Contribution of different sources of signal variance to T_2* and S_0 maps in the human brain at rest: a 7T study

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Purpose: Various noise sources affect BOLD fMRI time-courses and limit the benefits of high field fMRI. The aim of the present study was to investigate the contribution and the origin of non-thermal noise to fMRI signal fluctuations in the visual cortex at 7T during rest. The following noise sources were considered: 1) low frequency drifts; 2) effects related to the phase of respiration and cardiac cycles; effects due to fluctuations in the 3) respiratory flow rate and 4) cardiac rate; 5) thermal noise; 6) other sources, tentatively attributed to spontaneous neuronal activity. The variance explained by each noise source in BOLD-weighted single-echo, T_2* and S_0 images was then evaluated.

Prediction: T_2* signal fluctuations are expected for changes in intravoxel B_0 gradients, e.g. due to fluctuations in hemodynamic parameters (oxygen consumption, blood flow, blood volume), and in phase with respiration cycles. S_0 changes are related to fluctuations in real/apparent spin density (e.g. motion, B_0 drifts) and in T_1 (e.g. inflow, changes in blood volume).

Methods: Six subjects (4m/2f, age 33±4) participated in the study (IRB approved protocol). Subjects were asked to rest in the MR scanner with their eyes closed. Multi-echo GE-EPI BOLD fMRI was performed at 7T (GE Medical Systems) using 32 receive-only coil-elements (NOVA Medical) and the following parameters: TR=2s, FA=75°, N. slice=20, voxel-dim=2.5x2.5x2mm^3, slice-gap=2mm, SENSE-rate=3, N.scans=178. TEs=12/28.2/44.4ms were employed in odd scans (multi-echo set A)) and TEs=20.1/36.3/52.5ms in even scans (multi-echo set B)); the total acquisition length of a single EPI was 14.8ms. We also recorded the timing of physiological cycles (sampling rate = 250 Hz) by the use of a pulse-oximeter and the respiratory bellows provided with the MR scanner. We defined a region of interest (ROI) in the visual cortex by the use of a functional localizer (retinotopy, N. scans = 245). Separately for multi-echo set A) and B), we extracted T_2* and S_0 (S_0=S(TE=0)) by linear least square fitting of multi-echo data, assuming a mono-exponential signal decay. After standard image preprocessing, single-echo, T_2* and S_0 fMRI signals were converted to % signal change relative to their time average. Non-thermal noise sources 1)-4) were respectively modeled with: 1) three polynomial regressors; 2) eight RETROICOR regressors [1]; 3) two respiration volume per unit time (RVT) regressors [2] shifted at lag -8s and +8s (dual-lagged procedure, [3]); 4) two cardiac-rate regressors [4] shifted by lags of -4s and +8s [3].

The % fMRI signal variance explained (VE, %) by sources 1)-4) was computed as the R^2 value adjusted for the degrees of freedom, multiplied by 100. VE explained by noise source 5) at the voxel level was measured as the ratio of the signal variance due to thermal noise divided by the total signal variance of each time series, multiplied by 100. The variance due to thermal noise was estimated in each voxel from an image with no radiofrequency excitation and was scaled by the square of the signal at a fixed time point in the same voxel at each echo time. Projection of this variance to T_2* and S_0 images was performed according to the rules of linear least square fitting. The VE associated with spontaneous fMRI activity was determined from the residual signal variance after accounting for noise sources 1)-5). We computed VE attributable to sources 1)-6) for second-echo, T_2* and S_0 signals both at the voxel level and averaged within the ROI in the visual cortex.

Results: For each source, the explained variance in the visual cortex for second-echo, T_2* and S_0 signals of multi-echo set A) at the voxel and ROI level are shown in Fig. 1. Similar results were found for multi-echo set B). All non-thermal noise sources contributed to single-echo, T_2* and S_0 signal fluctuations. Low-frequency drifts and spontaneous activity were the major sources of non-thermal signal fluctuation. Both at the voxel and the ROI level, low-frequency drifts explained more variance in S_0 than in T_2* images (paired t-test, $p<0.01$). The opposite result was found for spontaneous activity ($p<0.015$) and changes in the respiratory flow rate ($p<0.065$); similar amount of variance in S_0 and T_2* images was explained by effects related to the phase of physiologic cycles and to fluctuations in the cardiac rate.

Conclusions: The reflection of low-frequency drifts in both S_0 and T_2* indicates that they have both an instrumental and a physiological origin, in agreement with previous work [5]. Effects related to the phase of physiologic cycles (e.g. blood pulsatility, head motion, B_0 changes in the head due to chest motion) and to fluctuations in the cardiac rate surprisingly contributed in similar amounts to T_2* and S_0 images. Fluctuations in respiratory flow rate showed a larger contribution in T_2* than in S_0 images, as expected considering that they may affect blood volume and flow. Finally, our results confirmed a TE dependence of spontaneous activity in the visual cortex, in line with previous work in the motor cortex [6]; nevertheless, residual spatially coherent spontaneous fluctuations were present in S_0 images.

References: [1] Glover et al., *Magn Reson Med,* 44:162-7, 2000. [2] Birn et al., *Neuroimage,* 31:1536-48, 2006. [3] Bianciardi et al., *Magn Reson Imag*, 27:1019-29, 2009. [4] Shmueli et al., *Neuroimage*, 38:306-320, 2007. [5] Yan et al., *Magn Reson Med*, 61:819-27, 2009. [6] Peltier and Noll, *Neuroimage*, 16:985-92, 2002.

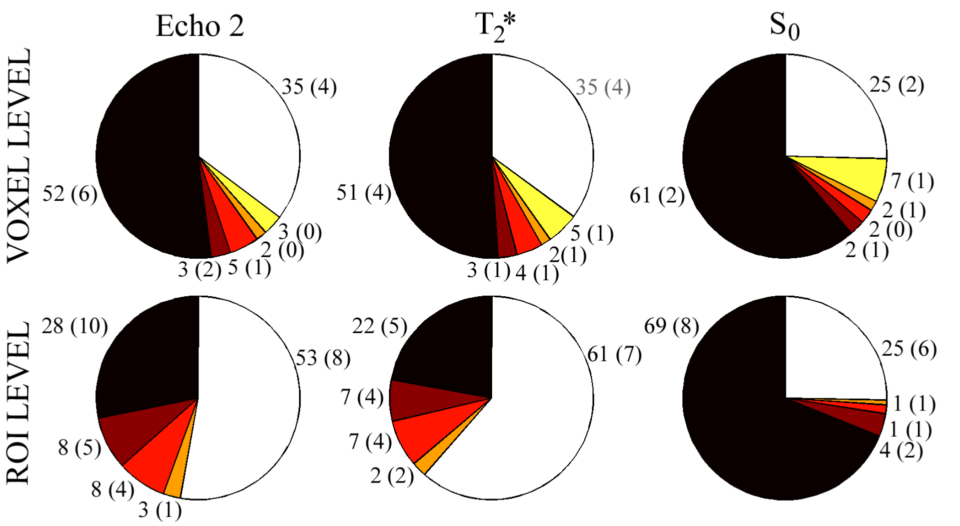

Fig. 1 Pie-charts showing the explained variance (VE, %) of fMRI data (second-echo, T_2* and S_0) relative to non-thermal noise sources 1)-4), thermal noise and spontaneous activity (average (s.e.) values across subjects). VE due to thermal noise is displayed at the voxel level only, since its contribution at the ROI level is negligible.