A fMRI Study in AnisometropicAmblyopes before and during occlusion therapy: Comparison 0f responders and non responders on basis of cortical activity pattern

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Introduction: Amblyopia us associated with functional loss of vision with no organic cause.This may be associated with decrease in colour vision, contrast sensitivity,Vernier acuity,Stereoacuity and spatial localisation. In our study, we observed BOLD responses on visual stimulation using black and white checkerboard flickering at 8 Hz in unilateral Anisometropic Amblyopes in response to occlusion therapy.

Material and method: 10 left eye affected amblyopes were recruited (mean age 12.10± 2.88yrs), all were started on occlusion therapy after appropriate refractive correction and followed for 4m+_6wks.Respoders and non responders (at least two line improvement in visual acuity was taken as responders) where compared on basis of fmri cortical activity,age,visual acuity at first and final follow-up, refractive error inboth eyes. The studies were carried out using 1.5T whole body MR scanner (Magnetom Avanto, M/s. Siemens Erlangen, Germany) with 12 channel head coil. Visual cues were projected using a MR compatible Binocular LCD goggles (NordicNeuroLab, Norway). The stimulus was developed using Superlab (version 4.2, Cedrus Inc, USA) and was presented to affected eye and fellow eye separately (with the other eye closed). 75 whole brain volumes were acquired using echo planar imaging (EPI) sequence, with parameters: no. of slices 29 (axial orientation), slice thickness: 4.5mm,TR:2000 ms, 64x64 matrix resolution (3.6x3.6x4 mm^3 voxel dimension), and FOV of 230mm. Pre and post-processing were carried out using SPM8 (Wellcome Department of Cognitive Neurology,London, UK). The BOLD clusters were converted from mni template to the Talairach and Tornoux coordinates, for estimation of anatomical areas. Two sample-t-test ($p<0.001$,cluster threshold 10) was used for group analysis.

Table 1. Clinical details of the subjects

Psychophysical tests	Responders (mean±SD)	Non-Responders (mean±SD)	p value
RE (log MAR) pre-occlusion	0.06±0.13	0.06±0.13	
RE (log MAR) Post-occlusion	0.06±0.13	0.06±0.13	
LE (log MAR) Pre-occlusion	0.68±0.16	0.86±0.21	0.180
LE (log MAR) Post-occlusion	0.32±O.15	0.86±0.21	
Refractive error RE (SE)	0.96±0.73	0.70±0.83	0.165
Refractive error LE (SE)	5.3±2.3	7.06±1.9	0.259

Table 1. BOLD activation on Amblyopic (Left) Eye viewing (flickering CB at 8Hz)

Clusters	Area of activation
Responders with respect to Non-responders	
42	Rt Insula BA13
43	Rt Inferior Occipital Gyrus BA19
40	Rt Middle Occipital Gyrus BA19
16	Lt Middle Occipital Gyrus BA19
5	Lt Middle Temporal Gyrus BA19
13	Rt Precuneus BA19
12	Rt Middle Temporal Gyrus BA22
6	Lt Superior Temporal GyrusBA38
5	Lt Middle Temporal GyrusBA39
9	Lt Superior Temporal Gyrus BA39
23	Rt Inferior Parietal Lobule BA40
11	Lt Postcentral Gyrus BA40
11	Lt Superior Temporal GyrusBA41
69	Rt PrecuneusBA7
Non-responders with respect to Responders	
11	Lt Anterior CingulateBA32

Results: On comparing age, visual acuity (both eye), refractive error (both eye) at baseline, there was no significant difference between responders and non-responders, but the two groups showed significant difference in cortical activation pattern on BOLD (Table 1, 2). On viewing with amblyopic eye, responders showed more cortical activation in visual cortex and visual association areas. Non-responders exhibited more activity in contralateral attention area.

Discussion: An increase in cortical activity in visual cortex areas on viewing with amblyopic eye in responders in comparison to non-responders may suggest that response to occlusion therapy is better if visual cortex is activated on BOLD task at 8 Hz in anisometropic amblyopia subjects[1]. Though there are various factors like visual acuity, age, severity and refractive errors, that can be indicative of the same, but fMRI based cortical pattern can better prognosticate the responders and non responders for amblyopia therapy.

Table 2. BOLD activation on Fellow (Right) Eye viewing (flickering CB at 8Hz)

Clusters	Area of activation
Responders with respect to Non-responders	
6	Right Cerebellum,post lobe
Non-responders with respect to Responders	
9	Lt Claustrum
10	Lt Anterior CingulateBA33

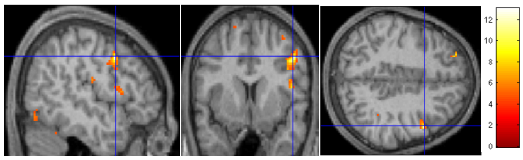

Figure 1. BOLD activation at baseline on 8 Hz flickering checkerboard viewing by amblyopic eye in

References:

1. Stewart CE, et al, 2007, Investigative Ophthalmology & Visual Science, 48, 2589-2594.