Retinotopic maps and hemodynamic delays in the human visual cortex measured using arterial spin labeling

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Introduction

Cortical representations of the visual field are organized retinotopically, such that nearby neurons have receptive fields at nearby locations in the image. Many studies have used blood oxygenation level-dependent (BOLD) fMRI to non-invasively construct retinotopic maps in humans [1]. However, the BOLD signal at 3T reflects primarily a change in venous oxygenation, which might lead to an apparent activation at a spatial location remote from the actual site of neuronal activation, thus reducing the specificity of the functional localization [2]. In contrast to BOLD signal, cerebral blood flow (CBF) as measured using arterial spin labeling (ASL) is not affected by remote draining veins, and therefore spatially and temporally more closely linked to the underlying neural activity. Furthermore, as the retinotopic stimuli are displayed one after another, the phase of each voxel's BOLD signal obtained from the temporal Fourier transform corresponds to the activation time when the stimulus reaches the receptive field of the voxel though with an additional delay due to the hemodynamic response. Thus, the relation between the observed response phase and the position of the stimulation in the visual field is biased by the hemodynamic delay t_H. Since the hemodynamic delay varies in a spatially dependent manner across the brain the magnitude of the bias is not uniform therefore tH needs to be measured for each voxel and a local correction is necessary for an accurate calculation of the retinotopic phase maps. In the present study, we determined retinotopic maps in the human brain using CBF and BOLD signals in order to compare their spatial relationship and the temporal delays of each imaging modality for visual areas V1, V2, V3, hV4 and V3AB. We tested the robustness and reproducibility of the maps across different sessions, calculated the overlap as well as signal delay times across visual areas. While area boundaries were relatively well preserved, we found systematic differences of response latencies between CBF and the BOLD signal between areas.

Methods

Five healthy subjects participated in the experiments on a 3T Siemens MAGNETOM Trio TIM scanner using a 12-channel head coil. The eccentricity and polar visual field maps were stimulated using expanding ring (45s for full expansion) and rotating wedge (30°, 45s for full rotation) stimuli. ASL images were obtained with a FAIR-QUIPSSII PASL encoding scheme with EPI readout that enables simultaneous acquisition of BOLD and perfusion weighted images. The BOLD signal is constructed as the running average of the control and tagged images and the perfusion as the running difference. Each PASL run consisted of 180 alternating tag and control images resulting in a total scan time of 7.5 min and repeated 6 times with the following sequence parameters: TI1=700 ms, TI2=1400 ms, TE=20ms, TR= 2500 ms, 16 axial slices , voxel size=3.5x3.5x3.5 mm^3, FOV=224 mm; FA=90º. High-resolution anatomical *T*1-weighted images were acquired using a 3D MP-RAGE sequence and 3D inflated brain surface were reconstructed using Freesurfer. Pre-processing was performed on the functional data including brain extraction, slice scan time correction, high pass filtering and motion-correction (FSL). To improve the signal-to-noise ratio, functional data were surface smoothed with a Gaussian kernel of 7 mm FWHM. The retinotopic phase maps were estimated by calculating the Fourier transform at the stimulation frequency. To develop a measure for the overlap, we expressed the phase maps of BOLD and perfusion runs as vectors $\vec{B}$ and $\vec{P}$ and plot the distribution of the cross-correlation coefficients calculated by $\vec{r_i} = xcorr(\vec{B}, mod \pm i.\pi/1000)$. To calculate the voxel specific t_H, we calculated the raw phase for the reversed (clockwise/contracting) and non-reversed data obtained from the stimuli moving in opposite directions. If the phase in the retinotopic map for the counterclockwise/expanding stimuli direction is Φa and for the clockwise/contracting direction with inversion Φb, then the phase induced by the hemodynamic delay t_H is equal to (Φb – Φa)/2 for that voxel. Therefore, we subtracted this voxel-wise determined t_H to create both BOLD and CBF retinotopy phase maps accurately with global phase correction.

Results

Figure 1 shows a color plot of the CBF responses to the rotating wedge and expanding ring stimuli on the inflated (A-C) and flattened (B-D) cortical surface representations. The color scale indicates the raw phase values between 0 and 2π for polar angle and eccentricity. Figure 2 shows the comparison of hemodynamic delay times (t_H) of BOLD and CBF signals for distinct visual areas. The calculated $t_H$values for BOLD signal were larger than those for CBF signal, implying an earlier perfusion response across the brain. We found that hV4 had the longest delay for both BOLD (5.34 ± 0.62 s) and CBF (3.16 ± 0.17 s) signals. Figure 3 shows the voxel-wise comparison of globally and locally corrected retinotopic phase maps, i.e. phase-maps obtained assuming a fixed t_H=5s across all voxels vs. individually estimated t_H for every voxel. The blue line shows the ideal curve that would appear if the vectors overlapped 100%. The green and red curves correspond to the correlation coefficient between CBF and BOLD signals as a function of phase-shift between the two, i.e. the distribution of the cross-correlation coefficients between the vectors $\vec{B}$ and $\vec{P}$ vs phase shift. Since we kept the $\vec{B}$ vector unchanged and shifted the $\vec{P}$ vector at each step for calculating the $\vec{r_i}$ vector, phase shifts on the negative direction indicate that $\vec{B}$ and $\vec{P}$ vectors align better when the voxel-wise phase values of the perfusion-based maps are slightly reduced. Figure 4 shows the reproducibility of visual area borders obtained in two separate experiments within the same subject. The contour lines (A-B) and the visual area borders (C-D) of the phase transitions estimated on the basis of two separate experiments exhibit a highly matched pattern (white-dashed lines and black-solid lines).

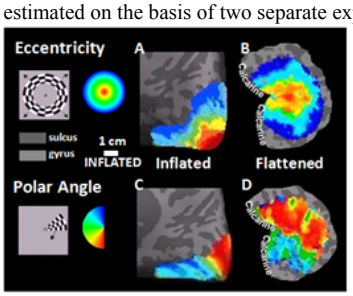

Figure 1

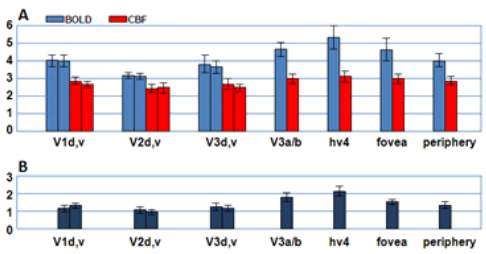

Figure 2

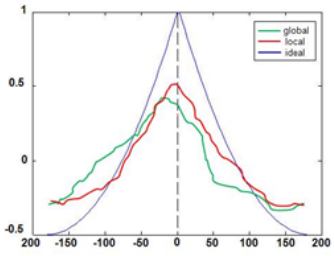

Figure 3

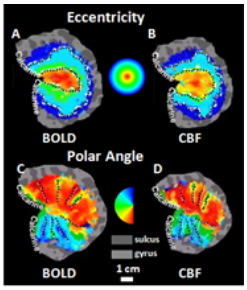

Figure 4

Discussion

The delineations of early visual areas were determined using the perfusion contrast MRI and their overlaps compared with BOLD signal retinotopy. The best match of the phase maps is obtained when the two are phase-shifted relative to each other. One reason for deviations observed between BOLD and perfusion signals is that the BOLD signal at 3T is primarily a change in venous oxygenation whereas ASL is more closely associated with the capillary bed. Our results are also provide explanation for the uncertainties concerning the spatial organization of the visual areas such as hv4 [4] due to the significant B0 inhomogeneities caused by the sinus vein masking the fine-structure of these areas.

References

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