Multi-Parametric Classification of fMRI-Activated Voxels Using Venous Vessel-Size, BOLD Latency and Susceptibility-Weighted Imaging

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Introduction

In order to increase the spatial specifity of *functional magnetic resonance imaging* (fMRI) based on the *blood oxygenation level dependent* (BOLD) effect by excluding macrovascular contributions, several approaches have been presented to identify large veins [1-10]. In the present study, some of the techniques mentioned above have been combined into a single set of experiments by the *multi-gradient-echo single-shot-sampling of spin-echo refocusing* (MESSER) sequence [10, 11] which is a single-shot parallel-imaging variant of *gradient-echo sampling of FID and echo* (GESFIDE) [12]. MESSER allows fast mapping of several parameters which are supposed to indicate the presence of large veins: From the transverse *gradient-echo* (GE) and *spin-echo* (SE) relaxation rates, R_2^* and R_2, the average venous vessel size, r_v, the change in resonance frequency, $\Delta\omega$, and the BOLD latency t_D can be estimated. To compare the results with a well-established external standard, MESSER was combined with high-resolution venograms based on susceptibility-weighted imaging to obtain a measure for the 'veinness', V_{SWI}, of a voxel. The purpose of this approach is twofold: Firstly, it was possible to study different parameters of activated voxels and their interrelationships. Secondly, based on these findings, the effectiveness of these parameters to detect large veins in order to increase specifity of BOLD-based fMRI could be evaluated.

Materials and Methods

Measurements were performed on a Siemens 3T Trio system with the MESSER sequence and an acceleration factor of three; a limited FOV of 154 × 154-mm; 64 × 64 matrix; SE echo time, $TE = 121$ ms; repetition time, $TR = 1050$ ms; 110-kHz receiver bandwidth; phase encoding direction from left to right; 7 slices (3-mm thickness). Eight healthy subjects were examined using visual stimulation with a short block duration of 10 s and a total of 15 blocks. fMRI analysis was performed by a linear correlation of the $-R_2^*$ and $-R_2$ time course to emulate an GE and SE experiment, respectively. A Fourier transformation of the time course yielded t_D [13] and r_v was estimated from the combined change in R_2^* and R_2 [10, 14-16]. Finally, $\Delta\omega$ was obtained by linear regression of the change in image phase as a function of TE. To obtain the venograms, a three-dimensional first-order fully flow-compensated spoiled GE sequence ($TE = 28.8$ ms, $TR = 50$ ms) with an isotropic resolution of 0.6 mm was used to obtain high-resolution phase images which were high-pass filtered to obtain maps of V_{SWI}. Activated voxels were classified by a K-means clustering algorithm using r_v, t_D and V_{SWI}. In addition, the interrelationship between these parameters among each other and with ΔR_2^*, ΔR_2 and $\Delta\omega$ was studied by a rank-correlation analysis (Kendall's τ).

Results

Fig. 1 displays representative maps of r_v and t_D overlaid onto V_{SWI}. Most of the venous structures, i.e. regions with a high V_{SWI}, correspond well with a high r_v and a late t_D. These qualitative findings could be verified by the cluster analysis which divided the ensemble into a macro- and a microvascular voxel population (Table 1). Besides r_v, t_D and V_{SWI}, ΔR_2^* is large for the cluster 'macro'. Both the microvascular and macrovascular $\Delta\omega$ have a mean value of almost zero indicating that large veins are not accompanied by detectable non-zero $\Delta\omega$ in our experiments. In the SE-activated ensemble, the mean r_v is lower than that of the R_2^*-activated voxels in the ensemble 'all', but higher than r_v of the microvascular ensemble. However, unexpectedly, V_{SWI} is slightly higher than in the GE-activated ensemble and t_D is relatively high. Thus, it is questionable whether the SE ensemble reflects microvascular effects in general which is commonly assumed. The correlation analysis revealed highly significant mutual correlation of 0.17 between V_{SWI} and r_v as well as t_D. In contrast, correlation of these three parameters with $\Delta\omega$ and ΔR_2 revealed much lower correlation coefficient below 0.1.

Discussion and Conclusions

The relatively good mutual correlation of venous vessel size, latency and venographic intensity suggests that these parameters can be used equally well to discriminate large veins. In contrast, a consistent change in resonance frequency for the macrovascular population was not observed in our experiments. Finally, it is questionable whether SE-BOLD contrast can be exclusively attributed to microvascular effects.

References

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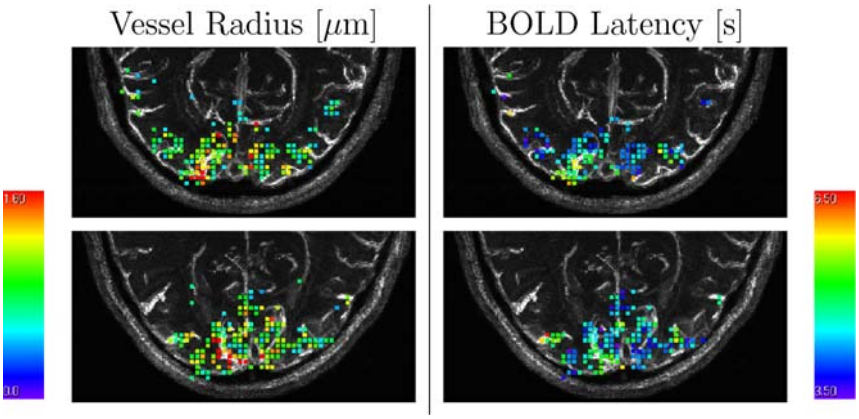

Figure 1: Representative maps of r_v (left column) and t_D (right column) in activated voxels overlaid onto venograms. Values of r_v are color-coded by the decadic logarithm of r_v in μm and values of t_D are color-coded in s. The activation patterns differ since only voxels whose value is in the color-coded range are included in the map.

	r_v [μm]	t_D [s]	V_{SWI}	ΔR_2 [1/s]	ΔR_2^* [1/s]	$\Delta\omega$ [rad Hz]
micro(6602)	5 ± 2.3	4 ± 1.2	0.15 ± 0.046	-0.13 ± 0.29	-0.27 ± 0.56	0.012 ± 0.41
macro(3179)	14 ± 8	4.5 ± 1.3	0.24 ± 0.13	-0.12 ± 0.6	-0.47 ± 1.1	-0.0079 ± 0.35
all(9781)	7.8 ± 6.4	4.2 ± 1.3	0.18 ± 0.093	-0.13 ± 0.42	-0.21 ± 1.3	0.0057 ± 0.39
SE(2063)	6.2 ± 4.2	4.7 ± 2.4	0.2 ± 0.11	-0.24 ± 0.61	-0.55 ± 2.9	-0.018 ± 0.54

Table 1: Average parameters of clusters. The number of voxels are listed in parentheses. The clusters 'micro' and 'macro' contain voxels with mostly micro- or macrovascular BOLD effects, respectively. Moreover, the table also lists the entire ensemble of voxels (all). The last line contains voxels activated only in the R_2 data (SE). Values given are mean and standard deviation.