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An improved model of motion-related signal changes in fMRI

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ABSTRACT

Head motion is a significant source of noise in the estimation of functional connectivity from resting-state functional MRI (rs-fMRI). Current strategies to reduce this noise include image realignment, censoring time points corrupted by motion, and including motion realignment parameters and their derivatives as additional nuisance regressors in the general linear model. However, this nuisance regression approach assumes that the motion-induced signal changes are linearly related to the estimated realignment parameters, which is not always the case. In this study we develop an improved model of motion-related signal changes, where nuisance regressors are formed by first rotating and translating a single brain volume according to the estimated motion, re-registering the data, and then performing a principal components analysis (PCA) on the resultant time series of both moved and re-registered data. We show that these "Motion Simulated (MotSim)" regressors account for significantly greater fraction of variance, result in higher temporal signal-to-noise, and lead to functional connectivity estimates that are less affected by motion compared to the most common current approach of using the realignment parameters and their derivatives as nuisance regressors. This improvement should lead to more accurate estimates of functional connectivity, particularly in populations where motion is prevalent, such as patients and young children.

Introduction

In-scanner head motion has been shown to be one of the largest sources of noise in resting-state functional magnetic resonance imaging (rs-fMRI). This challenge has recently been a topic of tremendous interest, in large part because even small amounts of movement can cause significant distortions to estimates of functional connectivity, and because uncorrected motion-related signals can bias group results if there are differences in head motion; see Maclaren et al. (2013) and Power et al. (2015) for review. Small, but significant, motion-related signal changes can remain even after realigning the images using rigid-body or affine transforms.

The most common current approach to deal with the residual motion-related signal changes is to regress out the 6 rigid body realignment parameters (3 translations and 3 rotations), as well as their temporal derivatives. Other variants of this approach additionally include time-shifted and/or squared versions of these motion parameters (Friston, 1996). However, these approaches assume that the motion-related signal changes are linearly related to the realignment parameters. This is not always the case. For example, at a curved edge of image contrast where motion in one direction causes a signal increase, the same motion in the opposite direction may not produce the same decrease, or even a decrease at all. Similarly, in a region with a nonlinear gradient in image intensity, a displacement in one direction would not produce the same magnitude signal change as a displacement in the opposite direction. Motion can result in sampling different proportions of tissue classes at any given location. Depending on the proportions sampled, resulting signal changes might be positive, negative or neither.

In this study, we develop an improved model of motion-related signal changes. First, in an approach similar to Wilke et al., we derive a voxel-wise estimate of the signal changes induced by the head motion during the scan by taking one of the acquired echo-planar imaging volumes and rotating and translating it according to the negative of the estimated motion parameters (Wilke, 2012). We will call this the "motion simulated" (MotSim) dataset. This MotSim dataset models the motion-related signal changes in the original data that are entirely due to motion. The MotSim dataset is then motion corrected with rigid body volume registration (MotSimReg). This MotSimReg dataset, which has been rotated and translated according to the estimated subject motion, and

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then re-registered, reflects imperfections introduced by interpolation and errors in estimating the motion (Grootoonk et al., 2000).

Three new models of motion-related signal changes will be evaluated and compared against the current common approach of including the 6 realignment parameters and their derivatives. Specifically, we derive nuisance regressors from 1) a temporal principal components analysis (PCA) of all brain voxels in the MotSim dataset (the “forward” model), 2) a PCA of the volume registered MotSim dataset (the “backward” model), and 3) a PCA of both the “forward” and “backward” models spatially concatenated (the “both” model). The use of temporal PCA to reduce a large array of potential noise regressors has been used previously for noise reduction in fMRI (e.g. to derive nuisance regressors from CSF and white matter in the CompCor technique, (Behzadi, 2007)); the beauty with the proposed MotSim PCA approach is that the noise time series are purely derived from the estimated subject motion and thus are unlikely to contain signals of interest (unless of course the neural signals of interest are correlated with the motion).

Materials and methods

Participants

Written informed consent was obtained from subjects prior to each scanning session in accordance with a University of Wisconsin Madison IRB approved protocol. Fifty-five healthy adults (27 females; 40.9 ± 17.5 years of age on average, range: 20–77 years) with no history of neurological or psychological disorders were scanned.

Data acquisition

Each subject was instructed to lie still in the scanner while keeping her or his eyes fixated on a cross. This resting condition (eyes open and fixating) has been shown to yield slightly more reliable results compared to either eyes closed or eyes open without fixation (Patriat et al., 2013). Each subject was scanned twice within the same session. All the scans were acquired using a 3 T GE MRI scanner (MR750, General Electric Medical Systems, Waukesha, WI). Each functional scan was 10 min in length and acquired with the same echo planar imaging (EPI) sequence (TR = 2.6 s, TE = 25 ms, flip angle = 60°, FOV = 224 mm × 224 mm, matrix size = 64 × 64, slice thickness = 3.5 mm, number of slices = 40). T1-weighted structural images were acquired before the functional images using an MPRAGE sequence with the following parameters: TR = 8.13 ms, TE = 3.18 ms, TI = 450 ms, flip angle = 12°, FOV = 256 mm × 256 mm, matrix size = 256 × 256, slice thickness = 1 mm, and number of slices = 156.

Motion dataset (MotSim)

In this study, we introduce new motion correction methods by extracting regressors from a dataset containing signal fluctuations solely due to motion. This motion dataset, that we refer to as, MotSim, was previously suggested by Wilke (Wilke, 2012). This motion dataset is obtained by extracting one volume from the original data and creating a 4D dataset by moving this one volume according to the inverse of the estimated 6 parameters of motion (Fig. 1). For the purpose of our study, the 4th volume, which also served as base for the motion realignment procedure, was chosen after the first two steps of preprocessing (removing the first three time points and performing slice-timing correction). We used linear interpolation for the resampling, the default in AFNI's 3dWarp. In a follow-up analysis, we repeated this using 5th order interpolation, and the main results were unchanged.

Motion regressors

In this study, four motion correction models were compared, all with the same number of regressors used the current standard (see model i). The models studied here are:

i. *12mot*: 6 parameters of motion derived from the re-alignment procedure + the derivative of each of these parameters.
ii. *12Forw*: First 12 principal components over the whole brain of the *MotSim* dataset (“forward model”).
iii. *12Back*: First 12 principal components over the whole brain after realigning the *MotSim* dataset, resulting in *MotSimReg* (“backward model”). Note that the realignment is estimated from the MotSim dataset, rather than applying the inverse of the transform that created the MotSim dataset.
iv. *12Both*: First 12 principal components over the whole brain after spatial concatenation of the motion dataset and the realigned *MotSim* dataset time series (“combined forward and backward model”).

12Forw and *12Back* differ from each other in that *12Forw* represents the *MotSim* dataset in its entirety whereas *12Back* only represents residual motion, such as interpolation errors and errors in the estimation of the amount of motion. Finally, *12Both* contains the regressors explaining the most variance across *12Forw* and *12Back*.

A temporal principal component analysis (PCA) generates a set of linear, uncorrelated components that reflect the main features of signal variations of the motion dataset. PCA has the benefit to minimize mutual information between the different principal components (PCs). The PCs are generated in order of decreasing variance explained (e.g. PC1 > PC2 > PC3…). Such a PCA decomposition approach has previously been used to derive nuisance regressors from CSF and other high variance voxels, primarily to model physiological noise (Behzadi, 2007). Here we use this idea to specifically derive noise regressors that will best model the signal changes induced by subject motion, and we evaluate the effectiveness of this approach at reducing the influences of subject motion. The principal components in the MotSim models were determined from a temporal PCA of all brain voxels, including edge voxels dilated 2 voxels out from the brain. We chose the first 12 principal components of each of the MotSim models in order to keep the number of nuisance regressors the same as the commonly used *12mot* model (6 realignment parameters and their derivatives). An additional model that has been suggested is the use of the 6 realignment parameters, the realignment parameters at the previous time point, and the square of each of these regressors (Friston, 1996), which we will call *24mot*. We will additionally evaluate this model, as well as using the first 24 principal components of the ‘Both’ model (*24Both*) in order to match the number of nuisance regressors.

Data preprocessing

Preprocessing of the rs-fMRI data was implemented using the software AFNI (Cox, 1996) (Fig. 2). The preprocessing steps included: removal of the first 3 volumes of data to remove the initial transient in the MR signal; slice-timing correction to correct timing difference due to an interleaved acquisition of slices within a volume; within-run volume registration to reduce the influence of subject motion within the scanner; motion regression; T1-to-EPI alignment; normalization of T1 data to a common MNI template space, and corresponding normalization of EPI data; spatial blurring (6 mm fwhm); and nuisance regression (with censoring,