Specificity and Sensitivity of Layer specific fMRI responses using GE and 3D GRASE at high fields.

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INTRODUCTION.

The possibility of measuring laminar specific activation in humans using fMRI [1, 2, 3] has the potential to significantly expand the study of systems and clinical neuroscience. In humans, investigations have focused on both flat [2] and convoluted [1, 3] cortical areas and using gradient echo (GE) BOLD [1, 2, 3]. Increased signal and contrast to noise at ultra-high fields [4] permit increases in the spatial resolution of the images. T_2* weighted images at ultra-high fields, while having an increased spatial specificity over lower field studies, remain sensitive to extravascular BOLD effects around large draining veins. On the other hand, T_2 weighted (Spin echo or GRASE [X] (which also has stimulated echo contributions)) BOLD has been shown to be particularly sensitive to smaller size vessels, making it desirable for functional mapping of columnar organizations in humans. However, it has not yet been demonstrated whether such specificity gains in high field T_2 weighted BOLD would be similarly advantageous in layer specific fMRI investigations and/or in regions outside of V1.

Here, we examine layer specific response profiles in two different visual areas (V1 and MT) within the same subjects. We report amplitude changes of BOLD (GE and GRASE) at different cortical depths in response to simple stimuli known to preferentially activate the targeted regions. Furthermore, in two of the three subjects we report layer specific tuning curves extracted from area MT in response to stimuli moving along four different axes. We show that for GRASE (unlike with GE): a) measurements are not biased towards the surface of the cortex and b) the specificity of the axis of motion tuning curves remains relatively flat throughout the layers.

MATERIAL AND METHODS. Measurements were performed at 7T (Siemens, Erlangen, Germany) using a using a custom 6 channel receive array and a separate open half-volume quadrature transmit coil. Three healthy volunteers participated in both studies (4 sessions: 2 GE sessions and 2 GRASE sessions). T_1 and proton density weighted (3D-MPRAGE) anatomical data were acquired for each subject in both sessions and were used for segmentation [5] and cortical layer sampling. Functional responses were measured with: 1) GE BOLD (TE = 17 ms, TR = 2000 ms resolution = 0.8 × 0.8 × 0.8 mm^3 (V1 experiment) and 1 × 1 × 1 mm^3 (MT experiment)); and 2) T_2 weighted high-resolution 3D GRASE with inner volume selection [6] (TE = 40 ms, slices = 12, TR = 2000 ms; resolution = 0.8 × 0.8 × 0.8 mm^3). Stimuli consisted of: a) flashing checkerboard presented in the lower right visual quadrant alternated with fixation and the presentation of a stimulus surrounding the targeted area; b) dots moving coherently along 4 axes alternating with static dots. Slice placement for the GRASE studies were based on previous GE sessions.

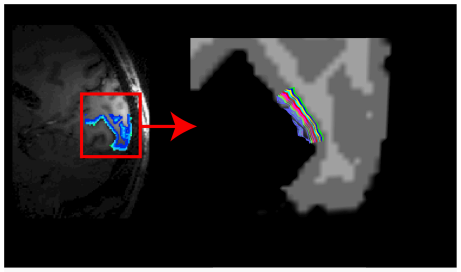

Figure 1

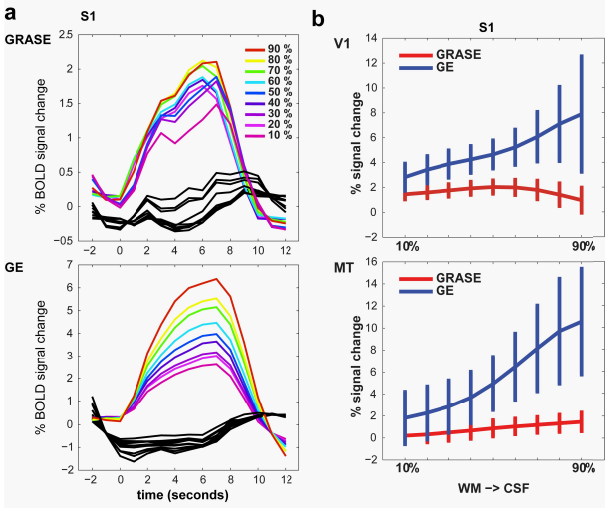

Figure 2

All functional data were co-registered to the anatomical data collected in the same session using a boundary-based registration as implemented in BrainVoyager (Brain Innovation, The Netherlands). Anatomical data were aligned across sessions. Anatomies collected from the GRASE session were used as a reference and segmented to extract layer profiles. Layer definition comprised of the computation of the distance of each voxel from the white/gray matter boundary and subsequent grid sampling as implemented in BrainVoyager. Figure 1 shows the results of the layer definition in one representative subject (Area V1). Anatomically defined layers were subsequently used to sample functional activation from the targeted areas.

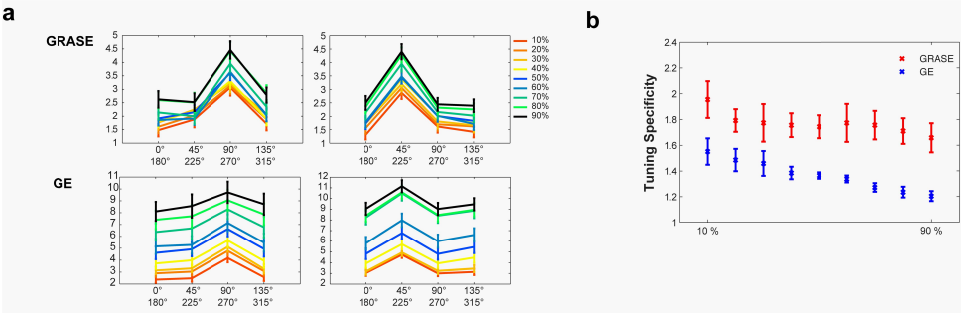

Figure 3

RESULTS. Figure 2a shows the layer dependent event related average response to the target (colored lines, different color represent different layer) and surround (black lines) in area V1 of one subject. Figure 2b shows for the same subject the layer dependent average BOLD response in area V1 (to target stimulus) and MT (to moving dots). Error bars represent the standard deviation of the response. Figure 3a shows for area MT the layer specific tuning curves extracted from one subject's responses to moving stimuli with both GE and GRASE. In figure 3b the specificity of the tuning curves (ratio between response to the most strongest stimulus and the average of the two closest stimuli) is reported across layers for both GE and GRASE.

DISCUSSION. In this work, we demonstrate that the increased specificity obtainable with GRASE might be preferred to GE when layer specific responses throughout the entire cortical depth are of interest (i.e. without removing superficial layers) and when total volume coverage is not limiting.

ACKNOWLEDGMENTS. Work supported in part by the National Institutes of Health (R01 EB000331, P30 NS057091, P41 RR08079, **P40 NS057091**). The 7 T magnet purchase was funded in part by the WM KECK Foundation.

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