

ASSESSMENT of NEURODEVELOPMENTAL OUTCOME IN TERM ASPHIXIATED NEONATES, TREATED WITH HYPOTHERMIA, USING TRACT-BASED SPATIAL STATISTICS

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Purpose

Our purpose was to examine white matter differences between hypothermia-treated term asphyxiated infants with severe, moderate and mild 2-years' neurodevelopmental outcome using TBSS.

Hypoxic Ischemic Encephalopathy (HIE) caused by perinatal asphyxia is one of the primary causes of morbidity and mortality among term infants[1]. Moderate hypothermia has been shown to increase survival and decrease late neurological impairment assessed at the age of 18 months[2]. Early biomarkers, accurately predicting later neurological outcome, are still needed, especially for the early evaluation of neuroprotective therapies.

MRI is increasingly being used to examine brain pathology among HIE infants. Brain edema, a consequence of perinatal asphyxia, can be visualized using diffusion weighted imaging (DWI). Already at 24 hours following the insult, decreased apparent diffusion coefficient (ADC) values can be measured using DWI. The number of lesions seen on DWI images, has been shown to correlate with later neurodevelopmental outcome[3]. However, because of the semi-quantitative visual assessment strategy implemented in most papers, a large number of infants are needed to be enrolled in any given investigation, which is not favorable in small pilot studies of possible new neuroprotective interventions.

Using diffusion tensor imaging (DTI), fractional anisotropy (FA) values can be calculated from the fitted tensor model, which indicate the degree of water diffusion anisotropy in a given voxel. The direction in which the diffusion of water is the greatest can also be determined, indicating the course of white matter bundles. From this information, direction-encoded FA maps can be calculated[4].

Tract-based spatial statistics (TBSS) is an analytical method developed for observer-independent quantitative statistical comparison of FA images. The applied strict alignment and spatial smoothing protocols, and the possibility of observer independent region of interest selection for voxel based statistics leads to increased sensitivity, objectivity and interpretability of multi-subject diffusion imaging studies compared to other methods [5]. These attributes augmented with bootstrap statistics allow for the comparison of FA maps even between relatively small patient groups.

Images for this section:

Our purpose was to examine white matter differences between hypothermia-treated term asphyxiated infants with severe, moderate and mild neurodevelopmental outcome using Tract-Based Spatial Statistics.

Fig. 1: Purpose

Methods and Materials

26 term asphyxiated infants, treated with hypothermia, were enrolled in our study. Neurodevelopmental outcome was assessed using Bayley Scale of Infant Development-II between 18 and 24 months. Asphyxia was considered 'severe' if both mental and motor scores were under 70 (10 cases), 'moderate' if scores were above 70 and abnormalities were seen on DWI images (10 cases) and 'mild' if scores were above 70 and no abnormality was seen on the DWI images taken between the 1st and the 7th day of life (6 cases).

A retrospective analysis of the 32-direction diffusion tensor data collected using a 3T MRI scanner between the 1st and 22nd day of life was performed. A tensor model was fitted to the DTI data, and FA maps were calculated from the tensor parameters. TBSS was performed according to the optimized protocol for neonates[6]. All diffusion-related calculations and statistics were performed using the FMRIB's FSL tools (FSL v. 4.1)[7].

Images for this section:

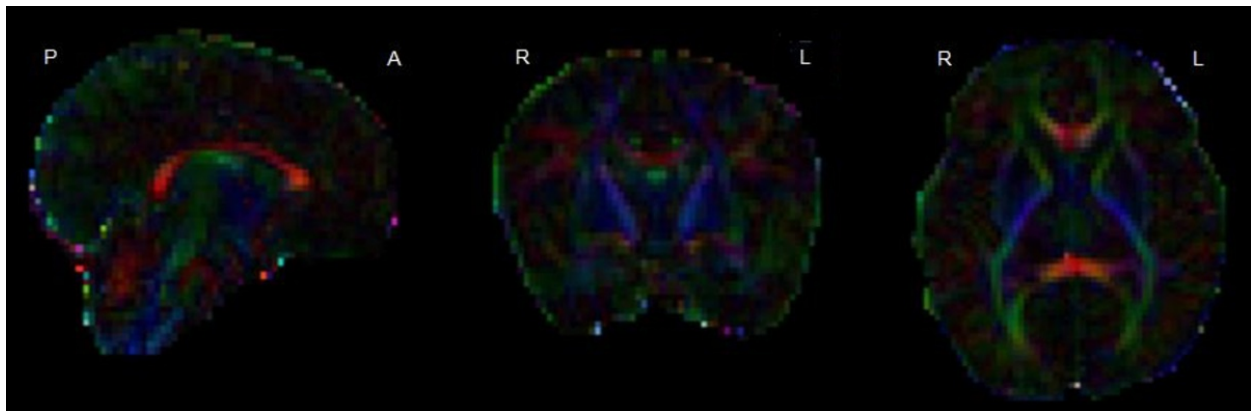


Fig. 2: Fractional Anisotropy (FA) maps were calculated using using FMRIB's FSL tools (FSL v. 4.1).

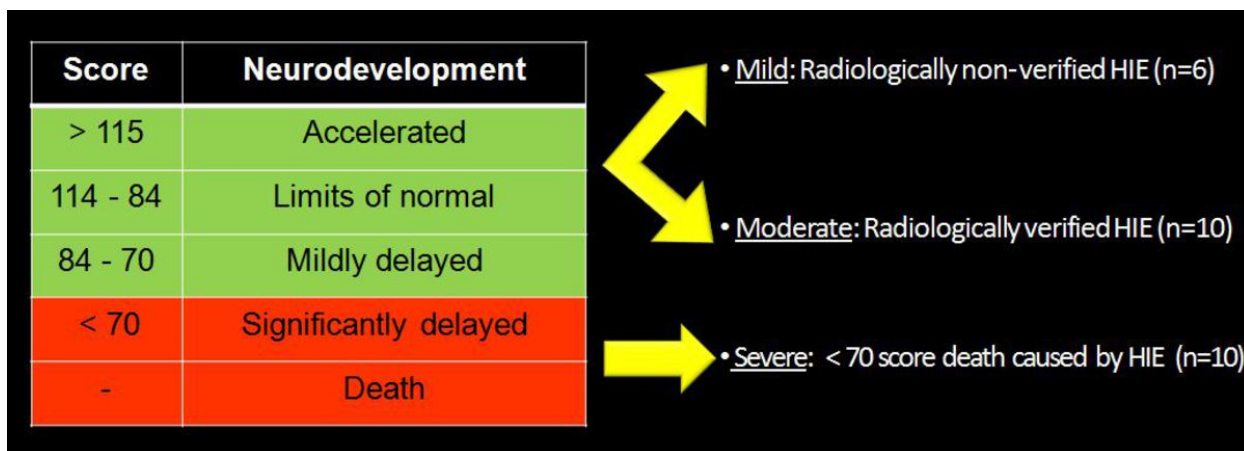


Fig. 3: Image showing the group selection criteria.

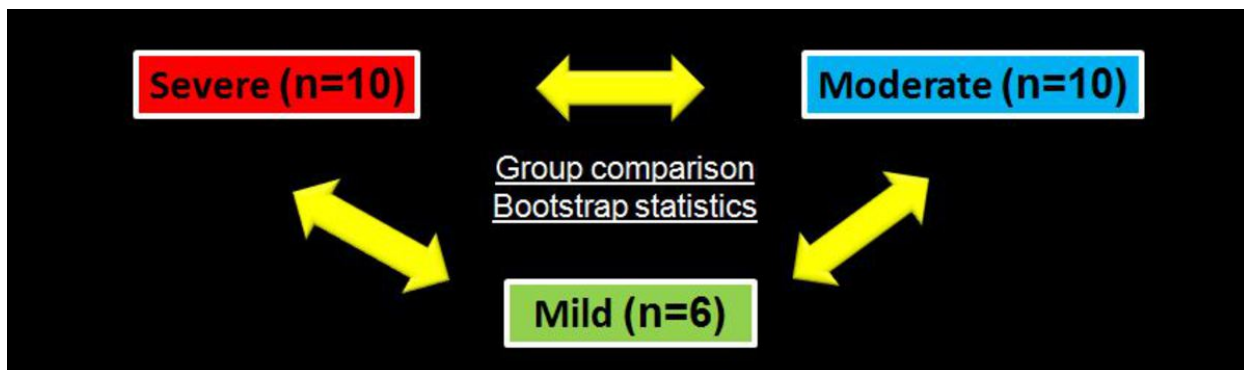


Fig. 4: Image showing bootstrap statistical comparison of the groups using Tract-Based Spatial Statistics.

Results

The 'severe' group showed significant decrease in FA values ($p < 0.05$, corrected for family wise error) along the left corticospinal tract compared to the 'moderate' group and a widespread diffuse decrease in FA values compared to the 'mild' group. No significant differences were seen between the 'moderate' and the 'mild' groups at this level of significance.

Images for this section:

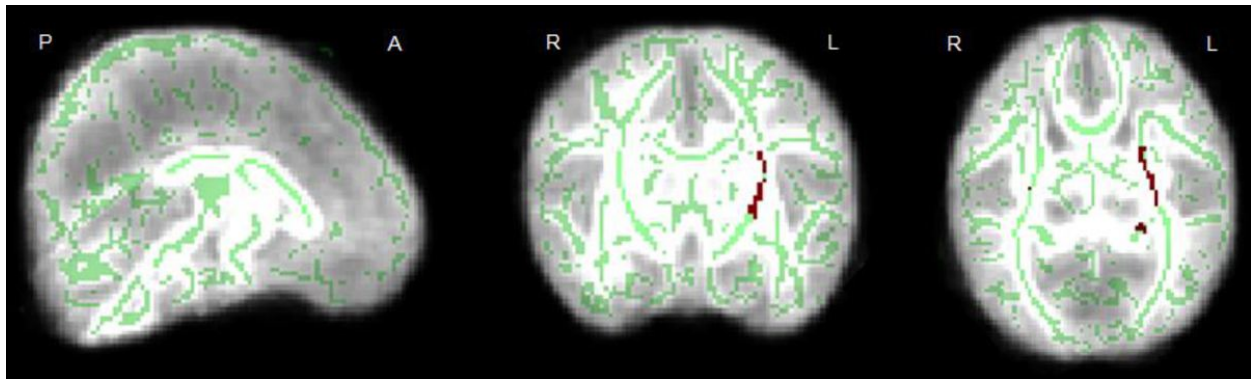


Fig. 5: The 'severe' group showed significant decrease in FA values ($p < 0.05$, corrected for family wise error) along the left corticospinal tract compared to the 'moderate' group. Green indicates the mean FA skeleton. Red indicates voxels with significant decrease in FA values of the 'severe' group, compared to the 'moderate' group.

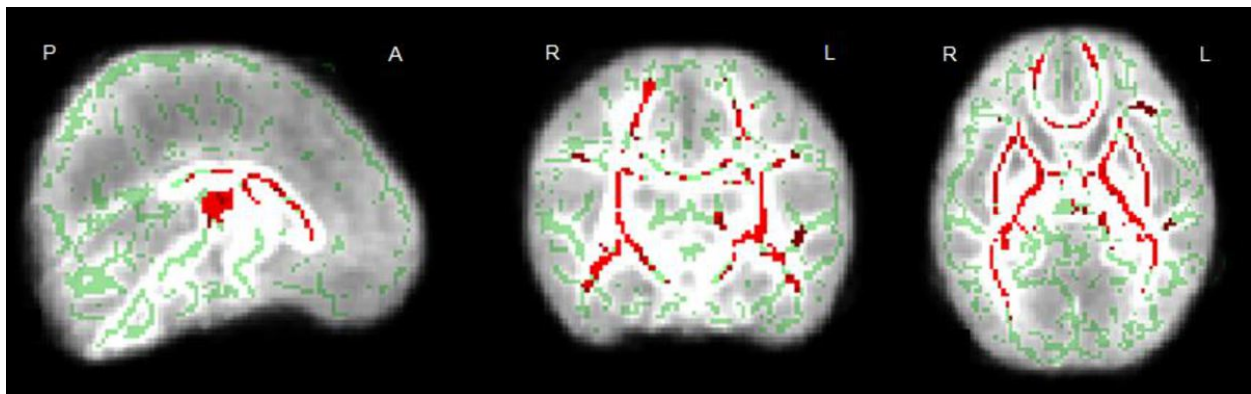


Fig. 6: The 'severe' group showed significant widespread diffuse decrease in FA values ($p < 0.05$, corrected for family wise error) compared to the 'mild' group. Green indicates the mean FA skeleton. Red indicates voxels with significant decrease in FA values of the 'severe' group, compared to the 'mild' group.

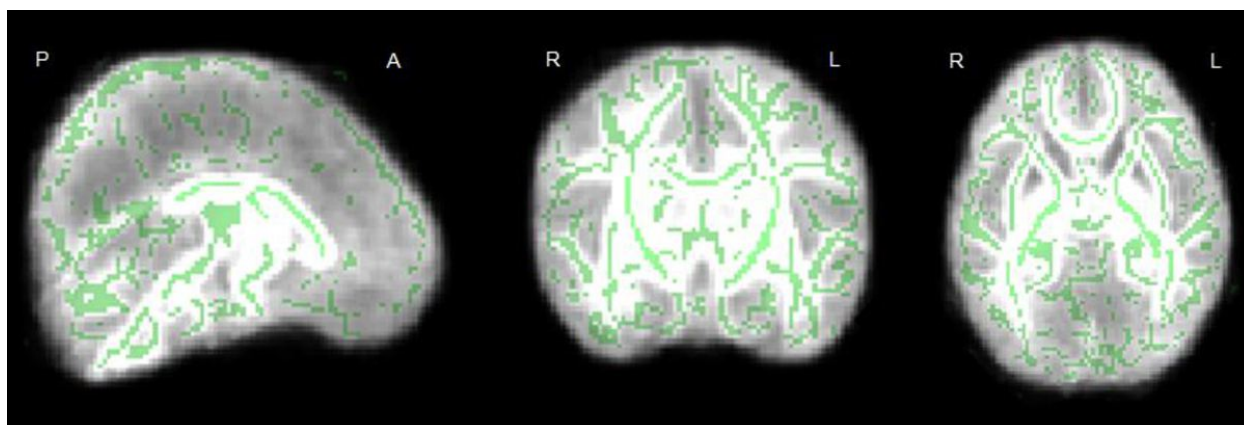


Fig. 7: No significant differences ($p < 0.05$, corrected for family wise error) were seen between the 'moderate' and the 'mild' groups. Green indicates the mean FA skeleton. Red indicates voxels with significant decrease in FA values of the 'moderate' group, compared to the 'mild' group.

Conclusion

To our knowledge, we were the first to compare the white matter of hypothermia treated term neonates suffering from perinatal asphyxia using TBSS. Our results show that TBSS is a promising technique to predict later neurodevelopmental outcome based on acute/subacute imaging data.

Images for this section:

Our results show that TBSS is a promising technique to predict later neurodevelopmental outcome based on acute/subacute imaging data.

Fig. 8: Conclusions

References

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