High resolution fMRI using a 3D mult-shot EPI sequence.

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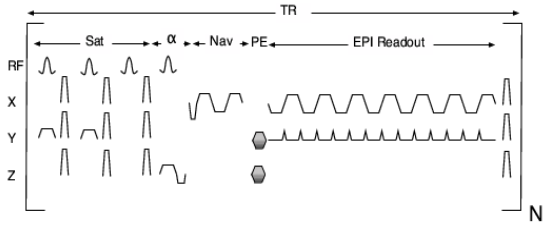
Introduction

The columnar architecture of the neocortex, an arrangement of neural function into patches ~0.5-1 mm across, is a fundamental scale of cortical organization. Columnar organization has been characterized in detail for some sensory brain areas (e.g. orientation preference and ocular dominance in primary visual cortex), and it is hypothesized that analogous columns are present in higher brain areas. Therefore, the ability to routinely and reliably measure activity at this scale, non-invasively in the human brain, would be one of the most important technical advancements in neuroscience since the original introduction of fMRI over a dozen years ago. Toward this end, we developed and implemented a zoomed, 3D, multi-shot EPI sequence for T2*-weighted blood oxygen-level dependent (BOLD) functional magnetic resonance imaging (fMRI), and we demonstrated the application of this sequence by measuring activity in visual cortex. We implemented a 3D (rather than 2D) sequence to enable the measurement of cortical activity with isotropic voxels, independent of the slice orientation relative to the folded cortical surface. We implemented a zoomed field of view to enable high spatial sampling resolution while maintaining a relatively high temporal sampling rate.

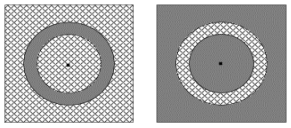
Methods



Pulse sequence: A 3D sequence was implemented which was comprised of a slab-selective main excitation followed by three navigator readouts, z-phase-encode gradient and an x-y EPI readout (notice absence of "echo-shifting"). Each main excitation pulse was preceded by two “y”-outer-volume suppression pulses and a fat-suppression pulse allowing fast acquisition of high-resolution images of a selected anatomical region.

Image reconstruction: The raw data were acquired and then reconstructed off-line using custom written C and matlab code. During image reconstruction, B0 [1] and pre-phase ghost corrections based on the navigator data were applied to each segment independently.

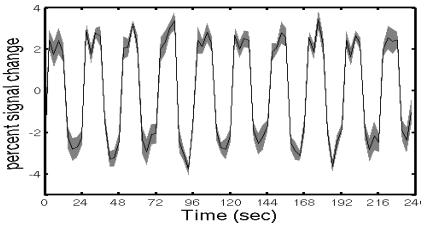
fMRI stimulus and analysis: The visual stimulus was a high-contrast, flickering (8 Hz) checkerboard restricted to a narrow annulus of the visual field (1.5-2.5 deg of visual angle) that alternated (24 sec/cycle) with the complementary “anti-annulus”. The annulus is known to evoke neural responses in a narrow strip of visual cortex. Consequently, large and medium draining veins which pool over larger regions of cortex will not exhibit BOLD signal changes in phase with the visual presentation of the annulus. Data were analyzed by: (1) highpass filtering the time series at each voxel to compensate for slow signal drifts [2], (2) dividing the time series at each voxel by its mean to convert the data from arbitrary image intensity units to percent signal modulation and to compensate for the distance from the receive coil, (3) fitting a sinusoid (24 sec period) to the time series at each voxel, and (4) computing the coherence between the time series and the corresponding best-fitting sinusoid and the phase of the best-fitting sinusoid. The coherence is a measure of stimulus-evoked contrast-to-noise, taking a value near 1 when the fMRI signal modulation at the block-alternation period is large relative to the noise (at the other frequency components) [3]. The phase measures the temporal delay of the fMRI signal relative to the beginning of the experimental cycle, and consequently labels cortical regions that responded to the annulus versus the anti-annulus. To visualize the results, the data were aligned with a high resolution T1-weighted anatomical scan of the entire brain (MPRAGE).

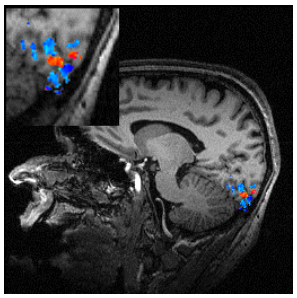


A section of acquired image demonstrates quality of images in the obtained time series.

Setup: The experiment was conducted on a Siemens Allegra 3T scanner fitted with a multi-channel occipital coil array (Nova Medical). Relevant sequence parameters were: TR=100 ms, TE=32 ms, field of view 192x48x30 mm^3. The selected volume was acquired every 3 sec at 1x0.98x1 mm^3 resolution. Six runs of 88 volumes (264 sec) each were acquired from a volunteer.

Results





A slice in sagital section overlaid with the corresponding average phase map shows clearly that the orange (annulus) response is flanked on both sides by blue (anti-annulus), consistent with the known retinotopic organization of visual cortex with the foveal representation further ventral/posterior and the peripheral representation further dorsal/anterior. A region of interest was selected, corresponding to the cortical representation of the annulus, using a the coherence threshold of 0.45 and phase lag of 0-90 degrees (i.e., a hemodynamic delay of 0-6 sec). The figure on the right shows the mean and standard error of the BOLD time series, across the 6 runs in the selected ROI. The reliability of the stimulus-evoked BOLD responses is high (small standard error relative to the mean amplitude of modulation), probably because of reduced partial voluming effects at high spatial resolution.

Conclusion

The present work demonstrates the application of a 3D acquisition to an fMRI experiment with 1x0.98x1mm^3 resolution. Because it is a 3D sequence and because of the surprisingly high reliability of the stimulus-evoked BOLD responses, we believe that it will be possible to refine and use this technique to routinely and reliably measure neural activity 0.5x0.5x0.5mm^3.

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References

[1] S. Thesen et. al. Absolute correction of B_0 fluctuations in echo-planar imaging, Proc. Intl. Soc. Mag. Reson. Med. **11**:1025 (2003)
[2] A. Smith et. al. Investigation of low frequency drift in fMRI signal, NeuroImage **9**:526-533 (1999)
[3] S.A. Engle et. al. Retinotopic Organization in Human Visual Cortex and the Spatial Precision of Functional MRI, Cerebral Cortex,**7**:181-192 (1997)
[4] N. K. Logothesis et. al. Nature, **412**:150 (2001)