Can functional signal change act as a filter for extracortical vein effects? Evidence from smoothing high resolution fMRI data

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Introduction

In fMRI classification and subsequent elimination of venous contributions is desirable to achieve higher spatial specificity. In particular, extracortical veins and larger venous vessels (e.g. the sagittal sinus) that drain activated areas lead to signal changes far from the site of neuronal activation [1-3]. Up to now a clear and direct identification of veins in the functional data set was not possible due to low spatial resolution. In addition, with EPI based techniques an accurate coregistration between functional and anatomical dataset was difficult to obtain. We used a flow-compensated 3D FLASH sequence [4] that virtually eliminates distortion and permits a sub-millimetre spatial resolution. This allows for direct vein classification and accurate coregistration. Model calculations have shown that veins should lead to very high signal changes which might be used to classify venous contribution based on their signal behaviour, however, an experimental verification is missing. We analyzed t-values and relative signal changes for both vein ROIs and grey matter (GM) ROIs in dependence of resolution by spatially smoothing high resolution data sets using different kernel sizes.

Methods

Three healthy subjects were studied after informed consent. MR imaging was performed on a 3 Tesla Magnetom Trio (Siemens, Erlangen, Germany) using a custom built eight channel occipital cortex array (Stark Contrast, Erlangen, Germany). Functional data sets were obtained using a 3D flow-compensated gradient echo FLASH sequence as implemented in the susceptibility weighted imaging (SWI) package. Imaging parameters: TR = 35 ms, TE = 28 ms, flip angle (α) = 15°, BW=100Hz/px, FOV = 144x108 mm2, slab thickness = 30 mm, acceleration = 2 (GRAPPA [5]). Spatial resolution was 0.75x0.75x0.75 mm3 (0.42 µl). A 192x144 matrix with 40 slices was used, resulting in an acquisition time of 118 seconds per 3D volume. Anatomical data sets were obtained using MP-RAGE with 0.75 mm isotropic resolution. The stimulus paradigm consisted of 4 volumes of rest, 4 volumes with subjects looking at a checkerboard flickering at 4 Hz., acquisition time ~16 min.).

Analysis

Realignment of the functional data and coregistration of the MP-RAGE was performed using weighting volumes (which required the SPM coregistration algorithm to be adapted). The required transformations were calculated with high convergence criteria and by using a multiscale approach down to a scale of 0.5 mm. Vessel enhancing diffusion filtering [6,7] was applied to the average rest-volume of the functional set (fig. 1) to obtain a venous mask where occasional misclassifications were corrected manually. For each subject an activated vein was chosen as the vein ROI and a GM ROI was chosen from an activated sulcus in the visual area as determined from the coregistered MP-RAGE. Further analysis was done by smoothing the data sets with spatial (Gaussian) filters with a FWHM of 1 to 6.25 pixels (resulting in resolutions of 0.75 mm to 5 mm). Average t-values and relative signal changes were calculated in the previously defined ROIs for each kernel.

Results

Fig.1 shows a single slice out of a 3D functional data set with extracortical veins clearly visible as dark spots (top) and a projection of an unthresholded 3D z-map that clearly shows the venous contamination of the statistical map (bottom). Fig. 2a shows the average t-values versus smoothing kernel FWHM for both vein and GM ROI, fig. 2b shows the relative signal changes (%), respectively. Error bars show the standard deviation over subjects. Average t-values of the vein ROI increase up to a value of about 10 (smoothing kernel of 2 mm) and then drops, the GM ROI increases slightly to a value about 2.2 with increasing smoothing kernel. The average values are quite different for both ROI types, but their standard deviations are quite large. In terms of signal change, the vein ROI shows 30% increase without smoothing which drops to 6%-7% for large kernel sizes – close to the value of the GM ROI (4%). This 4% signal change of the GM ROI is almost independent of smoothing. Most importantly, the variation is very small compared to the vein ROI.

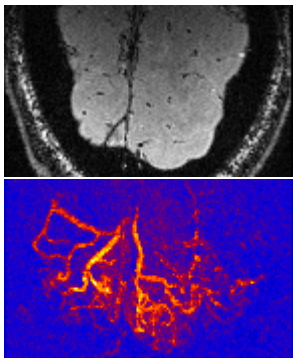

Fig.1 (top): Single slice out of the 3D data set with venous structures clearly visible. (bottom) 3D rendered projection of an unthresholded 3D z-map.

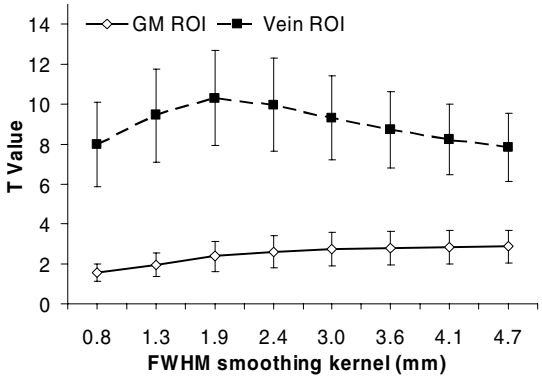

Fig.2a: Average t-values versus smoothing kernel for the vein ROI and the GM ROI. Error bars show standard deviations over subjects.

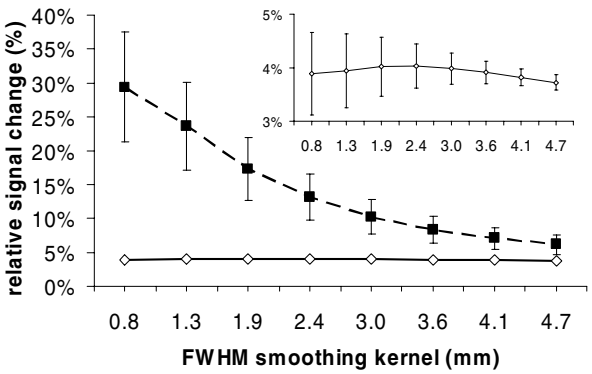

Fig.2b: Relative signal changes for the vein ROI and the GM ROI. Error bars show standard deviations over subjects. Note that error bars for GM ROI are smaller than the symbols. Insert shows zoomed GM signal change.

Discussion and Conclusion

The proposed high spatial resolution, 3D FLASH method delivers functional data that allow a direct classification of extracortical veins. Images are minimally distorted which simplify definition of grey matter ROIs due to accurate coregistration with anatomical images. Given our experimental parameters (B0, TE, etc) grey matter shows a t-value of about 2 and a signal change of about 4%. While t-values of the vein ROIs might not be optimal to discriminate between veins and grey matter due to large variations, relative signal change seems to be a better candidate due to very large signal changes at small smoothing kernels and due to the minimal variation in grey matter. The large variations in venous signal changes might be explained by the dilution effect (various distances from the activated grey matter) combined with interindividual differences in venous architecture, and variations in the orientation of the veins with respect to the static magnetic field. The small variation in the GM ROI might reflect the more homogeneous vasculature in GM. Our results hold promise – also for EPI-based methods were an anatomical discrimination is not feasible – to define a high resolution protocol where an easy venous filter can be constructed to disentangle grey matter activation and venous effects.

References

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