**Introduction:** In patients with optic neuritis (ON), location and severity of scotomas in the acute phase can vary greatly and may be central, paracentral, quadrantic, or small defects in the periphery. Over time the the Patients with ON undergo cortical and subcortical neuroplasticity as revealed by functional magnetic resonance imaging (fMRI) [1]. The heterogeneity of scotomas renders standard random effects group analysis [2] inadequate. In this particular case we do not expect a general effect [3] in visual cortex during improvement in visual performance, rather we expect an effect on average. This is due to the fact that certain voxels, for certain subjects will show an effect of an improvement in visual performance in certain parts of the visual field. Here we introduce a new method of modeling scotomas in fMRI, to reveal a clearer pattern of neuroplasticity, across a heterogeneous patient-population.

**Methods:** Sixteen patients were examined during their recovery from ON. The examinations were performed acutely and after additional 14 days, 3 months and 6 months, and consisted of fMRI during visual stimulation of their affected eye with a flashing checkerboard. Prior to each examination visual field maps (Figure 1) was recorded using Humphrey field analyser, and Humphrey's mean deviation (HMD), for the affected eye, was derived. HMD reflects the average (over the entire visual field) deviation in visual performance, from a matched control group of healthy subjects.
One contrast image from each of the 64 first level analysis were fed into a second level analysis, the corresponding designmatrix is shown in Figure 2A. The designmatrix includes two regressors per subject, one modeling a subject specific BOLD response (the first 16 columns), and another (the next 16 columns) models subject specific changes in HMD, due to recovery from optic neuritis.
To test for areas where on average, across subjects, there is an increase in BOLD-signal with an increase in HMD a t-contrast was applied to columns 17-32. This analysis models sessions as a random effect but subjects as fixed.
Changes in HMD can be modeled as an effect which is random across subjects by performing a third level analysis on the images of parameter estimates, from the regressors in column 17-32.

**Results:** The results of the second level analysis is shown in figure 2 and described in detail the figure caption. In short it is demonstrated that the model can indeed model subject- and location specific improvements in visual performance. The result of the third level, random effects analysis, was also as expected: only in the voxels corresponding to the most central part of the visual field (the occipital pole) did we se an effect of changes in HMD.

**Discussion**: During the last 10 years random effects analysis has become increasingly popular for group analysis of fMRI data. Whereas it is normally seen as a drawback, of a fixed effect analysis, that a large response in a single subject lead to a significant response in the group, it can, e.g. in the case of a very heterogeneous population, be considered as an advantage. In our example the fixed effect model was used to allow for different recovery rates in different patients at different locations. We successfully demonstrated that recovery from ON on average takes place in visual cortex and LGN, but for the individual subject happens at the locations where the scotoma is disappearing. A change in general is only found in the most occipital part of the visual cortex i.e. the center of the visual field, where almost all subjects experience an improved visual performance during recovery.


**References:**
[1] Korsholm et al. Brain (2007), **130**: 1244 -1253.
[2] Holmes NeuroImage (1998), **7** S754.
[3] Friston et al.Neuroimage. (1999), **10**(1):1-5.



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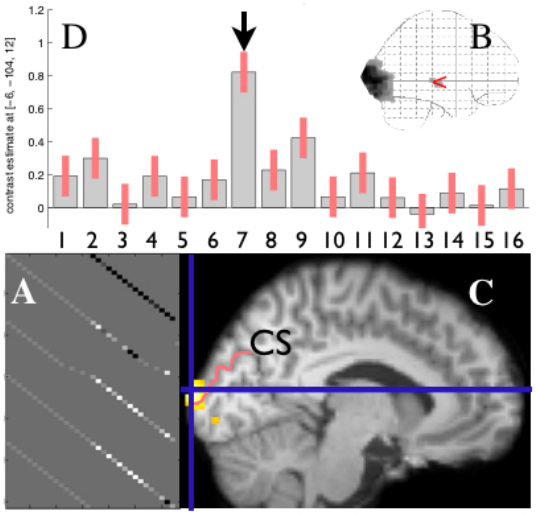


**Figure 2 (above):** The second level designmatrix **(A)** includes two regressors per subject, one modeling a subject specific BOLD response, while the other models subject specific changes in visual performance, due to recovery from optic neuritis. The maximum intensity projection **(B)** shows the voxels where there, on average across subjects, is a significant positive effect (t-test across all subjects) of an improvement in visual performance. This is the case for most of the visual cortex and lateral geniculate nuclei (red arrow). The maximum effect is found at MNI coordinate (-6,-104,12) (blue cross-hair in figure **(C)**) and is seen to be largely driven by subject 7 (black arrow in boxplot **(D)**). This boxplot shows the parameter estimates of the 16 regressors which models subject specific changes in visual performance. The voxels showing a significant effect of an improvement in the visual performance specific to subject 7 are superimposed (in color) on top of the spatially normalised structural image from that patient. These voxels are located above the calcarine sulcus (CS). This fits well with the fact that patient 7, in the acute phase, has a large scotoma in the lower visual field which has disappeared in the following examinations.

**Figure 1 (bellow):** The figure show Humphrey field perimetry maps from the affected eye of a typical group of patients recovering from optic neuritis. Each of the 15 patient (columns is examined 4 times (rows). It is seen that both scotoma location and recovery rate is very heterogeneous between subjects. The red and grey discs indicate the coverage or fMRI and Humphrey field perimetry respectively. Patient 7 is surrounded by a black line.