

## Differential involvement of long versus short range WM connections in CVI

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### Purpose:

Cortical/cerebral visual impairment (CVI) is the leading cause of pediatric visual impairment in developed countries, with nearly 19 per 1000 live births for infants born at 20-27 weeks gestation. While CVI has many causes, periventricular leukomalacia (PVL) due to perinatal hypoxia is the most common culprit. In preterm infants, the characteristic neuropathology of PVL shows widespread lesions involving brain regions responsible for visual and motor processing. Yet, despite its prevalence and breadth of impairments, very little is known about how the underlying structural and functional changes in the brain relate to the observed clinical deficits associated with CVI. This study utilizes HARDI tractography to characterize the structural connectivity deficits observed in CVI related to their specific visual deficits.

### Methods:

A HARDI [1] MRI protocol was used to acquire data from 3 CVI subjects as well as 4 age-matched controls for comparison. HARDI images were acquired using an eight-channel head coil on a 3 Tesla Philips Achieva system using a single shot EPI sequence (TE 73 ms, TR 17844 ms, 64 diffusion directions,  $B_{\max}$  3000 s/mm<sup>2</sup>,  $B_{\min}$  0 s/mm<sup>2</sup>, 2 mm isotropic voxel size). High resolution 3D T1 images were also acquired. HARDI volumes were corrected for eddy current artifacts and were skull-stripped with FSL. Orientation distribution function (ODF) calculation and subsequent white matter fiber tracking and reconstruction were performed using DSI Studio diffusion decomposition [2]. The brain was parcellated into discrete regions using Freesurfer in HARDI space. In house MATLAB software was used to generate connectivity matrices. Network Based Statistics (NBS) [3] was used to examine significant network differences. In addition, *a priori* determined white matter pathways associated with the dorsal and ventral streams were also examined. Pericalcarine, lateral occipital, and precuneus connections to portions of the cortex affiliated with the inferior and superior longitudinal fasciculi (ILF, SLF), and the inferior fronto-occipital fasciculus (IFOF) were assessed for number of fibers, tract volume, tract length, and QA.

### Results:

Both NBS and *a priori* t-tests on specific visual pathways suggest significant white matter connectivity changes in CVI compared to age-matched controls. Tractography based on the ODF (Figure 1) visualizes the pathways associated with the primary visual cortex of the left hemisphere in a sighted control and two individuals with CVI. At the network level, Using 68 ROIs from the Desikan atlas [4], the connectivity in the CVI group was significantly weaker compared to the control group ( $p = 0.028$ ). These networks included the occipital, temporal, and parietal regions (Figure 2). When dividing the Desikan atlas into smaller regions (184 total), step length showed significant network differences in terms of both intensity and extent ( $p < 0.03$ ). These networks consisted of occipital, parietal, temporal, and frontal regions (Figure 3). The preliminary results show significant decreases in long-range projection fibers between occipital and rostral portions of the frontal and temporal cortices ( $p = 0.0016$ ), without similar decreases in short-range fibers projecting to caudal portions of the temporal cortex and the parietal cortex ( $p = 0.47$ ). Further evidence supporting the preferential loss of short-range projections comes from the significant decrease in tract length observed in CVI compared to sighted controls for the ILF, SLF, and IFOF ( $p = 0.0053$ ). Tract volume is also significantly decreased in CVI compared to sighted controls ( $p = 0.03$ ).



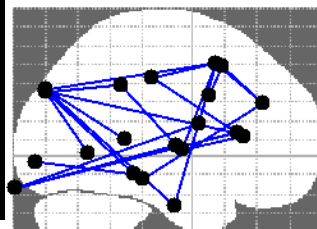
**Figure 1.** SLF, ILF, and IFOF of a control (a) and CVI subject (b). The loss of in all three pathways is evident, particularly the IFOF.

### Discussion:

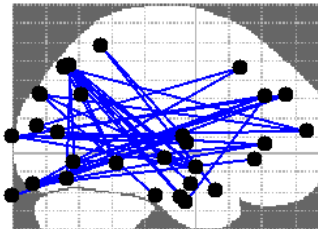
These results indicate that the long range pathways associated with both the dorsal and ventral streams are particularly affected in CVI. This suggests that the white matter injury may occur at a time when the heteromodal projection fibers are developing, which may explain the higher order visual processing and visual attention deficits observed in children with CVI.

### Conclusion:

This study will also provides the opportunity to investigate the neuroanatomical basis for visual dysfunctions observed in CVI and reveal how damage to the extrageniculostriate pathways correlates with specific deficits in visual dysfunction. Eventually this study can contribute insights towards the development of rehabilitation and education plans for clinicians and educators.



**Figure 2.** Network with significantly decreased fiber number in CVI.



**Figure 3.** Network with significantly decreased step length in CVI.

### References:

1. Tuch, D.S., et al., 2002. *MRM* 48: 577–582.
2. Yeh, F-C and Tseng, W-YI. 2013. *PLoS ONE* 8: e75747.
3. Zalesky, A., et al., 2010. *NeuroImage* 53: 1197–1207.
4. Desikan, R.S., et al. 2006. *NeuroImage* 31: 968–980.