Multi-modal Longitudinal Assessment of Infant Brain Organization in Perinatal Brain Injury

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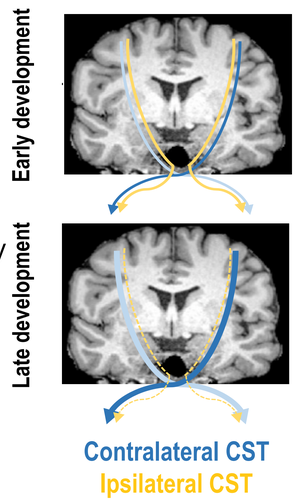
Background and Objectives:

- Perinatal brain injury (e.g. stroke or brain bleed in the prenatal and neonatal period) is a common cause of cerebral palsy (CP) and life-long motor impairment.
- During a period of heightened neuroplastic potential, early diagnosis and interventions may improve lifelong outcomes.
- The corticospinal tract (CST) is the primary pathway by which the cerebral cortex controls movement; CST organization impacts long-term motor function.
- **Objective: investigate longitudinal neuroplastic change in infants with perinatal brain injury by:**
  - Assessing CST excitability, integrity, and connectivity
  - Comparing motor outcomes from behavioral assessments to CST integrity/excitability



Study Timeline (corrected age of infant):

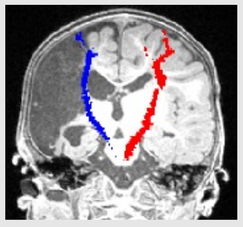
0-2 months | 3-6 months | 12 months | 18 months | 24 months

Assessments at each timepoint:

Visit 1

- MRI
  - Structural (T1, T2)
  - Diffusion
  - Multi-component relaxometry

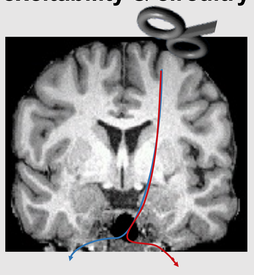
Diffusion MRI to assess brain connectivity



Visit 2

- TMS (for infants 3+ months corrected age)
- Age-appropriate Motor Assessments
  - General Movements Assessments
  - Hammersmith Infant Neurological Examination
  - Bayley - IV

TMS to assess brain excitability & circuitry



Motor development and CP diagnosis

Eligibility and Recruitment:

- Infants (N=50), corrected gestational age between original due date (term) and 6 months
- Radiologically-confirmed periventricular leukomalacia, acute unilateral or bilateral brain lesions (neonatal hemorrhagic or thrombotic stroke, intracranial hemorrhage)
- Exclusion: contraindications to MRI or TMS, other neurological conditions, metabolic disorders, disorders of cellular migration and proliferation, neoplasm
- In partnership with area NICUs (American Family Children's Hospital, Meriter)

Methodology and Pilot Data:

Magnetic Resonance Imaging (MRI)

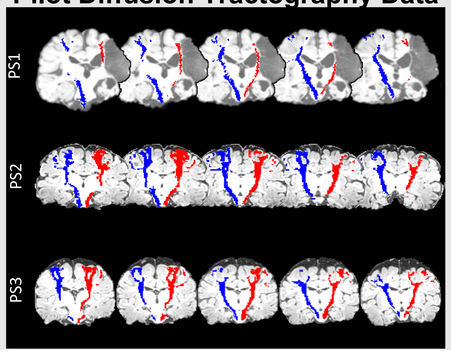
Obtained during natural sleep with infant-adapted protocols

- Structural (T1/T2)
- Diffusion (DTI/NODDI)
- Relaxometry (McDESPOT)

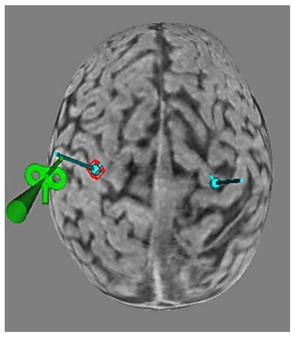
Key Data: Lesion location, corticospinal tract integrity (fractional anisotropy, mean diffusivity) and asymmetry

Imaging performed at Waisman Brain Imaging Core

Pilot Diffusion Tractography Data

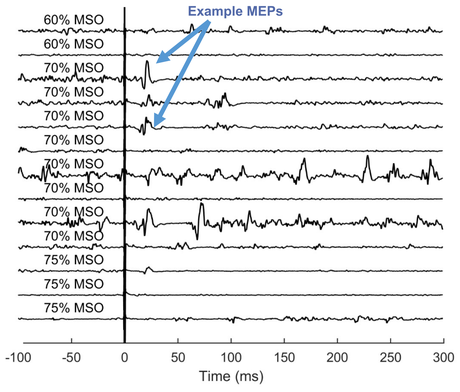


Transcranial Magnetic Stimulation (TMS)



Key Data: Motor evoked potential (MEP) presence/absence, resting motor threshold

Pilot TMS Data:



Stimulation: Right Hemisphere; EMG: Left Wrist
MSO = Maximum Stimulator Output

Safety of TMS:

- Our team has previously performed 14 single-pulse TMS assessments in 11 infants 3-23 months corrected age with diagnosis of perinatal brain injury. **No adverse events occurred.**
- All infants monitored by observation of infant status codes and stress responses, vital signs, parent report
- No adverse events were reported in the literature across >400 TMS sessions in children under 2 years old

Significance and Impact:

- Integrate non-invasive brain stimulation, neuroimaging and behavioral assessments to analyze associations between neuromotor development and potential diagnosis of CP
- Identify unique bioindicators of motor outcome and neuroplasticity after perinatal brain injury
- Inform early detection and diagnosis, facilitate early interventions tailored to individual developmental trajectories

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Lab Website: