Layer-specific differential activation in human V1 at 3 T using 3D-EPI

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Introduction

In a study at 3 T [1] it was shown that visual stimulation led to a larger signal change in the granular layer than in the infra- and supragranular layers of human primary visual cortex (V1). The underlying mechanism causing the response to simple stimulation to peak in this layer is unknown, but it is consistently found in animals as well [2-4] and shows that layer-specific effects can be depicted with fMRI. The temporal resolution in [1] however was very poor (~1 min/volume) which is unsuitable for most fMRI studies. The aim of the current study was two-fold: to significantly improve temporal resolution while maintaining spatial resolution and specificity by using an accelerated 3D-EPI sequence and to depict layer-specific *differential* activation by stimulating subjects with gratings of different colours. We expect that when using colour gratings, supragranular layers II&III in V1 will be relatively more active than when using achromatic ones due to the high density of so-called "colour blobs" in layers II&III.

Methods

Seven subjects were scanned after informed consent was given according to the guidelines of the local ethics committee. Functional scans were acquired on a 3 T whole body scanner (Siemens Medical, Germany) with a 3D-EPI sequence [5] using a 32-channel headcoil. Parameters were: FA 20°, voxel size 0.75x0.75x0.75 mm^3, matrix 192x256, 32 slices covering the calcarine sulcus (V1), TE/TR = 30/79 using 6/8 partial Fourier and a factor 4 acceleration yielding a volume repetition of 2.5 seconds. All experiments were accompanied by a T1-weighted MP-RAGE acquisition of 80 slices which had the same orientation, voxel size and FOV as the functional runs. Because EPI distortion could potentially corrupt the coregistration with the MP-RAGE, an inversion recovery EPI with T1 contrast was acquired with the same EPI parameters as the functional run (and the same shim settings). The MP-RAGE was normalised to this IR-EPI volume allowing non-rigid transformation in the phase encoding direction [6]. Finally, retinotopy [7] was performed to determine the location of V1 in each subject. The structural data were processed in FreeSurfer [8-9] to obtain the location of the WM-GM and the GM-CSF interfaces. These were used to plot profiles in the functional data perpendicular to the cortex.

The visual stimuli were taken from [10]. The paradigm consisted of 16 repeated segments. Within a segment, firstly 10 volumes of grey screen were presented (rest condition) followed by 3 blocks of 10 volumes, each block having a grating in a different "cone-contrast" direction. A short explanation (see [10] for details): the human visual system has three "channels", one detecting luminance contrast (ACH) and two referred to as the Red-Green (RG) and the Blue-Yellow (BY) pathway. These contrast channels act orthogonal to one another, such that a RG grating will not be detected by the other two. The levels of cone-contrast used in the experiment were matched at 34 times the average detection level threshold determined on three subjects using a staircase method. Summarising, this study aimed to excite the individual contrast pathways as performed in [10] and look at the laminar distributions of these activations.

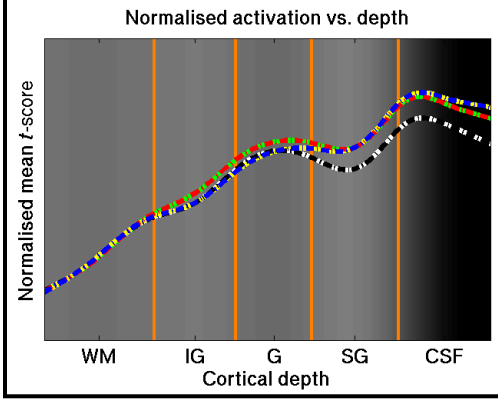

Figure 1: *Normalised activation profiles for Black/White, Red/Green & Blue/Yellow stimulation.*

Background grayscale is the average intensity of the rest condition showing a dark band at the granular layer. Due to decreased tSNR in CSF, t-scores are reduced superficial to the surface for all three conditions.

The relative contribution of the supragranular layer is larger for colour stimuli compared to the achromatic one (also see table 1).

	Difference between layers	
	IG vs G	G vs SG
RG vs ACH	0.646	0.063
BY vs ACH	0.979	***0.041**
RG vs BY	0.675	0.105

Table 1. *p-values of paired t-tests. The ratio of activation granular/supragranular is significantly different when comparing the blue/yellow condition and the achromatic condition. There is no significant difference between the infragranular and granular layer.*

Results and Discussion

The average signal change in response to colour gratings was ~1.7 times as strong as the response to achromatic stimuli. We were however most interested in the difference in shape, i.e. the relative contributions of each layer to the total signal change. To visualise this, fig. 1 shows activation profiles rescaled in such a way that values found just inside white matter were matched for the three conditions. Please note that this rescaling was done for illustration purposes only, statistical tests were performed on the original profiles.

First of all, the black/white profile in fig. 1 shows we succeeded in replicating the layer specific results found in [1] where black/white checkerboard stimulation was used along with much slower sequence. Using EPI we were able to increase slice coverage by a factor of 1.6 and still be 24 times faster in terms of volume TR.

Secondly, we assessed the shape differences of the three profiles. As an example, the BY curve in fig. 1 follows the ACH curve closely until the upper part of the granular layer. This indicates that the supragranular layers are relatively more active in the BY condition. To test significance of this, paired *t*-test were performed across subjects on the non-normalised curves. For each condition (ACH, RG, BY) the ratio between the activation in the middle of one layer (e.g. supragranular) with respect to another layer (e.g. granular) was calculated, yielding 7 ratios (1 per subject) for each condition. These ratios were pair-wise tested (RG vs. ACH, BY vs. ACH, RG vs. BY). The tests were performed on the IG, G and SG layers and results are shown in table 1. The BY stimulus elicited a significant difference with respect to the achromatic one between the granular and supragranular layer and the RG/ACH ratio got very close to significance between these layers. This seems to confirm the hypothesis that supragranular layers become more strongly activated when using colour (in addition to the global activation increase).

Conclusion

fMRI with laminar resolution was performed using accelerated 3D-EPI allowing 32 slices with 0.75 mm isotropic voxels with a volume repetition of only 2.5 seconds. This is a major improvement in terms of temporal resolution compared to [1] and opens the door to event related stimulus designs. Secondly, differential activation in the supragranular layers of V1 was shown by contrasting colour stimulation versus achromatic stimulation. A significant difference was found and is attributed to supragranular colour blobs showing increased activation in the colour conditions.

References

[1] Koopmans et al. (HBM, DOI: 10.1002/hbm.20936); [2] Goense et al. MRI 2006; [3] Harel et al. NI 2006; [4] Bissig et al. NI 2009; [5] Poser et al. ISMRM 2009; [6] Studholme, IEEE-TOMI 2000; [7] Engel et al., Cereb. Cortex 1997; [8] Dale et al. NI 1999; [9] Fischl et al. NI 1999; [10] Mullen et al. EJ. Neurosc. 2008;

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