Microstructural Visual Brain Reorganization in the Congenitally Blind and Acquired Blind

Vincent Lee[1], Amy C. Nau[2,3], and Kevin C. Chan[4,5]

[1]*Department of Radiology, University of Pittsburgh, Pittsburgh, PA, United States,* [2]*Sensory Substitution Laboratory, University of Pittsburgh, Pittsburgh, PA, United States,* [3]*Department of Ophthalmology, University of Pittsburgh, Pittsburgh, PA, United States,* [4]*Departments of Ophthalmology and Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, United States,* [5]*Center for the Neural Basis of Cognition, University of Pittsburgh and Carnegie Mellon University, Pittsburgh, PA, United States*

Introduction: There is mounting evidence that the plastic capabilities of the brain are not confined to critical periods during childhood. The visual cortex and associated regions are known to undergo experience-dependent modifications and cross-modal plasticity [1-3]. How neuronal reorganization contributes to enhanced function in the setting of blindness is a critical area for vision restoration research. Distinguishing the structural and functional differences in congenitally blind individuals completely deprived of visual input and adult, acquired blind who underwent normal visual cortical development compared to normals is needed. This information is critical for the eventual clinical decision making regarding who is a candidate for visual prosthetics and when the therapy should be prescribed [4]. Any rational therapy aimed at restoring vision must be predicated on an understanding of the remaining faculties of a brain deprived of visual input. In this study, we used fractional anisotropy (FA) from diffusion tensor imaging (DTI) to compare nerve fiber organization among Congenitally Blind, Acquired Blind and Normally Sighted brains.

Methods: We enrolled 26 adult subjects for this study grouped as follows: Healthy Normally Sighted Controls (Normals, n=6), Congenitally Blind (CB, n=4), and Acquired Blind (AQ, n=16). All subjects were scanned on a whole body TrioTim 3 Tesla scanner (Siemens AG, Erlangen, Germany) using an approved Institutional Review Board protocol for DTI acquisition with additional MR sequences including MPRAGE for calibration and normalization. DTI was acquired in 12 isotropically distributed directions using an interleaved spin-echo echo-planar sequence (TE/TR=93/4800 ms, b-value = 0 and 1000 s/mm^2, voxel size = 1.875 x 1.875 x 3.2 mm^3 and matrix size = 128 x 128 x 36). The FA maps were prepared for voxel-wise analysis using all but the parametric testing procedures of Tract-Based Spatial Statistics (TBSS) from FSL [5]. For statistical analysis, custom-written, voxel-wise non-parametric Kruskal-Wallis (KW) and Mann-Whitney (MW) tests were employed. In conjunction, the same non-parametric models were used to analyze FA averages from 2 regions of interest (ROIs): 1) whole brain global fiber tracts generated from TBSS and 2) intersection of (1) and Juelich Optic Radiations from FSL anatomical template, which represents major fiber bundles connecting to the visual cortex (Figure 1).

Results: Figure 2 presents the results of post-TBSS processing and voxel-wise non-parametric analysis of FA of all subjects. The H-statistics results of KW analysis in Figure 2A showed voxels with statistically significant FA differences (H critical = 7.38; $p \leq 0.025$) particularly at the bilateral optic radiation (arrows) among all 3 subject groups. The Z-score results from two-sided MW tests with multiple comparison corrections showed statistically significant voxels in the optic radiation between CB and Normals (Figure 2B) and between AQ and Normals (Figure 2D) (Z critical = 2.40; $p \leq 0.00833$) but not between CB and AQ (Figure 2C). The voxel-wise non-parametric tests also uncovered statistically significant clusters in major tracts or surrounding brain regions with less direct connections to the visual cortex, such as the inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, lingual gyrus, and cingulate gyrus (data not shown). Other major tracts or brain regions appeared to be relatively intact. In the ROI-based quantitative non-parametric analysis of FA averages, no statistical significance was found in the whole brain fiber tracts among 3 subject groups (KW test: H=3.77; $p \geq 0.05$). MW tests over the same ROI confirmed this finding (CB vs AQ: Z=1.60; AQ vs Normals: Z=0.147, $p \geq 0.05$) with a marginally significant difference between CB and Normals (Z=2.13; p=0.0167). In the optic radiation, CB possessed the lowest FA (FA=0.345±0.046) compared to AQ (FA=0.374±0.037) and Normals (FA=0.407±0.015) (KW test: H=7.16; p=0.028). MW tests showed significant differences between CB and Normals (Z =2.56, $p \leq 0.00833$) and marginal significance between AQ and Normals (Z=1.92; $p \leq 0.025$) in the optic radiation, while no apparent difference was found between CB and AQ (Z=1.32; $p \geq 0.05$).

Discussions and Conclusion: This study demonstrated the existence of definite brain areas with significant FA differences among congenitally blind, acquired blind and normally sighted individuals. Since both congenitally blind and acquired blind subjects showed lower FA than normal controls in the major fiber tracts connected to the visual cortex, our results suggested that plastic changes may occur in both early blindness and late onset of blindness after completion of traditional critical period of visual brain development. The inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, lingual gyrus, and cingulate gyrus possess indirect connections to the visual cortex [6,7] and are involved in visual processing such as object recognition, dreaming, and other complex visual functions [8,9]. Whether the significant FA differences in these brain regions offer the potential for cross-modal plasticity and vision restoration bears further investigation. Future studies will assess how the duration of blindness affects FA changes among acquired blind patients, and how specific training protocols will reorganize the microstructures in the above brain regions in both congenitally blind and acquired blind patients.

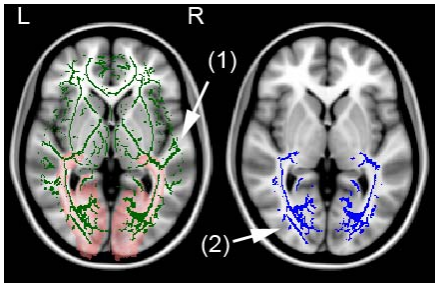

Figure 1: (Left) Whole brain global fiber tracts (1) from TBSS overlaid on T_1-weighted MNI Template and Juelich Optic Radiations (pink). **(Right)** Intersection of fiber tracts and Juelich Optic Radiations representing major fiber bundles connecting to visual cortex (2).

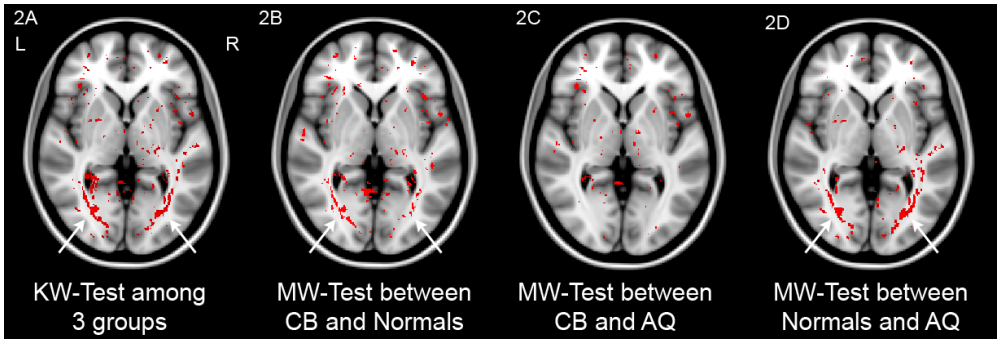

Figure 2: Results from non-parametric voxel-wise analyses of FA maps. Voxels with statistically significant differences (red) were found in the bilateral optic radiation (arrows) in Kruskal-Wallis H-statistics (H critical=7.38; $p \leq 0.025$) among all 3 groups **(2A)** and in Mann-Whitney Z-scores (Z critical=2.40; $p \leq 0.00833$) between CB and Normals **(2B)** and between AQ and Normals **(2D)** but not between CB and AQ **(2C)**.

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