Effects of chest motion and respiratory pressure wave in the brain investigated using high spatial resolution fMRI at 7 Tesla

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Introduction: Respiration generates fMRI signal instability in the brain by several different mechanisms, including: 1) chest motion, which produces bulk magnetic susceptibility variations in the brain; 2) pulsatile motion of blood and CSF due to respiratory waves in arterial and venous pressure. The effects produced by these two mechanisms in fMRI images have distinct spatial distribution, and their relative contribution varies with the fMRI acquisition parameters. In particular, effects due to chest motion are expected to: a) be in phase with respiration (e.g. as measured with a respiratory bellow or an airway flow spirometer); b) have a negligible dependence along the *X* (L/R) and *Y* (P/A) directions [1] and a have a strong dependence (~$1/r^3$ for phase (Φ) fMRI signals [1] , and ~ $1/r^8$ for magnitude (M) fMRI signals according to our simulations, r = distance from the center of the lungs) along the *Z* direction (I/S); c) decrease with decreasing slice thickness (M fMRI signals only); d) increase linearly with the static magnetic field (B_0). Effects due to the respiratory pressure wave are expected to: a) not have a precise phase relationship with respiration, because of the different arrival times of the traveling wave in different brain areas; b) contribute more in large vessels, ventricles, and subarachnoid space, and have a spatial distribution similar to those effects caused by the cardiac pressure wave; c) increase with decreasing the voxel size because of reduced partial volume effects; d) produce higher contrast changes for higher B_0, especially in vessels, because of longer T_1 values. We investigated the relative contribution of these effects, their spatial distribution, and the performance of different correction methods by acquiring whole-brain high-spatial-resolution M and Φ resting-state fMRI at 7 Tesla.

Methods: Two subjects (2m, age 22, 41) participated in the IRB-approved study. GE-EPI BOLD-fMRI was performed at 7 Tesla using 32 receive-only coil elements and parameters: echo-time (TE) = 22 ms, repetition time = 5 s, flip angle = 85°, N. slices = 94, slice orientation = axial, voxel-size = 1.2×1.2×1.2 mm^3, N. scans: 100, GRAPPA acceleration factor: 4, nominal echo spacing = 0.75 ms. Cardiac pulsation and respiration were monitored/recorded by a piezoelectric finger pulse sensor and by airway flow spirometry via mouth-piece (1 kHz sampling rate). M signal fluctuations were converted to % signal changes relative to their time average (M/M_0, %). For each voxel and time-point in the Φ time-courses, the first Φ time-point was subtracted, and phase wraps over time were removed. The background spatial low-frequency Φ variations were fitted for each slice and time point with a 4th order polynomial function. These signal fluctuations appeared to be correlated to and in phase with respiration, and were employed, on a voxel-by-voxel basis, as physiological noise regressor (Φnoise-regressor) for both M and Φ fMRI data [2]. Φ data were converted to fractional resonance frequency shifts (ω/ω_0, ppm) according to: $\omega/\omega_0 = \Phi/(2\pi\gamma_T B_0 TE)$, with $\gamma_T B_0$ = 297 MHz. Temporal drifts of M and Φ fMRI signals were modeled with 3rd order polynomials and removed. Effects in-phase with the respiratory recordings (including effects due to chest motion and a portion of the effects due to respiratory pressure wave) were modeled either with: a) Φnoise-regressor; b) 2 RETROICOR regressors (design matrix: Xr-retroicor-in-phase = [$\cos(\theta_r)$, $\cos(2\theta_r)$], θ_r = respiratory phase as in [3]). Effects out-of-phase with the respiratory recordings (including part of the effects due to respiratory pressure wave) were modeled with 2 RETROICOR regressors (Xr-retroicor-out-of-phase = [$\sin(\theta_r)$, $\sin(2\theta_r)$]). We also considered a comprehensive model of effects related to respiration with either: a) Xr-retroicor-full = [Xr-retroicor-in-phase Xr-retroicor-out-of-phase], as in [3]; b) Xr-mix = [Φnoise-regressor Xr-retroicor-out-of-phase]. Effects related to the cardiac pulsation were modeled with 4 RETROICOR cardiac regressors (Xc), as in [3]. For each voxel in both M/M_0 and ω/ω_0 fMRI data, the amplitude of signal changes (SC) due to each design matrix was computed as the standard deviation of the fitted signal over time; the % signal variance explained (VE, %) by each design matrix was computed as the R^2 value adjusted for the degrees of freedom, multiplied by 100. For each design matrix, we computed average slice profiles of SC and VE in the *Z*, *X* and *Y* directions.

Results and Discussion: For an example data-set and each design matrix, SC and VE profiles along the three directions are shown respectively in Fig. 1 and 2. For Xr-mix, SC and VE in three reformatted image planes are shown respectively in Fig. 3 and 4. Respiratory effects constitute a major noise component in ω/ω_0 data (VE due to Xr-mix on average across the brain equal to 64.16 ± 0.03 % and 50.15 ± 0.03 % for subject 1 and 2), and a smaller but not negligible component in M/M_0 data (VE equal to 5.11 ± 0.01 % and 1.92 ± 0.00 %). In ω/ω_0 time-courses, the ratio between effects out-of-phase and effects in-phase with respiration for subject 1 and 2 was: 0.53, 0.50 for SC; 0.24, 0.21 for VE; their ratio was higher in M/M_0 time-courses (0.96, 1.1 for SC; 0.58, 0.67 for VE). In ω/ω_0 images, both effects in-phase and out-of-phase with respect to respiratory recordings varied mainly across the *Z* direction; their variation across the *X* and *Y* direction was smaller but still significant ($p < 0.05$). In M/M_0 images, effects due to respiration are mainly visible in large vessels, ventricles, and subarachnoid space; the slice profiles of SC due to respiratory effects (modeled with Xr-mix) were highly correlated with those of cardiac effects ($p < 10^{-33}$ for both subjects). These results indicate that: chest motion is an important respiratory-related source of signal instability in ω/ω_0 data, whereas its contribution to M/M_0 data is attenuated here probably due to the use of thin slices; pulsatile motion is the major respiratory-related source of signal instability in M/M_0 data. On average across the brain, Φnoise-regressor explained more variance than Xr-retroicor-full in ω/ω_0 data ($p < 0.05$), but this was not the case in M/M_0 data. Xr-mix explained more variance than Xr-retroicor-full in both ω/ω_0 and M/M_0 data ($p < 0.05$). These results suggest that retrospective and prospective correction methods of respiratory effects based on the measure of off-resonance changes in Φ data might only correct for effects in-phase with respiration; for high spatial resolution M fMRI data, these procedures could be combined with methods that account for effects out-of-phase with respiration.

References: [1] Van de Moortele et al, *Magn Reson Med,* 47:888-95, 2002. [2] Bianciardi et al., *ISMRM 20th Annual Meeting*, Abstract n. 2198, 2012. [3] Glover et al., *Magn Reson Med,* 44:162-7, 2000.

- Φnoise-regressor - Xr-retroicor-in-phase - Xr-retroicor-out-of-phase - Xr-retroicor-full - Xr-mix - Xc