



Rationale

- In spite of its good spatial selectivity, fMRI currently suffers from uncertain interpretation of data in quantitative hemodynamic terms.
- We combined quantitative optical imaging of hemodynamic signals directly with concurrent BOLD fMRI in the rat somatosensory cortex in order to better understand the temporal and spatial relationships of the two modalities.

Challenges

- To perform direct optical imaging with a small bore MRI magnet, a long optical fiber bundle is needed to reach the CCD camera system outside the fringe magnetic field.
- All head holder and stimulator electrodes must be non-magnetic.
- Care must be taken to minimize magnetic susceptibility distortions from the craniotomy and the optical set up.

Methods – Animal holder

- A plastic stereotax and animal cradle were constructed (Figure 1) designed to fit within the MRI scanner's gradients.
- The RF surface coil, mirror and fiber bundle is rigidly held over the animal's head.
- A dielectric mirror was selected which minimally affected the RF coil tuning.

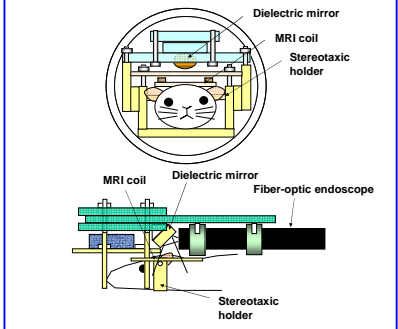


Figure 1. Front and side schematics of the MRI compatible animal cradle and probe assembly.

Methods – Illumination and light detection

- The high-density coherent fiber-optic bundle (10,000 fibers) is coupled to the optical signal detector: a CCD camera (Roper Scientific) (Figure 2).
- Illumination is achieved using a non-coherent bundle that runs parallel with the high-density coherent one.

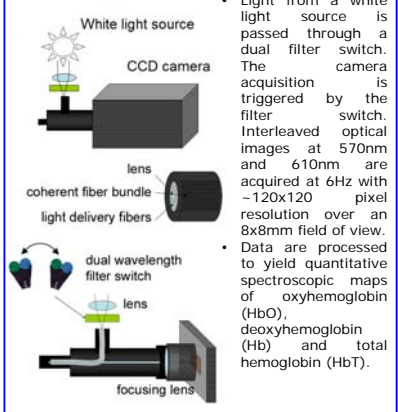


Figure 2. Optical imaging: illumination and light detection assembly.

Methods – Animal preparation

- Animals were anesthetized with halothane for surgery, then alpha-chloralose infusion.
- A ~5x5mm area of skull was thinned to translucency above the left somatosensory cortex (whisker representation).
- A circular 'well' of silicone caulk was built up around the thinned skull region, topped with an angled silica wafer to avoid specular reflections.
- The 'well' was completely filled with transparent Fomblin perfluorocarbon liquid to avoid any air-tissue interfaces.
- Thin non-magnetic (silver) wires were implanted under the skin of the whisker pad and connected to an electrical stimulator using RF filtered wires through the magnet's Faraday shield.

Methods – MRI

- Scans were acquired on a 4.7T/33cm bore Oxford magnet interfaced to a Bruker Biospec Avance console.
- 12cm i.d., 380mT/m gradients were used.
- A small 7mm diameter surface coil was placed directly on the skull, around the thinned skull area.
- fMRI scans were acquired using single shot gradient recalled echo epi-planar imaging (GRE-EPI). Voxel size 300x300x600µm, TR 500ms, TE 35ms, 5 oblique slices (Figure 3A).
- High resolution structural scans were acquired using a 'conventional' gradient echo sequence. Voxel size 75x75x300µm TR 500ms, TE 10ms.

Methods – Protocol

- Pulsed electrical stimuli were applied to the whisker pad at 1, 1.5 or 2mA in 10s blocks with 36s inter-block interval.
- A 'sync' pulse programmed from the MRI scanner was also recorded by the optical imaging system to allow accurate temporal registration of the data.

Results – T2* relaxation maps

- Maps of T2* relaxation time, Figure 3B, show relatively uniform relaxation up to the edge of the cortex: i.e. minimal artifacts from the thinned skull area.
- T2* maps also highlight veins penetrating cortex and also with in deep white matter.

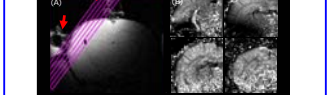


Figure 3. (A) Oblique slice positioning on coronal localizer image. The edge of the silicone well is also visible (arrows). (B) Coronal T2* maps of live rat brain at 4.7T.

Results – Functional correlation maps

- Structural scans, single shot EPI and correlation maps from an fMRI acquisition are shown in Figure 4.
- Superficial veins are apparent in the structural scans which can form 'fiducials' to aid spatial registration with optical images.
- Localized signal loss in the EPI images are likely due to larger surface veins.
- Nevertheless, focal areas of activation to whisker pad stimulation are clearly seen.

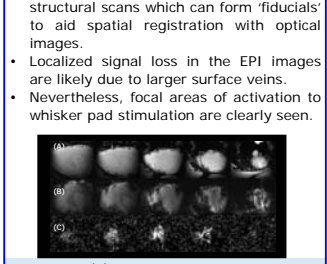


Figure 4. (A) High resolution oblique GRE images (B) single-shot GRE-EPI images, (C) Standard correlation maps from one stimulation run (5 stimulus repetitions).

Results – Registration of MRI and optical data

- Cortical surface is reconstructed from oblique structural MRI images (Figure 5A).
- Superficial veins form 'fiducials' to aid spatial registration with optical images.

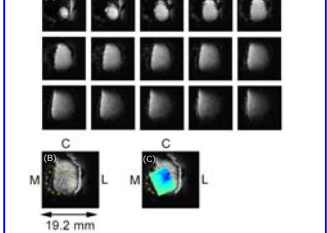


Figure 5. Reconstruction of cortical surface (B) using structural MRI series (A). The location of silicon 'well' is shown in yellow. (C) Registration of optical field of view using surface vessels as 'fiducials'.

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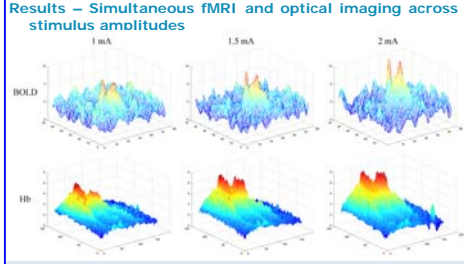


Figure 6. Parametric surfaces of BOLD and Hb responses at 3 stimulus intensities. Maps were calculated as mean of images 2-5sec following the stimulus onset normalized by the pre-stimulus baseline.

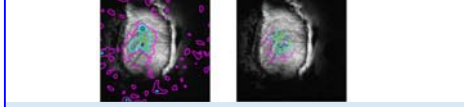


Figure 7. Contours of 0.8, 0.6 and 0.2*max of BOLD (left) and Hb (right) superimposed on MRI surface reconstruction.

Results – Trial-to-trial correlation of MRI and optical data

- There is close to linear correlation between amplitudes of BOLD and optical signals (Figure 8).

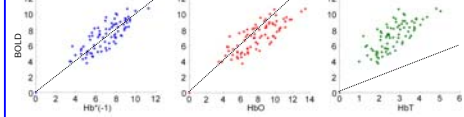


Figure 8. Trial-to-trial correlation of peak amplitudes of MRI and optical measures. The dotted line corresponds to x=y.

Results – Comparison of functional timecourse of BOLD and optical measures

- Timecourses were extracted from ROI within the 0.4*max contour.
- BOLD response from the brain surface is delayed relative to deeper layers.
- BOLD surface response peaks earlier than optical measurement of Hb (the same time as HbO).
- BOLD surface response decay is similar to Hb.

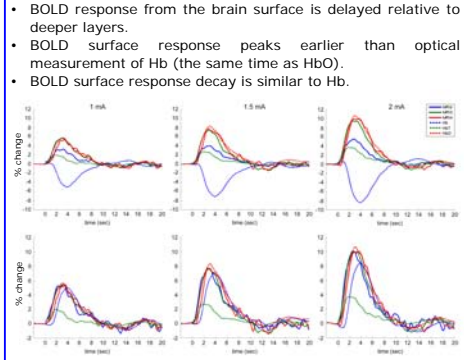


Figure 9. Temporal characteristics of BOLD and optical hemodynamic measures. Bottom row: MRI amplitude normalized to slice 4 (the surface slice); Hb inverted to allow comparison of risetimes.

Results – Comparison of BOLD response with spontaneous 'vasomotor' oscillations

- Spontaneous oscillations are evident in all measured parameters: Hb, HbO, HbT and BOLD. No stimulus was present. Compare the spatial profile to Figure 6.

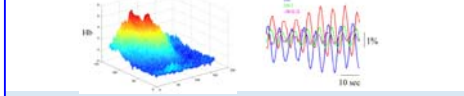


Figure 10. (A) Parametric surfaces of Hb during spontaneous oscillations calculated as mean of 5 images at the maximum amplitude divided by the mean of 5 images at the minimum. (B) Timecourse of spontaneous oscillations in the region inside 0.5*max contour – comparison of Hb, HbO, HbT and BOLD.

Conclusions

- Comparison of the timecourse of BOLD fMRI recorded from the brain surface layers and optical measurements demonstrate contribution of both Hb and blood volume (as demonstrated previously by Obata et al., Neuroimage, 2004). Short TR (500msec), small surface transmit coil (7mm diameter) and high field (4.7T) increase contribution of T1 to the BOLD signal resulting in increased 'in flow effects'.
- BOLD signal from the brain surface is delayed comparing to deeper layers. This might correspond to delayed activation of pial veins.
- There is close to linear correspondence between the amplitude of BOLD and optical measures on a trial-to-trial basis. This also indicates that trial-to-trial variability reflects fluctuations in cortical (neuronal) responsiveness.

Obata T, Liu TT, Miller KL, Luh WM, Wong EC, Frank LR, Buxton RB. Discrepancies between BOLD and flow dynamics in primary and supplementary motor areas: application of the balloon model to the interpretation of BOLD transients. Neuroimage 2004, Jan 21(1):144-53.