Separating BOLD activation from stimulus-correlated motion by means of linear source extraction applied to multi-echo data

P. F. Buur[1], C. W. Hesse[1], and D. G. Norris[1,2]

[1]F.C. Donders Centre for Cognitive Neuroimaging, Nijmegen, Netherlands, [2]Erwin L. Hahn Institute for Magnetic Resonance Imaging, University Duisburg-Essen, Essen, Germany

Introduction

The majority of fMRI studies use the BOLD effect as contrast mechanism for functional activation, which affects local signal intensity by a change in the relaxation parameter R_2^* ($1/T_2^*$). However, the functional signal is often obscured by additional sources that contribute to the MR signal such as subject motion, inflow and the respiratory and cardiac cycle. To a great extent, these sources manifest themselves as fluctuations in the initial signal S_0. Here, a novel approach is presented which seeks to separate the R_2^* and S_0 signal components. The method makes no explicit assumptions about activation time-course or location and is based on a simple linear mixing model of how the sources R_2^* and S_0 project onto the measured data. From the signal intensity (Eq. 1), an expression for how the signal change depends on changes in R_2^* and S_0 can be derived (Eq. 2, μ indicates mean value over time). Using this knowledge, it is possible to extract R_2^* and S_0 time courses from multi-echo data acquired at different echo times TE. The efficacy of this method is demonstrated in a paradigm where functional activation and subject motion occur simultaneously.

$$S(t) = S_0(t) \cdot \exp[-TE \cdot R_2^*(t)] \qquad \text{(Eq. 1)}$$

$$\Delta S/\mu S = \Delta S_0/\mu S_0 - TE \cdot \Delta R_2^* \qquad \text{(Eq. 2)}$$

Methods

Six subjects were scanned at 3T (Siemens TIM Trio, 12 channel head coil, flip angle 78°, TR 2020 ms, 30 slices, 10% slice gap, voxel size 3.5x3.5x5mm^3). Five echoes (after each excitation) were acquired at TE = 9, 21, 33, 44, 56 ms using an in-house GE-EPI ME sequence. Short echo times were achieved using GRAPPA with threefold acceleration, 6/8 partial Fourier and a bandwidth of 2520 Hz/pixel. Visual activation was elicited using a reversing checkerboard pattern (20s) separated by a baseline fixation cross (30s). Subjects were instructed to slightly nod their heads every other stimulation block. Prior to source extraction, motion parameters were estimated from the third echo using SPM5 and subsequently applied to all echo data.

Assuming the echo signals to be linear mixtures of the activation (R_2^*) and motion artefact (S_0) sources, the sources are extracted on voxel-by-voxel basis using Eq. 3. $\mathbf{x}(t)$ is a matrix (with size being the number of echoes by the number of time points) containing the measured echo time courses rescaled according to the left-hand side of Eq. 2. $\mathbf{A}$ is a 5-by-2 matrix with two columns describing how the sources $\mathbf{s}(t)$ are mixed into the echo time courses (the 'source projection' vectors). Following from the right-hand side of Eq. 2, the column values are a constant number and the echo times for S_0 and R_2^* respectively. Multiplication of $\mathbf{x}(t)$ with the pseudoinverse of $\mathbf{A}$ (from the left) "unmixes" the signal and yields an estimate of $\mathbf{s}(t)$, a matrix containing the two sources (with size being the number of sources by the number of time points). The first row of $\mathbf{s}(t)$ contains the extracted S_0, the second row contains the extracted R_2^*. Since the scaling of the columns of $\mathbf{A}$ is arbitrary, the scaling of extracted sources has no physical meaning; hence, they are rescaled to lie between 0 and 1.

$$\mathbf{x}(t) = \mathbf{A}\mathbf{s}(t) \Rightarrow \mathbf{s}(t) = \mathbf{A}^{-1}\mathbf{x}(t) \qquad \text{(Eq. 3)}$$

Results

Figure 1 shows typical motion parameters for one of the subjects. As expected given the movement instruction, movement was greatest along the *y*- and *z*-axes and around the *x*-axis. Translations ranged from 0.5 to 5mm, rotations ranged from 1 to 8 degrees. In Figure 2, average time courses from a small ROI in visual cortex (red box) are plotted for the extracted S_0 and R_2^*. The signal from the third echo is included for reference. The effect of motion (see Fig. 1) is clearly visible in the single echo signal (top). The S_0 component captures most of the movement-induced intensity fluctuations (middle), whereas the R_2^* component is almost artefact-free and follows the expected pattern of activation.

Time courses for an ROI outside the visual cortex are shown in Figure 3. Again, the S_0 component contains the motion-related variance to a high degree. Although no significant intensity fluctuations are expected in the R_2^* component as this region is not activated, it can be seen that part of the motion effects project onto this component. Compared with S_0 the artefact amplitude in the R_2^* component is quite small relative to the background noise, which is consistent with the notion that in the absence of activation, the "unmixing" projects mainly noise. The results shown here are representative for the data obtained across all six subjects.

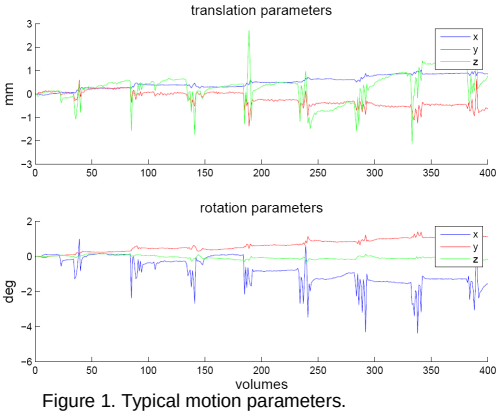

Figure 1. Typical motion parameters.

Discussion

Using a simple linear mixing model of how the sources R_2^* and S_0 project onto the measured data, this approach successfully separates activation and task-correlated motion. Starting with Eq. 1, the only assumption in constructing the source projection vectors used for source extraction is an exponential signal decay. Combined with an optimal weighting scheme in which the CNR of each separate echo is taken into account (1), the sensitivity of the method can be further improved. Also, with the number of receive coils increasing rapidly it becomes feasible to go to higher acceleration factors and collect more echoes, which in turn can help to increase accuracy and robustness of the source estimates obtained using this method. After the extraction procedure, the data can be used normally for statistical inference.

Ultimately, the quality of this approach is limited by the accuracy of the mixing model. In the examples shown in Figures 2 and 3, part of the motion is reflected in the R_2^* component. It is quite reasonable to assume that errors in the realignment procedure (2) or susceptibility effects due to the large movements (3) can lead to a slight misspecification of the model. However, it should be bourn in mind that the movements in this experiment are quite extreme.

In this experiment, the application of the method to remove the effects of subject motion from the data is demonstrated. As in principle, all physical processes that give rise to changes in S_0 can be separated from those in R_2^*, the approach also holds promise to reduce physiological fluctuations from the cardiac and respiratory cycle and might therefore be valuable in the analysis of resting state data (e.g. 4, 5).

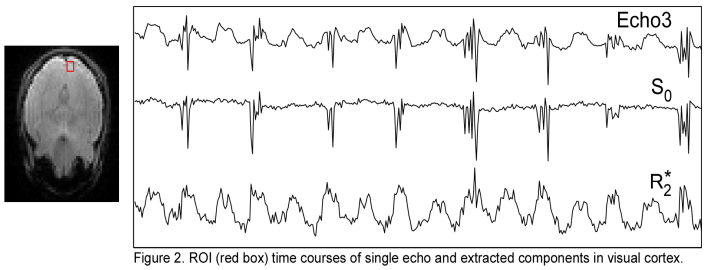

Figure 2. ROI (red box) time courses of single echo and extracted components in visual cortex.

Figure 3. ROI time courses of single echo and extracted components in non-activated region.

References: (1) Poser, BA, 2006, Magn Reson Med., 55, 1227-35. (2) Grootoonk, S, 2000, NeuroImage, 11, 49-57.
(3) Wu, DH, 1997, J Magn Reson Imag, 7, 365-70. (4) Birn, RM, 2006, NeuroImage, 31, 1536-48. (5) Shmueli, K, 2007, NeuroImage, 38, 306-20