Tissue Changes underlying MRI changes detected in Descending Corticospinal Tract following Ischemic Stroke

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ABSTRACT

Insufficient cerebrovascular perfusion and low oxygen delivery to the brain are common in the perinatal period and increase risks of brain damage, causing stroke. Little is known about the tissue changes underlying these imaging changes but these changes are assumed to be early Wallerian Degeneration.

The purpose of this study was to investigate the tissue changes underlying the magnetic resonance imaging changes detected in the descending corticospinal tract (DCST) following ischemic stroke.

Seven day old Wistar pups were exposed to either a sham surgery or a transient unilateral cerebral stroke.

The animals were subjected to a sham surgery or a transient unilateral cerebral hypoxia-ischemia (HI) procedure.

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METHODS AND MATERIALS

- Model of Hypoxia Ischemia
  - Forty Three Wistar pups from pregnant rats
  - Seven day old Wistar pups–right common carotid artery exposed surgically, ligated and transected followed by 60 minute exposure to hypoxia (8% O2, 92% N2, 35°C).

- MR Imaging
  - Imaging at 2 hours, 24 hours, 1 week and 4 weeks post surgery (9.4 T Bruker Biospin).
  - T2 scans 25-30 slices (0.5 thick) from the cerebrum to the medulla were acquired.

- Histology
  - Animals perfused 24 hours post MRI, brains paraffin embedded, sections cut (6 μm thick), stained with SMI312, Fluorojade, GFAP, ED1 and MBP.

Data Analysis

- Sections analyzed at cortex, cerebral peduncles, pons.
- Images of SMI312, GFAP, MBP captured digitally and analyzed for optical density using Image J.
- Fluorojade and ED1: Mean number of positively stained neurons shown.
- Optical density values (G). Low optical density values = less staining.

RESULTS

- Progression of histological changes in directly damaged regions (ischemic cortex) and remote regions connected to the cortex (DCST).
- Decreased SM312 staining in ipsilateral CP at acute timespans (2hour-1day) and ipsilateral DCST (CP) at chronic times (1-4 weeks) post HI.
- Decreased MBP staining in the ipsilateral CP at 1-4 weeks post HI.
- Increased Fluorojade stained cells in ipsilateral cortex at all times (2h, 24h, 1d, 2d, 1w, 4w) post HI and ipsilateral CP at 2d post HI.
- Increased GFAP staining in ipsilateral cortex seen by 1d post HI and up to 4w post HI. GFAP staining visible in CP by 2d post HI.
- No significant ED1 staining in CP but slight ED1 staining observed visually by 2d post HI.

CONCLUSIONS

- Axonal degeneration of the DCST in neonates, as a result of a unilateral cerebral HI episode, can be detected using histology in the cortex, cerebral peduncles within hours post injury.
- This is the first study to show that the progression of these histological changes reflect the changes that occur during Wallerian degeneration in the DCST.

Future Directions:
- Evaluate tissue changes at other regions of DCST like internal capsule, medullary pyramids and at more chronic timepoints to see how these tissue changes evolve over time.
- Correlate MRI and histological data.

REFERENCES