasive bedside technique that has been used in the preterm population and has the potential to provide additional biomarkers of cerebral development.

FDNIRS-DCS acquisition system

Probe placement on neonatal forehead

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Hypothesis

Cerebral blood flow (CBF_i) and oxygen metabolism ($CMRO_{2i}$) indices acquired by advanced NIRS reflect cerebral development and are associated with neuromotor status at term-equivalent age (TEA) in preterm infants.

Aims of the study

1. To examine changes over time in advanced NIRS measures and their associations with the neuromotor status in infants born preterm.
2. To explore the relationship between GA and trajectories of brain hemodynamics and oxygen metabolism.

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Methods

- Prospective observational cohort study
- Inclusion criteria
  - Infants born between 29-36 $^{6/7}$ GA
  - Admitted for ≥48 hours at CHUSJ NICU
- Exclusion criteria
  - Chromosomal or major congenital anomaly, moderate to severe HIE, stroke, not likely to survive
  - Under child protection services
- Demographic and neonatal data were collected from medical charts.
- Advanced NIRS was performed from one week of life to TEA.
- Change in NIRS parameters was determined using the first and the closest to TEA values.

Main outcome

- Abnormal neuromotor exam at TEA, defined as abnormal ATGNA + abnormal GMA results

1. Amiel-Tison and Gosselin Neurological Assessment (ATGNA) :
   - 35 items determining the neurological status
   - Previously validated in the preterm population to discriminate those with DD

   (Simard MN, 2009)
2. General Movement Assessment (GMA) :
   - Observation of spontaneous movements for 1-3 min
   - Based on pattern recognition
   - Can predict cerebral palsy and milder deficits

   (Einspieler C, 2005)

Statistical analysis

- Logistic regression analysis to examine relationship between changes in NIRS parameters and neuromotor status
- Univariate linear regression analysis to examine relationship between GA and NIRS slope

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Results

- Valid NIRS data after quality assessment (at least 2 measurements) :
  - Change in CBF_i : n = 48
  - Change in $CMRO_{2i}$: n = 26
- Abnormal neuromotor exam at TEA :
  - n = 33 (39%)

Characteristics of the study population

	All participants (n=85)
Mean gestational age (SD), weeks	33.4 (1.78)
Mean birth weight (SD), grams	1877 (595)
Male，n （%）	44 (52)
Multiple births, n (%)	30 (35)
Antenatal corticosteroids, n (%)	65 (76)
Urgent Cesarean section, n (%)	39 (46)
Surfactant administration, n (%)	15 (18)

NIRS and neuromotor exam at TEA

- Adjusting for GA, there was no correlation between NIRS parameters trajectories and the neuromotor exam at TEA.
  - CBF_i (OR 1.27; 95% CI 0.31-5.15)
  - $CMRO_{2i}$ (OR 0.30; 95% CI 0.05-1.91)

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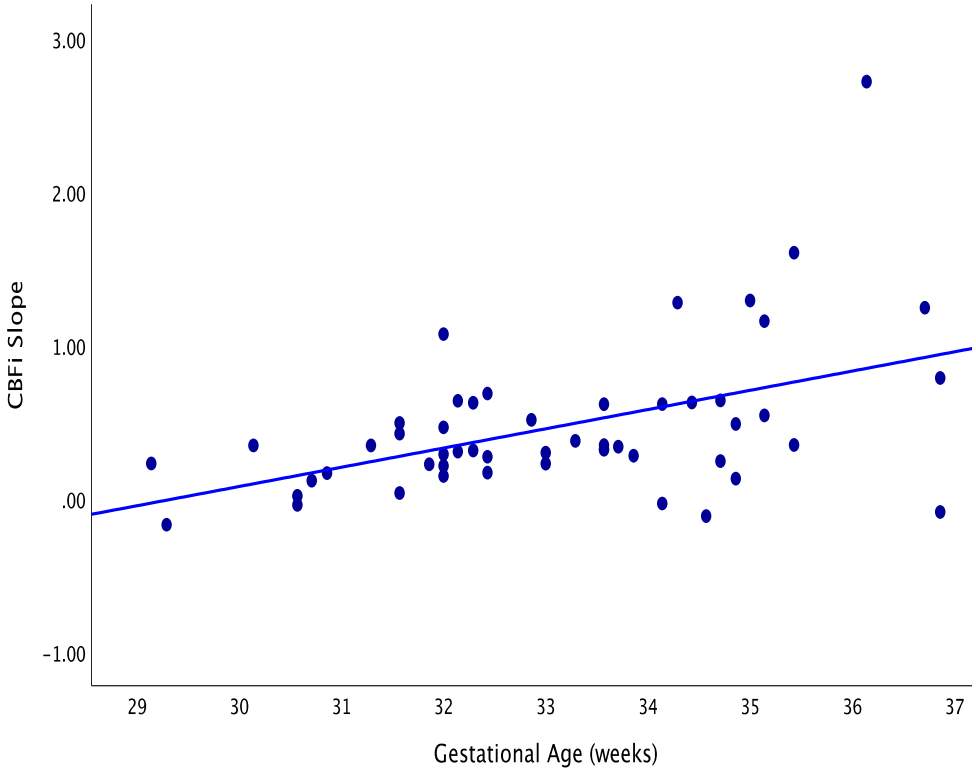
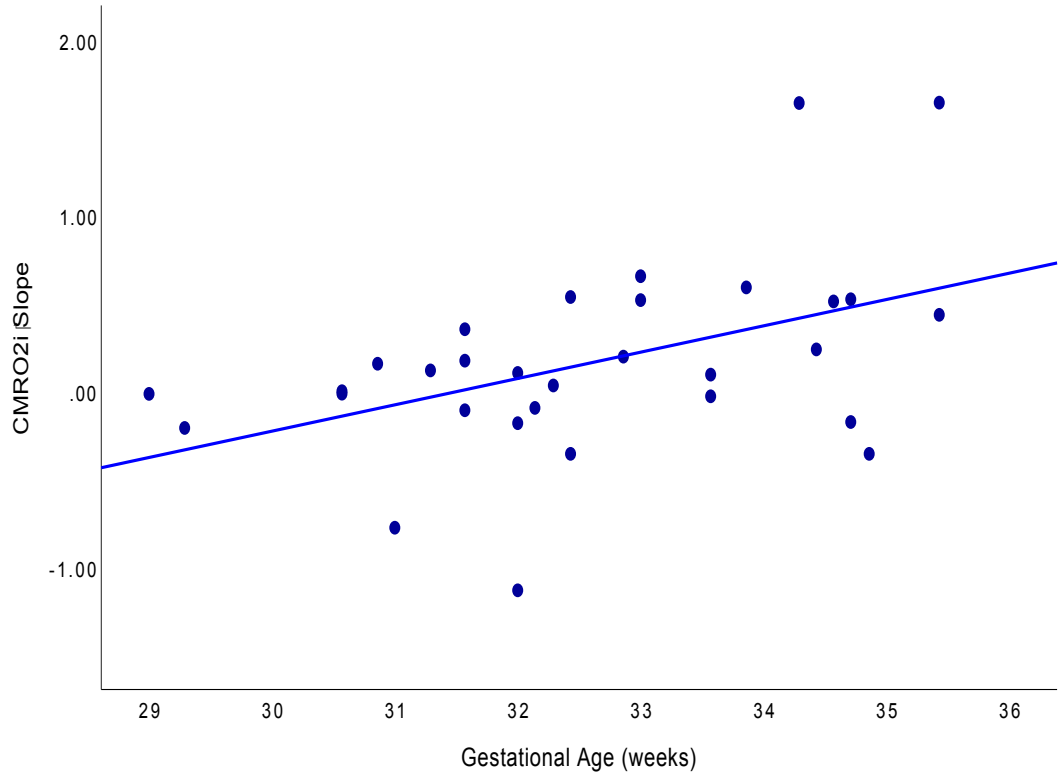
GA and CBF_i slope



(β=0.49; P<0.001)

GA and $CMRO_{2i}$ slope



(β=0.56; P=0.003)

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Discussion

- In our study, we found a significant correlation between GA and a more rapid increase in CBF_i and $CMRO_{2i}$.
  - With the physiological maturation and growth of the newborn's brain over time, we expect an increase of cerebral blood flow and oxygen metabolism.

    (Roche-Labarbe N, 2012)
  - With advancing GA, infants are on average born with an already more mature and voluminous brain, which affects cerebral blood flow and oxygen consumption.

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Discussion

- In our study, we did not find any correlation between NIRS trajectories and the neuromotor assessment at TEA.

Advanced NIRS monitoring :

- Advanced NIRS provides information on brain hemodynamics and oxygen metabolism.
- Advanced NIRS has the potential to assess brain growth as CBF_i and $CMRO_{2i}$ are associated with brain volume.
- Advanced NIRS trajectories can be used to screen abnormal brain metabolic activity. (Dehaes M, 2015)

Neuromotor assessment at TEA :

- The ATGNA and GMA reflect the global and structural integrity of the brain and can indicate cerebral alterations. (Gosselin J, 2007) (Peyton C, 2016)
- The ATGNA was shown to predict developmental delay. (Simard MN, 2011)
- The GMA can predict neurological impairment such as cerebral palsy. (Burger M, 2009)

➜ These parameters highlight different information on the infant's neurological and neuromotor state.

➜ Therefore, combining them could be useful to enhance risk prediction.

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Limitations

- Small sample size (recruitment still ongoing)
- FDNIRS-DCS data quality may be affected in infants with small head
- Lack of hemoglobin values from blood sampling at TEA
- Regional variations of cerebral development (Lin PY, 2013)
- Possible impact of systemic conditions on brain hemodynamics and metabolism

Conclusions

In this population, there was no correlation between advanced NIRS cerebral parameters and infant neuromotor status at TEA.

There was a significant association between GA and a more rapid increase in cerebral blood flow and oxygen metabolism.

The use of advanced NIRS as a non-invasive and bedside technique to monitor the brain hemodynamics and oxygen metabolism in the preterm population shows promising results.

In infants born 29-36 weeks' GA, advanced NIRS and the neuromotor status at TEA provide complementary information that could help for a better risk stratification.

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Perspectives

- As this cohort grows until 2 years corrected age :
  - Increasing sample size
  - Optimizing NIRS measurements and hemoglobin collection (non-invasive oximetry at TEA)
  - Assessing frequent neuromotor exams over time
- Our main goal will be to examine the combination of markers that optimizes the prediction of infants born 29-36 weeks' GA at highest risk of developmental delay.

Thank you ! To all the families who participated in this study

To our team and research professionals

CRSNG NSERC

CIHR IRSC
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