Methodology for Sub-Millimeter Resolution fMRI in Awake Monkeys at 7T

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Introduction: Functional MRI with its capability of simultaneously sampling a large number of voxels is an appealing method for mapping the topological organization of higher order visual areas. The scale of the macaque cortex compared to humans should enable us to carry out studies at improved resolutions with respect to the intrinsic scales of the cortex. This is made possible by small and tightly spaced RF coils and a reduced phase-encoding field of view in EPI. However, functional imaging of awake monkeys also introduces dynamic image shifts and distortions in EPI due to B_0 offsets and gradients, which are induced by movements of the animal's body during the scan. In this work we developed a series of methods designed to mitigate the issues of imaging the awake monkey at 7T: a reduction of the movement dependent distortions through favorable choice of slice, read and phase encoding directions, the use of receive coil arrays for parallel imaging, and the use of an image post-processing motion correction algorithm. We validated the methodology by mapping the retinotopic organization of area MT and neighboring area V4t [1,2] with 0.75mm isotropic resolution.

Fig. 1: Eight channel array coil.

Methods: We developed multi-channel array coils for use in a horizontal 7T whole-body MRI scanner equipped with a 36cm diameter head gradient set (Siemens Medical Solutions, Erlangen Germany). A four- and an eight-channel phased array coil (Fig.1), with, respectively, 5cm and 3.5 cm coil diameters, were designed to fit juvenile male rhesus monkeys. The monkeys were placed in a sphinx position and their heads were fixed with a head-post during the visual fixation task [3]. EPI Data were acquired with TR/TE=2000/19ms, ES=0.60ms, 0.75 mm isotropic resolution, 72 FOV, and 36-42 slices. At each TR, half of the k-space volume was acquired alternating between odd and even k-space lines of the full k-space volume. The final images were reconstructed from each k-space sub-volume by a SENSE reconstruction algorithm. Proton density weighted GRE images were used as sensitivity profiles in this algorithm.

Interference patterns, which appear in areas where ghost artifact and image overlap, can be strong at high field strengths when using small voxel sizes. The Fourier transformation of the time course has elevated amplitudes at the Nyquist frequencies in voxels that correspond to areas with overlap of artifact and image due to the alternating k-space trajectories used in even and odd time points. Multiplication of a filter function with the time spectrum for removal of the Nyquist frequencies from the spectrum, followed by a back-transformation restores a time course, which is almost free of interference patterns.

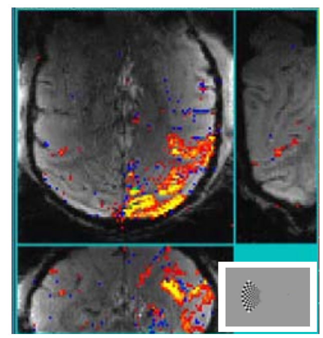

Fig. 2: Raw EPI images with functional overlay.

We chose coronal slices as the imaging plane, because body motion induced gradients are mostly perpendicular to the horizontal plane. With this slice orientation and accelerated data acquisition body motion of the monkeys effectively induce B_0 offsets within the imaging plane, which lead to shifts of the images but little distortions. To address this problem we developed a new motion correction algorithm, which is designed to correct for shifts between near identical images of the same object. For this purpose we calculate the complex ratio $R_{12}=I_1 \cdot I_2^*/|I_1 \cdot I_2^*|$ of an image I_1 and reference image I_2. The transformation of the ratio R_{12} into Fourier space results in a two-dimensional delta function and a shift of its peak off the center of Fourier space represents the pixel shift of the image I_1 in respect to I_2. This shift value is then used to correct the image I_1 without loss of information by making use of the Fourier shift theorem [4].

Results: We acquired whole brain EPI volumes with isotropic 0.75mm resolution in awake monkeys, which were trained to perform a visual fixation task. Fixation behavior was typically better than 90% within a $2^o \times 2^o$ fixation window as measured by an IR based eye-track system [3]. Raw EPI images acquired with the eight channel coil have SNR values of 50-90 and show little distortions (Fig. 2). After temporal filtering and motion correction the alignment of the images in phase encoding direction (direction of shift due to offsets in B_0) was less than 0.3 pixel widths or 0.15mm for a 0.75mm pixel size. The alignment in slice selection and frequency encoding direction is typically within a few percent. As much as 90% of all images in the time course of a session were accepted for statistical analysis. The 10% rejected due to strong distortion or failed alignment typically coincided with bad eye fixation. Figure 3 shows a flattened representation of parts of the superior temporal sulcus (STS) around area MT with responses to a static horizontal meridian stimulus ($p<10^{-5}$). The positions of the meridians shown as black (VM) and white (HM) lines are based on phase-encoded retinotopic mapping experiments.

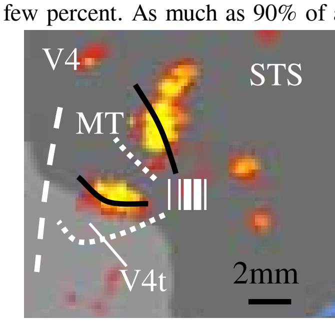

Fig. 3: Activation map of the vertical meridians of MT and V4t. Indicated are VM, black lines and HM white lines

Discussion: The use of multi-channel coil technology and accelerated EPI as well as a newly developed motion correction algorithm enabled us to significantly improve image alignment and quality for data acquisition in sub-millimeter fMRI of awake monkeys. The methods mitigate time dependent distortions and shifts from body movement and the images can directly be used to register to anatomical volumes. Relative to all earlier fMRI studies in awake behaving macaques we were able to reduce the voxel volume by a factor of 5 and achieve image quality and resolution that is sufficient to resolve the topological structure of MT and V4t [1,2]. Our results further demonstrate the potential of sub-millimeter resoultion fMRI with awake monkeys for bridging the gap between information gained from decades of invasive electrophysiological measurements and more recent human fMRI studies.

References: [1] Rosa M.G.P. et al., Phil. Trans. R. Soc. B (2005) **360**, 665; [2] Gattass R. et al., Phil. Trans. R. Soc. B (2005) **360**, 709; [3] Vanduffel W. et al., Neuron (2001) **32,** 565; [4] Reddy B.S. et al., IEEE Trans. Im. Proc. (1996) **5**(8) 1266;

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