Neurological perturbations and language impairments in very preterm infants

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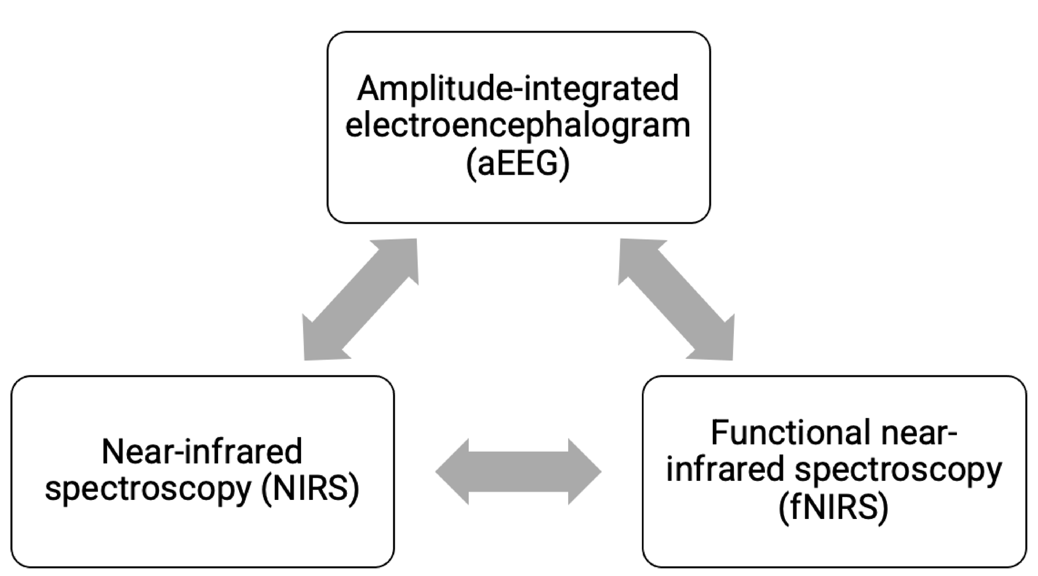
Background & Significance

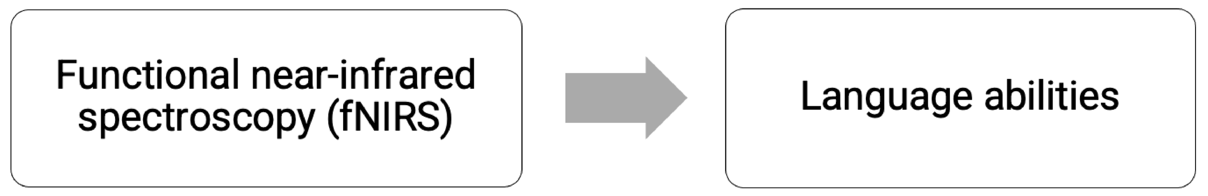
- 30% to 45% of preterm infants experience a language delay or disorder *(Pritchard et al., 2014)*
  - Substantial heterogeneity exists in language outcomes of preterm infants
  - Additional investigation into the underlying mechanisms of language development in preterm infants is needed
- Early neuromonitoring and neuroimaging metrics currently used in the neonatal intensive care unit (NICU) are currently unable to predict long-term language outcomes
- Recent approaches emphasize simultaneous use of multiple neuromonitoring modalities, such as amplitude-integrated electroencephalography (aEEG) and near-infrared spectroscopy (NIRS), for continuous monitoring of cerebral function in the NICU
  - It is unclear whether aEEG and/or NIRS can reliably index functional-related outcomes
- A better understanding of the structural and functional architecture of the language system in preterm infants may help explain the heterogeneity in language abilities
- Neuromonitoring and neuroimaging metrics may emerge as early biomarkers for predicting adverse language development

Aims

1) Determine the extent to which aEEG, NIRS, and functional NIRS (fNIRS) are concordant in detecting neurological perturbations



2) Examine the association between the functional architecture of the language system at 36 weeks post-menstrual age and language development in very preterm infants at 9 months corrected age



Research Design & Methodology

Study Population

- 30 very preterm infants (gestational age < 32 weeks) who received neonatal care at the University of Iowa Stead Family Children's Hospital
- Inclusion Criteria: Primary caregiver is a native English speaker, ≥18 years, and the legal guardian.
- Exclusion Criteria: Grade III or IV intraventricular hemorrhage with progressive ventricular dilation; periventricular leukomalacia; hypoxic-ischemic encephalopathy; major brain malformations or abnormalities; diagnosis of genetic syndrome or major congenital abnormalities; severe hearing, visual, or physical impairment

Multimodal neuromonitoring and neuroimaging techniques

- **aEEG** is a compressed form of electrocortical activity recording that allows evaluation of baseline brain wave activity and detection of seizures (Figure 1)
- **NIRS** measures cerebral regional oxygen saturation (rSO²) and allows for calculation of cerebral fractional tissue oxygen extraction (FTOE) (Figure 2)
- **fNIRS** quantifies changes in concentrations of oxyhemoglobin (HbO²) and deoxyhemoglobin (HHb) in cortical brain structures and can be used to measure resting brain function, or cerebral network connectivity, in clinic settings (Figure 3)

*Note. Brain metrics will be measured at **36 weeks post-menstrual age** during the infant's NICU hospitalization*

Figure 1. CFM Olympic Brainz Monitor and hydrogel electrodes located at the C3, P3, C4, and P4 regions according to the 10—20 International System of Electrode Placement

Figure 2. INVOS 7100 (Medtronic, Dublin, IR) and cerebral sensors

Figure 3. NIRSport2 (NIRx Medical Technologies LLC) and illumination emitters and SiPF detectors located bilaterally in frontal and temporal brain regions

Language abilities

- Expressive and receptive communication skills will be assessed with the Bayley Scale of Infant and Toddler Development, Fourth Edition (Bayley-4) at 9 months corrected age

Covariates

- Infant sex, plurality (singleton, twin, triplet), NICU length of stay, socioeconomic status (SES), and maternal antenatal and postnatal steroids

Analytic Approach

- Aim 1: Correlate Burdjavlov scoring of cerebral maturation (aEEG), cerebral oxygenation (NIRS), and functional connectivity strength of the language network (fNIRS)
- Aim 2: Utilize linear mixed effects models with maximum likelihood estimation and an unstructured covariance matrix
  - Fixed effects include functional connectivity markers (i.e., coherence values), infant sex, plurality, length of stay in NICU, socioeconomic status, and maternal antenatal and postnatal steroids
  - Random intercept for participant

Clinical Implications

- Improved prediction for risk of later language delays and disorders based on neuromonitoring and neuroimaging biomarkers at critical timepoints
  - Families of very preterm infants could be counseled on the increased risk of language impairment
  - Infants could receive more comprehensive proactive screening and intervention for language delays
- Earlier language services are imperative, as language development may be more amenable to environmental factors (e.g., infant's home learning environment) than other domains (e.g., motor development)

Project Timeline

	F23	SP24	S24	F24	SP25
Protocol approved by UI-SFCH IRB					
Orient NICU staff to neuroimaging and neuromonitoring techniques					
Begin enrollment					
Gathering & processing neuromonitoring and neuroimaging data (aEEG, NIRS, fNIRS)					
In-person evaluation with the Bayley-4 at 9-months corrected age					
Data analyses					
Manuscript & conference preparation					

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