Relationship between Visual Functional Connectivity and Duration of Blindness Depends on Onset of Visual Deprivation

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Target audience: Scientists and clinicians interested in neuroplasticity and vision.

Purpose: Visual deprivation is known to induce plasticity of the visual system, which can be observed through alterations in functional connectivity (FC) as measured by fMRI (1). Understanding plasticity of the visual system and developing biomarkers to noninvasively measure its effects are critical for any vision restoration device that depends upon an intact visual cortex (e.g., retinal implants). While it is known that visual cortex functional remodeling will differ between congenitally blind subjects and those who lose vision later in life, how these FC changes accrue over time and how this relationship between FC and duration of blindness differs between early and late acquired blindness are unknown. Therefore, the purpose of this work was to model the effects of previous visual experience on visual FC in blind subjects.

Methods: We recruited 18 subjects after obtaining informed written consent including 11 acquired blind, and 7 congenitally blind subjects. MR images were collected on a 3T Siemens Allegra scanner. We collected 8 minutes of images at rest using a single-shot gradient echo EPI pulse sequence with the following parameters: TR/TE=2000/26 ms, 20.5x20.5 cm2 field of view, 64x64 imaging matrix, and 36 contiguous 3.24 mm thick axial slices. Images underwent slice timing correction, realignment, normalization to MNI space, and masking with a gray matter mask. Images were smoothed with a Gaussian kernel of FWHM = 5 mm. Nuisance covariables were then regressed out using a general linear model (GLM). Image data and the covariables were temporally filtered with a pass band from 0.01 to 0.1 Hz. The covariables included the motion parameters from realignment, the average time course from the white matter, the average time course from the CSF, the average time course from the entire brain, and a constant. Then a visual functional connectivity map was constructed for each individual by computing the average correlation coefficient between the visual cortex (using either striate or extrastriate cortex as the seed ROI) and each voxel in the brain. We then modeled the effects of visual experience by fitting these FC maps with a GLM with predictors including duration of blindness, a dummy variable for congenital blindness, and the interaction of these two effects. T score maps were thresholded at a family wise error corrected $p<0.01$ (corrected at the cluster level). We also computed the average FC for each individual using voxels where significant effects were detected by the voxel-wise analysis. We used 5 regions of interest, which represent large modules of FC networks as provided by a previously published atlas (2). These modules include somatosensory/motor, auditory/insula/limbic, task-positive, task-negative, and visual networks. Finally, we plotted FC versus duration of blindness in each of these ROIs by group and tested for correlation using a Spearman correlation to ensure results were not overly influenced by outlying blindness durations. P values less than 0.05 were considered significant.

Results: The results of voxel-wise statistical testing using the extrastriate cortex as the seed are shown in Figure 1. From the maps, we can observe that many more voxels show a significant group by interaction effect compared to a simple correlation with duration of blindness, indicating that the relationship between extrastriate FC and duration of blindness is significantly different between groups. A similar trend was observed using striate cortex as the seed (data not shown). To observe these relationships more directly, we summarized FC for each subject in 5 ROIs and plotted the results against duration of blindness. An example scatter plot of extrastriate FC in the somatosensory/motor ROI versus duration of blindness for both group is shown in Figure 2, while all correlation tests are summarized in Table 1. Both the example plot and the summary statistics show that the slope of the FC versus duration of blindness relationship is of opposite sign, with only exceptions in two ROIs where the slope in the acquired group is close to zero.

Discussion: This work represents an early step toward understanding plasticity in the visual system and how it depends upon prior visual experience. These results suggest that alterations in FC due to visual deprivation progress over time. However, the direction of this progression in congenitally blind subjects is actually the opposite of the direction observed in subjects with acquired blindness. In the long term, biomarkers of visual functional connectivity could aid in the screening of patients who may receive vision restoration devices. Our findings indicate that longitudinal measures of FC and not only FC alone may be essential for characterizing the state of the visual system.

References: 1. Liu Y, Yu C, Liang M, et al. Whole brain functional connectivity in the early blind. Brain : a journal of neurology 2007;130(Pt 8):2085-2096. 2. Jones DT, Vemuri P, Murphy MC, et al. Non-stationarity in the "resting brain's" modular architecture. PloS one 2012;7(6):e39731.
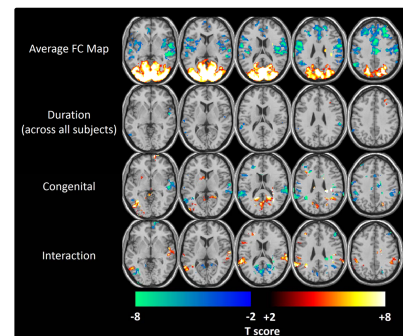

Figure 1. Summary of voxel-wise statistical testing (FWE corrected p<0.01). Row 1: T score for average visual FC map in all blind subjects. Row 2: T score for significant relationship between FC and duration of blindness. Row 3: T score for group-wise differences. Row 4: T score for group by duration interaction.
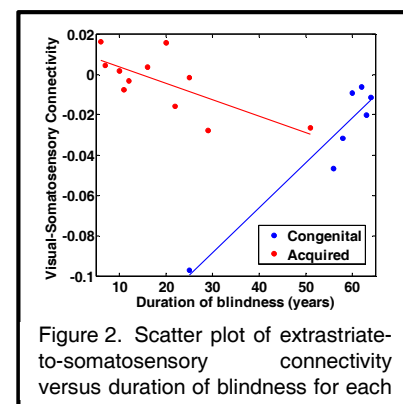

Figure 2. Scatter plot of extrastriate-to-somatosensory connectivity versus duration of blindness for each

Table 1. Spearman correlation coefficient for FC vs. duration of blindness by group (*p<0.05, **p<0.1).

	Striate		Extrastriate	
	Congenital	Acquired	Congenital	Acquired
Somatosensory/Motor	0.85*	-0.67*	0.71**	-0.70*
Auditory/Insula/Limbic	0.71**	-0.39	0.71**	-0.75*
Task-positive	0.04	-0.4	0.75**	-0.45
Task-negative	0.64	-0.72*	0.75**	-0.37
Visual	-0.89*	-0.05	-1.00**	0.22