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A dual echo approach to motion correction for functional connectivity studies

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ABSTRACT

The effect of subject head movement on functional connectivity as measured by BOLD (blood oxygen level dependent) fMRI was investigated; movement mainly introduced increases in connectivity into the dataset. The effect of movement on connectivity is an important consideration when comparing patients suffering from neurological conditions to healthy controls, since it is well known that patients affected by such conditions are prone to move more in the scanner than healthy subjects. A method of motion correction utilising a dual echo EPI sequence is described. The first echo is acquired soon after the slice excitation ($TE_1 = 10$ ms) when BOLD contrast is low and the MR signal is mainly sensitive to movement related effects, while the second echo is acquired at an echo time ($TE_2 = 30$ ms) at which the MR signal is sensitive to both BOLD and movement related effects. To correct for additional signal variance introduced by subject movement, the second echo image is divided by the first echo image at each time point across the length of the scan. This procedure is easy to implement and requires no extra scan time. This method proved superior to the standard means of correction whereby realignment parameters and their first order derivatives are used as covariates of no interest in a linear regression model.

Introduction

Over the past few years, BOLD (blood oxygen level dependent) functional connectivity MRI (fcMRI) has become an important tool in studying the brain. fcMRI involves measuring the temporal correlation of BOLD signal fluctuations between different regions of the brain (Biswal et al., 1995; Li et al., 2009; Rogers et al., 2007; Zhang and Raichle, 2010).

One of the most commonly used methods of functional connectivity imaging is seed-based correlation mapping (Zhang and Raichle, 2010). This method involves selecting a region of interest in the cortex and extracting its timecourse (in this case the variation in BOLD signal intensity across time) and calculating the Pearson correlation coefficient of this timecourse with every other grey matter voxel timecourse. Functional connectivity studies have the advantage over traditional task-based fMRI studies that they can be carried out at rest, when the subject is not engaged in an experimentally prescribed task. A consistent resting state network was first identified in an fcMRI study by Greicius et al. (2003). The network was termed the default mode network (DMN). This network shows a high degree of functional connectivity when the brain is at rest but is attenuated when it is involved in a specific activity. A considerable amount of research has gone into determining the effect neurological conditions may have on this network (Broyd et al., 2009). Changes in functional connectivity in the DMN have been observed in many neurological disorders, including Alzheimer's disease (Greicius et al., 2004; He et al., 2007), depression (Greicius et al., 2007; Sheline et al., 2010) and schizophrenia (Liang et al., 2006; Pomarol-Clotet et al., 2008).

Neuronal activity in the brain causes BOLD signal changes of just a few percent. The low percentage change in signal that the technique depends upon makes it susceptible to a wide range of effects which may compromise data quality. Subject movement is one of the most common causes of unwanted MR signal fluctuations. The relative change in signal intensity due to head movement can range from 3 to 7% depending on the extent of the gaps between slice profiles (Muresan et al., 2005).

Minimising effects introduced by head movement in the scanner is especially important when comparing patients suffering from neurological conditions to healthy controls, since it is well known that patients suffering from such diseases are prone to move more in the scanner than healthy subjects. For example, in one fMRI study, a group of stroke patients exhibited twice as much movement as their age matched controls (Seto et al., 2001). In functional connectivity studies, the effect of head motion in the scanner is to increase temporal variance of the MR signal which obscures the detection of functional connectivity.

Methods exist to minimise the negative impact of head movement on fMRI data quality. Realignment is a standard pre-processing step which is widely used in fMRI studies. There are a number of ways in which it can be implemented in practice, but the essential idea is the same: all brain volumes are aligned to a single scan volume (often the first in the time series). This process produces a set of affine transformation parameters that record how volumes have been realigned across the length of the

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scan. They therefore act as an estimate of subject head movement. A standard method of motion correction is to use these realignment parameters as nuisance regressors to account for the effect of movement on the MR signal from each voxel timecourse. The main focus of this correction method is to remove motion related signal variance. This method is somewhat limited however in that it will not reduce spin history related movement effects.

Following RF excitation, the longitudinal magnetisation of a spin system in an external magnetic field will return to its magnetisation at thermal equilibrium (M_0). The magnetisation will not necessarily have fully recovered to this equilibrium value by the time of the next slice excitation. Nevertheless, after a number of excitations, the longitudinal tissue magnetisation will reach a steady state. This equilibrium is dependent on the flip angle of the excitation pulse used, its repetition time (TR) and the tissue's longitudinal relaxation time (T_1). Movement of an object in the scanner will change the steady state magnetisation by changing the time between slice excitations in the tissue comprising the object. This will cause movement related changes in tissue magnetisation which are often referred to as spin history effects. Spin history effects can be partially removed by using the first order time derivatives of the realignment parameters as covariates of no interest in the design matrix. However, these effects cannot be corrected for completely as realignment parameters are a set of (six) global parameters whereas spin-history effects occur on a voxel-wise level. Spin history effects can also persist through several volumes; these delayed effects are not accounted for at all by this correction method.

The aim of this investigation is twofold: to determine the extent to which movement affects functional connectivity in the brain and to evaluate the efficacy of correction methods based on a dual-echo EPI sequence (Buur et al., 2009; Talagala et al., 1999) to reduce movement related effects in fcMRI.

Material and methods

Participants

Eight healthy volunteers (four male; mean age and SD = 24 ± 4 years) with no history of trauma or neurological disease were scanned. Written informed consent was obtained from all subjects. The study was approved by the local ethics committee (College Ethics Review Board, University of Aberdeen).

Magnetic resonance imaging

Measurements were carried out on a Philips 3T Achieva scanner (Philips Medical Systems, Best, The Netherlands) using a 32 channel receive-only phased-array head coil. A dual echo EPI sequence was used for fcMRI. Following a slice-selective excitation pulse, gradient echo images were acquired at two different echo times, $TE_1 = 10$ ms and $TE_2 = 30$ ms. Imaging parameters were TR = 2 s; flip angle = 78°; matrix size = 96 × 96; field of view = 240 × 240 mm^2; number of slices = 25; slice thickness = 4 mm parallel imaging method = SENSE; acceleration factor = 3; number of dynamic scans = 300; 4 dummy scans; slice orientation = axial oblique. In addition, a high resolution T_1 weighted structural scan was obtained. Scan parameters were: TR = 8.2 s; TE = 3.8 ms, flip angle = 8°, matrix size = 240 × 240 × 125, field of view = 240 × 240 × 160 mm^3, voxel size = 1.0 × 1.0 × 1.0 mm^3, total acquisition time = 5 min 35 s.

Experimental paradigm

Two fcMRI scans were acquired for each participant. In one of the scans, the subject was asked to lie still and in the other, to carry out a set of head movements. The order of these scans was randomised across subjects in order to prevent any effects introduced by habituation to the scan environment. During the movement scan, the subject was first instructed to lie completely still, 'think of nothing in particular' and to fixate on a cross for 26 s. This period was followed by 24 s during which an arrow was presented to the subject in alternating up and down directions, changing every 4 s. The subject was instructed to move his/her head in the direction indicated by the arrow. Movement in the up-down direction is expected to have the strongest effect on the MR signal as slices were acquired perpendicular to this direction. This paradigm was repeated across a ten minute scan. Instructions as to the degree of movement required were explained to the subject prior to the beginning of the experiment. The subject was asked to carry out head movements of a few centimetres and was told to practice these movements before going into the scanner. The participant was also given two trigger buttons (one in each hand) and instructed to press the buttons alternately as the arrows were displayed on the screen. This condition acted as a control task for the still scan, ensuring the subject was fully awake and that the same degree of attention was focused on an external task. Data from subjects whose correct button press responses fell below 95% would not be included in the study. During the still scan, the same experimental paradigm was used as during the movement scan, with the exception that the participant was asked to use only the buttons when the arrows appeared on the screen rather than moving his/her head.

Quantifying the degree of head movement

The degree of head movement in each scan was quantified using the metric below (Buur et al., 2009), which can be calculated from the realignment parameters:

$$\sum_{n=2}^{N}\sqrt{\left(T_{z,n}-T_{z,n-1}\right)^2+\left(\frac{r_y}{4}\left(R_{x,n}-R_{x,n-1}\right)\right)^2+\left(\frac{r_x}{4}\left(R_{y,n}-R_{y,n-1}\right)\right)^2} \quad (1)$$

N is the number of elements, T_z is the translation in the z direction in mm, R_x is rotation in the x direction in rads and R_y is rotation in the y direction, r_y and r_x are the diameters of the head in the y and x directions, set to 18 cm and 16 cm respectively.

Data pre-processing

Standard fMRI pre-processing was carried out using the Statistical Parametric Mapping software package SPM8 (http://www.fil.ion.ucl.ac.uk/spm). All pre-processing steps were applied to both the still and motion datasets. Pre-processing steps included realignment, slice-time correction, spatial normalisation and smoothing using a 6 mm FWHM Gaussian kernel. A study specific, binary grey matter mask was created and applied to the functional images in the following manner: Segmented grey matter images from subject T_1 scans were normalised and smoothed. These images were averaged across subjects and thresholded at a probability value of 0.1. Any functional data not included in the bounds of the mask was excluded from any further analysis.

Voxel timecourses were low-pass filtered (cut-off frequency = 0.1 Hz) and baseline corrected using a second order cosine basis set to remove low-frequency signal drifts. A study specific binary whole brain mask was created from the average grey and white matter of all subjects using the same method as for the grey matter mask. The global signal across each scan was calculated by averaging across all voxels within the whole brain mask. This global signal was then removed by linear regression using the approach described by Fox et al. (2005) . It is important that the global signal is regressed out during pre-processing for any meaningful comparison to be made between the correction methods described below. This is because global signal effects will be present in the first echo (TE_1) timecourse and will therefore be removed by correction methods involving the use of this timecourse.