

Testing Repeatability of DTI-ALPS in Assessing the Brain Glymphatic System of Neonates with Prenatal Opioid Exposure

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Background: Prenatal opioid exposure (POE) is a public health concern with risk for neonatal opioid withdrawal syndrome and poor neurodevelopmental outcomes. The glymphatic system is a waste clearance pathway in the brain, and its dysfunction may contribute to adverse outcomes in infants with POE. Diffusion tensor imaging analysis along the perivascular space (DTI-ALPS) has recently been proposed as a method to assess the glymphatic system. This project aims to test the reproducibility of DTI-ALPS in neonates and assess correlations of DTI-ALPS with POE.

Methods: This prospective, HIPAA compliant, IRB-approved study included neonates with POE and control neonates not exposed to prenatal opioids. MRI including DTI was performed at <48 weeks postmenstrual age. Blinded repeat manual ROIs were drawn along the corticospinal projection fibers to measure ALPS values on the DTI-FA maps in subject space (SS) and template space (TS) using DSI Studio software. Intraclass correlation coefficients (ICC) were used to assess repeatability and reproducibility. Linear regression assessed the association of POE and ALPS index with demographic and exposure related covariates.

Results: There were 36 subjects – 19 with POE and 17 unexposed controls. There was good to excellent ICC (0.74-0.95) of ALPS indices between the two trials in SS and TS. However, comparing ALPS indices between SS and TS showed poor ICC (0.14-0.37). With linear regression, there was no significant association between POE and brain ALPS indices obtained through SS or TS measurements.

Conclusions: Despite good intra-technique repeatability of ALPS measurements in subject space or template space in the neonatal brain, there was high variability with ALPS indices measured between the two techniques. Our results suggest a greater need for standardization of methods for calculating the ALPS index in neonates. Greater reproducibility in metrics will be needed before reliably assessing the clinical correlations of glymphatic system function measured by DTI-ALPS.