Investigation of cardiac and respiratory pressure waves in the brain by high resolution echo-planar imaging at 7 Tesla

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Purpose: Recent work [1] showed the feasibility of mapping the propagation of the cardiac pressure wave in the brain by echo-planar imaging (EPI) with short repetition time (TR). We further investigated the cardiac and also the respiratory pressure wave in the brain by means of high spatio-temporal resolution EPI at high magnetic field strength. Specifically, we studied the feasibility of mapping the arrival time and the bulk flow velocity change of each pressure wave, which are respectively related to the velocity of the traveling wave and to the wave pressure change. We also investigated the acquisition time needed to estimate these parameters with an error less than 5%.

Methods: Two subjects (1m/1f, age 41/23) participated in the IRB-approved study. Gradient echo EPI was performed at 7 Tesla using 32 receive-only coil elements and parameters: echo time = 22 ms, TR = 51 ms, flip angle = 85° , 1 axial slice, in plane voxelsize = $1.2 \times 1.2 \text{ mm}^2$, slice thickness (TH) = 1.2 mm, N. scans: 1200, GRAPPA factor: 4, nominal echo-spacing = 0.75 ms. Cardiac pulsation and respiration were monitored/recorded by a piezoelectric finger pulse sensor and by an airway flow spirometer via mouth-piece (1kHz sampling rate). A 2nd order Fourier series was employed to model the effects related to the phase of cardiac pulsation and respiration (4 cardiac and 4 respiratory RETROICOR regressors [2]). In each voxel, magnitude EPI signals were converted to % signal changes by dividing the signal at each time point by the mean signal across time; temporal drifts (3rd order polynomials) were removed. The EPI signal variance explained (%) by cardiac and respiratory RETROICOR regressors was computed as the R² value adjusted for the degrees of freedom, multiplied by 100. To analyze the respiratory pressure wave, EPI time-courses were low-pass filtered (cut-off frequency 0.6 Hz). To analyze the cardiac pressure wave, EPI time-courses were band-pass filtered between 0.6 Hz and 2.5 Hz. For each voxel, and for each (cardiac or respiratory) peak, we considered a



window of 3 wave cycles (~ 3 s and ~ 13 s respectively for cardiac and respiratory effects) of the EPI time-course, and then averaged this window across peaks to obtain an average cardiac and an average respiratory EPI waveform (the number of consecutive averaged peaks, Nav, was varied between 1 and 55 for the cardiac waveform, and 1 and ~10 for the respiratory waveform). The same averaging process was performed to the cardiac and respiratory recordings (down-sampled at 1/TR) to obtain average reference pressure waveforms. From each average EPI waveform (cardiac and respiratory) we estimated two parameters: a) the arrival time (AT, s) of the pressure wave with respect to the peak of the average reference pressure waveform; to obtain AT we computed the phase of the spectral density of the correlation between the average EPI waveform and the average reference pressure waveform; AT was then computed as the phase at the wave (cardiac/respiratory) frequency divided by 2π and by the value of the wave frequency; b) the change in bulk flow velocity (Δv , cm/s) due to the pressure change, as TH/TR·log(S_{max}/S_{min}) (S_{max,min} = maximum, minimum signal in the first cycle of the average EPI waveform), assuming T₁ shortening due to inflow effects; in vessels, this is an upper estimate of the change in bulk flow velocity because of additional shortening of apparent T₁ due to possible blood volume effects or T₂* changes. Assuming as a gold standard the two parameters computed for the maximum Nav, we computed the error in the estimate of these parameters for lower Navs as: error_{AT}(Nav) = 100*abs(AT(Nav)-AT(Nav_{max}))/AT(Nav_{max}); error_{Δv}(Nav) = 100*abs(Δv (Nav) - Δv (Nav_{max}))/ Δv (Nav_{max}). The error was then averaged (± s.e.) across voxels where the variance explained by cardiac or respiratory RETROICOR regressors was > 2%.



Results: For an example data-set, we show: an EPI image (averaged across 60 time-points) in Fig. 1A; the variance explained by the cardiac and respiratory RETROICOR regressors respectively in Fig. 1B, C; the signal time-course (only 20 s) from a scalp vessel (blue arrow in Fig. 1A) and its amplitude spectrum in Fig. 2A, B: note the presence of respiratory (~0.24 Hz), cardiac (~ 0.98 Hz, and higher harmonics) components, and also of interaction terms (~0.98 ± 0.24 Hz, and higher harmonics). For Nav_{max} we show: the average EPI waveforms in Fig. 3A, B (three voxels, blue: scalp vessel, red: cerebrospinal fluid - CSF-, green: gray matter, see arrows in Fig. 1A); AT and Δv maps in Fig. 4 (mask: variance explained > 2%). error_{AT} and error_{Δv} for subject 1 (solid lines) and subjects 2 (dashed line) are shown in Fig. 5A, B: for both subjects, errorAT is below 5% for Nav < 26 (cardiac) and < 7 (respiration); error Δv is < 5% for Nav < 46 (cardiac) and < 10 (respiration).

Discussion and conclusions: The cardiac and respiratory pressure waves explain a fraction of variance greater than 2% mainly in large scalp and brain vessels and in the CSF. AT varied of few hundred ms within the CSF and across vessels; Δv varied between 0.3 and 1.5 cm/s. In single slice high resolution EPI, we have demonstrated the feasibility of mapping the AT of cardiac and respiratory pressure waves in \leq 30 s, and to estimate the bulk flow Δv in \leq 45s with an error less than 5%. These results are promising for the estimation of the velocity of the traveling wave and of the wave pressure change, which are indicators of vessel elasticity and of CSF response to vascular compliance.

References: [1] Tong and Frederick, *Neuroimage*, 61:1419-27, 2012. [2] Glover et al., *Magn Reson Med*, 44:162-7, 2000.