A quadrant-specific monocular visual functional MRI paradigm designed to minimize attention and loss-of-fixation biases

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Introduction: Visual functional MRI is a useful way of studying cortical organization and reorganization in health and disease. Previous designs have used whole[1] or hemi-field[2] stimulation. We have developed a novel quadrant specific stimulation paradigm in a group of healthy subjects, and tested the minimum duration of stimulation required to demonstrate occipital activation. Using red/green filter goggles to isolate each eye, this technique tackles several design issues, which have not been fully addressed in previous studies. It enables both eyes to be tested within the same scanning run, which is important to minimize sources of differential attention and habituation bias across the run, and allows maintenance of fixation even if the subjects studied are patients with complete monocular visual loss. The quadrant specific stimulation offers improved spatial resolution without extensive post-processing, which is often necessary in formal retinotopic mapping protocols.

Methods: Seven volunteers with normal visual function were recruited (mean age 29.7, standard deviation 3.6, 6 females). They viewed red or green checkerboard stimuli on a 30x28 degree of visual angle rectangular projection screen, whilst wearing transparent goggles which had a green filter over one eye and a red filter over the other. The red checkerboard was designed to be of zero contrast when viewed through the green filter and vice versa. In this manner monocular stimulation was achieved. Subjects were instructed to fixate on a central blue cross which appeared black to each eye through the goggles. They viewed 8Hz reversing checkerboard stimuli covering either a peripheral quadrant or a central circle. In the blocked design, each session consisted of 4 runs, each run lasting approximately 5 minutes. Within each run were 10 epochs of alternating stimulation and rest, each lasting 16 seconds. After run 2 the orientation of the goggles was reversed i.e. if the red filter previously covered the left eye, it now covered the right. During the rest period the subjects continued to fixate on the central cross and the grey background screen was presented without checkerboards. To ensure that attention and fixation were maintained the subjects were instructed to press a button with their right index finger when the fixation cross changed to a hash symbol (#). This occurred at a random frequency several times during each scanning session during rest epochs and responses were recorded.

All scans were performed on a 1.5T Signa Excite whole-body MRI System, with an 8 channel head coil. Thirty eight near axial slices (2 mm thick, 1mm gap) covering the whole brain and parallel to the AC-PC line were acquired with TE 50ms, TR 3950ms, field of view 20cm, matrix size 64x64.

Analysis was performed using statistical parametric mapping software (SPM2). The button press response vectors were entered into the design matrix as covariates of no interest to account for the resulting motor activations. At the first level, the resulting maps were thresholded at a familywise error rate of $p<0.05$, and the percentage of runs resulting in the anticipated unilateral occipital activation above or below the calcarine fissure was calculated. The maps from the first level analysis were then entered into a second level random effects analysis and the results thresholded at $p<0.001$. Regions of interest were created from each maximal quadrant-specific activation cluster and applied to the other statistical parametric maps. The resulting parameter estimates were used to quantify the specificity of activation.

Results: As expected from visual anatomy, we found quadrant specific activation localizing to the contralateral hemisphere of the occipital lobe, with the lower quadrants represented above and the upper quadrants below the calcarine fissure. Stimulation with the central circle resulted in bilateral occipital activation. (Figure) The specificity of lateralization to right or left occipital cortex and localization above or below the calcarine fissure was confirmed quantitatively.

The extent of activation and the threshold at which it was detectable showed considerable between-subject variation at the first level. After 4 runs of stimulation, we were able to reliably demonstrate anatomically appropriate activation for 90% of the conditions. This percentage fell to 77% for 2 runs and 50% for 1 run.

Conclusions: We show that quadrant specific visual fMRI is feasible at 1.5T with a scan time of 20 minutes. Our paradigm has several technical advantages. We suggest that the technique that we have developed would be particularly suited for studying diseases in which radiological correlations with clinical visual field defects were of interest. We offer it as a method of improving spatial resolution compared with whole field stimulation, without the post-processing requirement of a formal retinotopic mapping protocol.

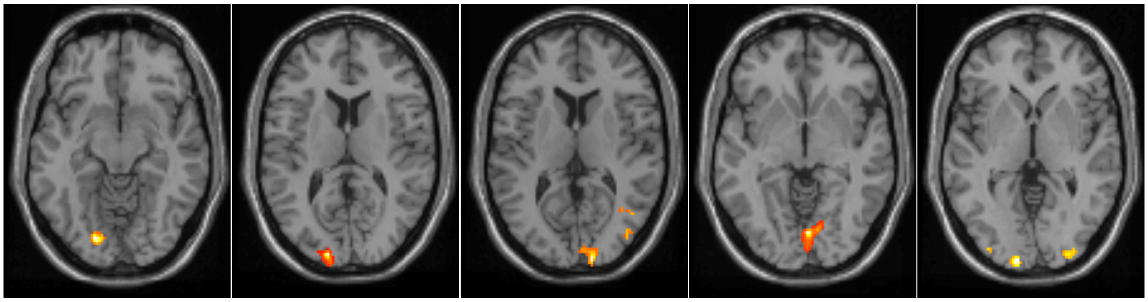

Figure: Statistical parametric maps showing results of the second level random effects analysis from the 7 subjects following stimulation of the right eye. From left to right the maps show stimulation of the upper temporal, lower temporal, lower nasal and upper nasal quadrants and the central circle. Shown in neurological convention i.e. reader's left=left. Results are overlaid on to a canonical single subject brain.

References: 1. Toosy A T, Hickman S J, Miszkiel K A, Jones S J, Plant G T, Altmann D R, Barker G J, Miller D H, Thompson A J. Adaptive cortical plasticity in higher visual processing areas after acute optic neuritis. Ann. Neurol. 2005; 57: 622-633.

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