

On the Optimal Strategy for Tackling Head Motion in fMRI Data

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1 INTRODUCTION

The blood oxygen-level-dependent (BOLD) signal measured with functional magnetic resonance imaging (fMRI) in the brain is a mixture of fluctuations from both neuronal and non-neuronal origins, the latter being responsible for inducing BOLD signal changes that account for a substantial amount of its variance (Caballero-Gaudes and Reynolds 2017).

One of the most problematic sources of noise is head motion. Because fMRI volumes are acquired over multiple slices, the movement of the head causes excitation of different slices at subsequent time points relative to previous ones. These so-called ‘spin history’ effects lead to motion-related changes in BOLD signal intensity that obfuscate the measurement of localized haemodynamic responses (Parkes et al. 2018). This will cause distortions and signal dropouts in brain regions prone to these effects.

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In general, the effect of head motion is predominantly seen in voxels at the edges of the brain and in voxels lying close to tissue boundaries due to the differences in proton density and relaxation parameters across brain tissues (Liu 2016). Nonetheless, any brain region might suffer from detrimental effects of head motion.

There are two main types of head motion: gradual head shifts and sudden movements of the head known as motion outliers (Liu 2016). To compensate for head shifts, it is common practice to realign the data (as part of typical fMRI preprocessing) by estimating the position of the head in space at each volume relatively to a reference volume using rigid body transformations. In a rigid body transformation, head position is described at each timepoint by six motion parameters (MPs): translational displacements along X, Y, and Z axes; and rotational displacements of pitch, yaw, and roll. In order to exclude the variance of the BOLD signal associated with head shifts, these 6 MPs are commonly included as nuisance regressors in a General Linear Model (GLM) analysis of the fMRI data. Because residual BOLD variance associated with head shifts can still be present, additional MP-derived regressors have been suggested, namely the temporal derivatives of the MPs (Power et al. 2013). Motion outliers induce the most critical BOLD signal changes. These can be identified as spikes in the data and cause large variations in image intensity. Such spikes are not accurately estimated using rigid body transformations, and thus the motion correction step or the regression of the MPs fail to account for them. As a solution, several metrics have been proposed for the detection of motion outliers, the most common being the Framewise Displacement (FD) and the Derivative or root mean square VARIance over voxels (DVARS) (Power et al. 2013). Then, motion outliers can be corrected through motion censoring (or scrubbing), whereby additional scan nulling regressors (with 1s at the volumes where motion spikes are detected and thus to be censored, and 0s elsewhere) are regressed out from the fMRI data (Siegel et al. 2014). Alternatively, volumes associated with motion outliers can be interpolated based on non-corrupted volumes (Rudas et al. 2020; Mckechanie et al. 2019; Mazaika et al. 2009; Caballero-Gaudes and Reynolds 2017).

Both task-related activation maps and measures of functional connectivity depending on both short- and long-range connections might be affected by both types of head motion (Power et al. 2014; Seto et al. 2001). Resting-state fMRI studies have demonstrated that head motion can introduce systematic bias to

connectivity estimates by creating spurious but spatially structured patterns in functional connectivity (Maknojia et al. 2019; Parkes et al. 2018; Power et al. 2014). In task-based fMRI studies, head motion is particularly problematic when it correlates with the experimental tasks leading to false brain activations. If not properly accounted for, head motion will bias the statistical results, reducing the sensitivity and specificity for detecting task-specific BOLD responses (Caballero-Gaudes and Reynolds 2017; Power et al. 2014; Seto et al. 2001).

Despite all the known effects of head motion on the quality of fMRI data, and several correction options, there is still no consensus regarding the optimal number of MP-related regressors to consider for tackling head shifts, nor the most appropriate approach to mitigate motion outliers.

Also, there is a lack of studies in determining the extent at which the effects of head motion differ between groups in clinical studies. This is particularly relevant in task-related functional connectivity fMRI studies, which are rapidly increasing in clinical research.

In this study, we started by testing the number of MPs (between 6 and 24) that would improve the ability to accurately detect task-specific BOLD responses on fMRI data collected from 8 participants performing a perceptual decision-making task. Then, we tested motion censoring and volume interpolation approaches for tackling motion outliers, with the volumes to be censored detected with the FD and DVARS metrics, whereas volumes to be interpolated were identified with FD. The best approach (and metric) was also determined based on the quality of the data analyses. The effect of different approaches for correction of head motion on task-related activation maps was also compared between a control group of healthy participants and a clinical group of patients with Multiple Sclerosis.

2 METHODS

2.1 Participants

This study includes 4 patients with Multiple Sclerosis (MS) and 4 healthy controls. Patients were recruited at the Coimbra Hospital and University Centre (CHUC) and met the criteria for MS diagnosis according to McDonald Criteria (Thompson et al. 2018). All participants gave written informed consent. Local ethics committee approved the study.

2.2 Data Acquisition

Imaging was performed on a 3T Siemens MAGNETOM Prisma Fit MRI scanner (Siemens, Erlangen) using a 64-channel RF receive coil, at the Portuguese Brain Imaging Network (Coimbra, Portugal). fMRI data was acquired using a 2D simultaneous multi-slice (SMS) gradient-echo echo-planar imaging (GE-EPI) sequence (6× SMS and 2× in-plane GRAPPA accelerations), with the following parameters: TR/TE = 1000/37 ms, voxel size = 2.0×2.0×2.0 mm³, 72 axial slices (whole-brain coverage), FOV = 200×200 mm², FA = 68°, and phase encoding in the anterior-posterior direction. A short EPI acquisition (10 volumes) with reversed phase encoding direction (posterior-anterior) was also performed prior to each fMRI run, for image distortion correction. A 3D anatomical T1-weighted MP2RAGE (TR = 5000 ms, TE = 3.11 ms; 192 interleaved slices with isotropic voxel size of 1 mm) was also collected for subsequent image registration.

2.3 Behavioral Task

The imaging session contained two functional runs for collection of BOLD signals during the performance of a perceptual decision-making task on biological motion (BM), each consisting of 507 volumes (approximately 8.37 minutes). This task comprised three categories of visual motion stimuli: global biological motion; local biological motion; and scrambled motion. Biological motion stimuli were built based on human motion capture data collected at 60 Hz, comprising 12 point-lights placed at the main joints of a male walker. Each BM perception run consisted of 12 blocks of 40 seconds: 4 or 5 blocks (depending on the starting block) of the point-light walker facing rightwards or leftwards (global biological motion), 4 or 5 blocks showing only the point-light located at the right ankle and moving rightwards or leftwards (local biological motion), and 3 blocks of point lights randomly positioned across the y axis, while maintaining their true trajectory across the x axis (scrambled motion). After each stimulus presentation, the participants reported the direction of motion of the dots (left or right) by pressing one of two buttons. Figure 1 is a schematic representation of the visual stimuli.

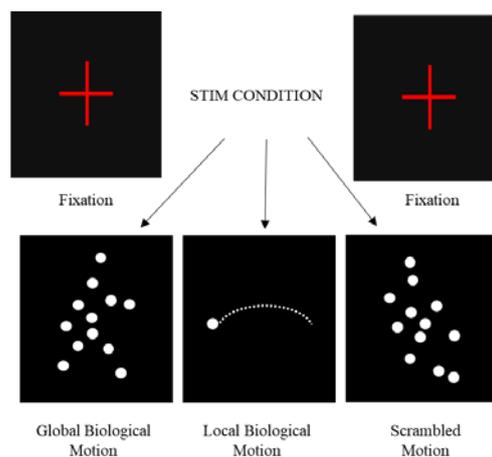


Figure 1: Schematic representation of the visual stimuli.

2.4 Data Processing

2.4.1 Pre-processing Steps

fMRI data were preprocessed using the MATLAB® software, with SPM12 and the PhysIO toolbox (Kasper et al. 2017), except for image distortion correction which was performed using FMRIB Software Library (FSL). The first part of the pre-processing pipeline included: 1) slice timing correction; 2) realignment of all fMRI volumes relative to the first volume; 3) correction of geometric distortions caused by magnetic field inhomogeneity; 4) bias field correction. The second part of the preprocessing was related to regression of non-neuronal fluctuations such as cardiac and respiratory signals, WM and ventricular CSF average BOLD fluctuations and head motion spikes. First, image coregistration (anatomical to functional) and segmentation of the structural image were done to extract WM and ventricular CSF masks. Noise fluctuations (cardiac and respiratory signals, WM and CSF average BOLD fluctuations) including 6 and 24 MPs were computed with PhysIO toolbox and then regressed out of the BOLD signal. After determining the optimal set of MPs, motion outliers were either regressed out of the BOLD signal (by adding scan nulling regressors consisting of 1 at the volume to be censored and 0s elsewhere) or interpolated. These were identified with the FD or DVARS metrics. The pre-processing was completed with spatial smoothing with a 3 mm full-width-at-half-maximum (FWHM) isotropic Gaussian kernel and high-pass temporal filtering with a cut-off period of 108 s.

2.4.2 Motion Processing

The first step is to study the number of MPs (between 6 and 24) needed to correct the effects caused by head shifts and consequently which one would improve the ability of our models to accurately detect task-specific BOLD. Here, we tested 6 and 24 MPs because they represent the two extreme cases complexity-wise (Maknojia et al. 2019). The 6 MPs were computed as part of the volume realignment step and the 24 MPs which correspond to squares of the 6 MPs and temporal derivatives were computed with PhysIO toolbox. Then we regressed out these MPs from the BOLD signal.

To test which strategy is best to correct the motion outliers' effects (modelling or interpolation), we start by detecting the outlier's volumes with the two most used metrics: FD and DVARS.

FD is a scalar quantity to express instantaneous head motion and it is computed through the time series of the six MPs obtained during the motion correction step (Power et al. 2013).

DVARS is a measure computed from the data itself and does not depend on the MPs. It represents how much the intensity of a volume changes in comparison to the previous one (Power et al. 2013).

After identification of motion outliers, we tested modelling strategies through motion censoring (with 1s at the volumes where motion spikes are detected and thus to be censored, and 0s elsewhere) and regression and volume interpolation to correct motion outliers' effects in data.

Modelling strategies were firstly implemented with motion outliers being identified with FD and secondly with motion outliers being detected by DVARS. We used PhysIO toolbox to apply FD metric with a threshold of 0.5mm and FSL utility *fsl_motion_outliers* to compute the DVARS for all volumes; motion outliers were identified by thresholding the DVARS at the 75th percentile plus 1.5 times the inter-quartile range.

The last method we used to repair the volumes most affected by movement was a linear interpolation (INTERP) with the ArtRepair software (Mazaika et al. 2009). Motion outliers were identified with FD metric with a threshold of 0.5mm.

2.5 Statistical Analysis

For the purpose of mapping the regions involved in our perceptual task, the GLM framework was used. GLM is a common way to analyse fMRI and it is basically a linear regression represented by:

$$y = X\beta + \varepsilon \quad (1)$$

with y the time series from one voxel, X the design matrix, β the model parameters, ε , the normally distributed error (or residuals) with zero mean (Pernet 2014). Onsets and durations of each experimental condition were included in the model of the BOLD signal as regressors of interest representative of our task. We ended up with three regressors representing periods showing global biological motion, local biological motion, and scrambled motion. These regressors were built based on unit boxcar functions with ones during the respective periods, and zeros elsewhere and convolved with a canonical, double-gamma hemodynamic response function (HRF). The HRF-convolved regressors were then included in a GLM (X , the design matrix) that was subsequently fitted to the fMRI data. After the fitting, the β 's are estimated, weighting the relevance of each regressor in explaining the variance of the data. Here, we set to study brain regions that are activated when global biological motion stimuli are present more than when scrambled motion versions appears. Thus, the areas associated with this condition were localized according to the following contrast: [global biological motion – scrambled motion].

Because many voxels are tested simultaneously, the chance of observing false positives (i.e., the Family Wise Error (FWE) rate) is very high in the absence of any correction. To address this issue, we used a FWE correction method based on Random Field Theory (RFT), and we only considered activations as significant those with a threshold of $p < 0.05$ (the probability that we will observe a false positive is only 5%).

GLMs were estimated for each participant containing the two runs of the behavioral task and statistical maps with voxels exhibiting significant changes specified by the contrast [global biological motion – scrambled motion] were identified with a cluster threshold of $p < 0.05$ (FWE corrected).

After determining the optimal set of MPs (6, see Results below), the subsequent analyses regarding motion outliers were performed only considering 6 MPs. In this way, each participant ended up with 5 GLMs consisting of: 1) only 6 MPs, 2) only 24 MPs, 3) 6 MPs and motion outliers regressors detected with FD, 4) 6 MPs and motion outliers regressors detected with DVARS, 5) interpolated volumes.

From the resulting activation maps, the maximum (Z -max) and mean (Z -mean) Z -score values were extracted. Also, we quantified the amount of variance of the average BOLD signal

across each activation map that was explained by the MPs R^2 (BOLD/Motion). Despite the MPs are regressed out from the data and motion outliers corrected, head motion may not be fully corrected, thus leaving residual contributions in the BOLD signal (Abreu 2017). The R^2 (BOLD/Motion) measure was estimated by the coefficient of determination adjusted for the degrees of freedom, R_{adj}^2 which is defined according to (Montgomery, Peck, and Vining 2012):

$$R_{adj}^2 = 1 - \frac{N - 1}{N - P - 1} \frac{\sum_{i=1}^N \varepsilon_i^2}{\sum_{i=1}^N (y_i - \bar{y})^2} \quad (2)$$

where \bar{y} is the average BOLD signal, N is the number of volumes and P the number of motion regressors; ε denotes the residual of the model under analysis, which is described by $\varepsilon = y - \beta X$, where X is the matrix containing the MPs, and β the associated weights estimated using a GLM framework.

These were the metrics we compared to assess the quality of each method. The Z values indicate the sensitivity of the model in detecting brain regions that are associated with our behavioral task. The higher the values of Z the higher is the quality of the method. The lower the values of R^2 (BOLD/Motion) the less variance of the BOLD signal is explained by motion so the better is the method.

In order to statistically compare the performance of the methods tested here, a two-way mixed ANOVA (one between-subjects and one within-subjects factors) was performed. Prior to these analyses, the requirements of the statistical tests described next were verified. For the two comparisons the between-subjects factor is “Group”, which has two nominal unrelated or independent categories: Multiple Sclerosis (MSC) and control (CNT) participants. The within-subjects factors are the “MPs” (number of motion parameters) and “Correction Method” for the first and second comparison respectively.

3 RESULTS

3.1 6 MPs vs 24 MPs

Group mean Z-max, Z-mean and R^2 (BOLD/Motion) values of the models with 6 MPs and 24 MPs are represented in Table 1. As evidenced, the Z-max and Z-mean values are systematically higher when using 6 MPs. No differences were found in the

R^2 (BOLD/Motion) values. The two-way mixed ANOVA showed that the comparison between these values concerning the main effect “MPs” was statistically significant ($p < 0.05$). The “Group” main effect proved to be non-significant ($p > 0.05$) for this R^2 (BOLD/Motion) values. The two-way mixed ANOVA showed that the comparison between these values concerning the main effect “MPs” was statistically significant ($p < 0.05$). The “Group” main effect proved to be non-significant ($p > 0.05$) for this comparison. There was also no statistically significant interaction between “Group” and “MPs” ($p > 0.05$). Figure 2 shows the activation maps of one participant when using 6 vs 24 MPs.

Table 1: Metrics to assess the quality of the models using 6 MPs and 24 MPs. Values are presented as mean \pm standard deviation in each group of participants.

		Metrics		
MPs	Group	Z-max	Z-mean	R^2 (BOLD/Motion)
6	MSC	8.015	5.974	-0.012
		\pm 0.500	\pm 0.317	\pm 0.000
	CNT	7.094	5.631	-0.011
		\pm 1.050	\pm 0.300	\pm 0.001
24	MSC	7.648	5.814	-0.012
		\pm 0.766	\pm 0.283	\pm 0.000
	CNT	6.875	5.536	-0.011
		\pm 1.264	\pm 0.365	\pm 0.001

3.2 FD vs DVARS vs INTERP

Table 2 depicts group mean Z-max, Z-mean and R^2 (BOLD/Motion) values of the models used to test the different methods for correction of motion outliers. Despite Z-max and Z-mean values are higher for the interpolation method, the two-way mixed ANOVA showed that the comparison between these values was not statistically significant ($p > 0.05$) considering both “Correction Method” and “Group” main effects. No statistically significant differences were found to the R^2 (BOLD/Motion) values. There was also no statistically significant interaction between “Group” and “Correction Method” ($p > 0.05$).

Table 2: Metrics to assess the quality of the models using FD, DVARS and INTERP methods to correct motion outliers' effects. Values are present Values are presented as mean \pm standard deviation in each group of participants.

Correction Method	Group	Metrics		
		Z-max	Z-mean	R^2 (BOLD/Motion)
FD	MSC	8.015 ± 0.496	5.971 ± 0.311	-0.012 ± 0.000
FD	CNT	7.070 ± 1.213	5.632 ± 0.310	-0.011 ± 0.001
DVARS	MSC	8.015 ± 0.500	5.974 ± 0.317	-0.012 ± 0.000
DVARS	CNT	6.983 ± 1.234	5.603 ± 0.336	-0.005 ± 0.017
INTERP	MSC	8.035 ± 0.505	6.022 ± 0.321	-0.012 ± 0.000
INTERP	CNT	7.105 ± 1.054	5.641 ± 0.288	-0.006 ± 0.011

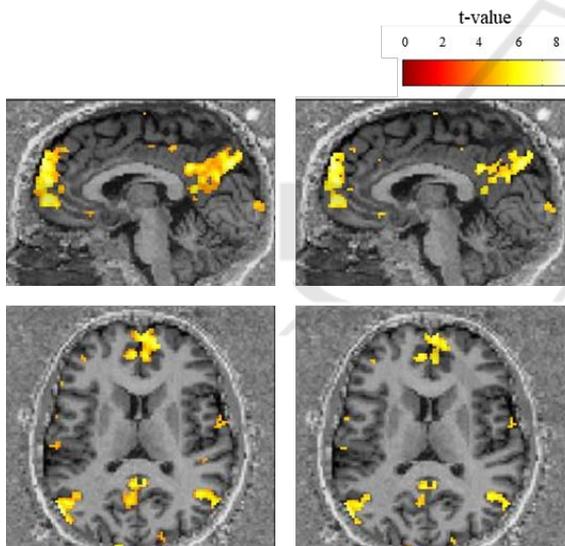


Figure 2: Activation maps of one participant, resulting from the contrast [global biological motion – scrambled motion]. On the left is represented an activation map resulting from a model with 6 MPs. On the right is represented an activation map resulting from a model with 24 MPs. The model with 6 MPs (left side) shows that task-specific brain regions are detected with higher sensitivity relatively to using 24 MPs (right side). Results are presented at a voxel p -value < 0.05 , FWE corrected for multiple comparisons. Color bar scale represents t-values. The t-value is the result of the statistical test (t-test) in each voxel and measures the size of the difference calculated between the BOLD signal in the presence of biological motion stimulus and the BOLD signal during the presence of scrambled motion stimulus. The higher the t-value the most correlated is the BOLD signal with the task condition or the specified contrast in a given brain region, thus more sensitive is that (group of) voxel(s).

4 DISCUSSION

Due to the lack of consensus on how to deal with the head motion effects in fMRI data analysis, in this study we compared different strategies to compensate for head motion, in the context of a perceptual decision task performance between MS patients and controls. We started by testing if including temporal derivatives of MPs would improve the results of our analyses. Next, we compared three methods to correct the effects of motion outliers. Two of them were modelling approaches (censoring) based on two different motion outliers detection algorithms: FD and DVARS. The third strategy used was interpolation of volumes affected by motion, INTERP.

The first comparison, 6 vs 24 MPs, revealed that higher Z-score values are obtained when considering 6 MPs, suggesting that task-specific brain regions are detected with higher sensitivity relatively to using 24 MPs. This is further supported by the activation maps resultant from both models. Head shifts are usually corrected through regression of MPs, but there is still no consensus regarding the optimal number of MPs to include. Our results using just 6 MPs are consistent with literature reporting that adding temporal derivatives can result in loss of degrees of freedom and therefore loss of valuable information. (Yang et al. 2019).

Regarding the second comparison, the Z-max and Z-mean values are higher for the interpolation method. Although the two-way mixed ANOVA showed that the comparison between the values obtained with the different methods was not statistically significant ($p > 0.05$), we suggest the use of the interpolation method. However, further studies with more data are needed to reach a definite conclusion about which method is best to correct the effects of motion outliers. Furthermore, it is important to discuss the impact of modelling motion outliers and interpolation in the data.

Modelling motion outliers is a widely used technique to correct sudden movements of the head, however it creates temporal discontinuities. Interpolation overcomes this problem and avoids side effects in the high-pass filter (Michielsen et al. 2011). However, volume interpolation induces synthetic data, and the duration of the censored segment, as well as the type of interpolation (linear, Fourier, wavelets or splines), may produce different effects that depend on the choice of these parameters (Caballero-Gaudes and Reynolds 2017). To our

knowledge these effects and the negative impacts of using interpolation are still largely unknown. Although the two approaches are widely used, to our knowledge there are no studies that contemplate the question, with a direct comparison on the same data, about which strategy is best to correct motion outliers: modelling or interpolation. Because there are no negative effects reported when using interpolation and that it appears as an alternative to solve the data loss caused by censoring, we further suggest that this method may be the best one to adopt to mitigate the effects of motion outliers. Nevertheless, we believe further studies with a higher number of participants will allow to derive conclusive results and to a greater consensus on which strategy to use. Thus, our study paves the way towards finding an optimal motion correction strategy.

In both comparisons, the main effect of group and also the interaction of correction approach with group proved to be not significant, which means that there are no differences provoked by head motion correction effects between groups. So, the quality of head motion correction is mainly due to the method. This is an important issue to consider in fMRI studies in clinical context, as previous reports show group differences in head motion between control and patient groups (Seto et al. 2001). This is particularly relevant in task-related and resting-state (RS) functional connectivity fMRI studies, which are rapidly increasing in clinical research (Goto et al. 2016). Previous studies show that group differences in head motion between control and patient groups cause group differences in the resting-state network with RS-fMRI (Lee, Smyser, and Shimony 2014; Song et al. 2012; Maknojia et al. 2019). To our knowledge there is a lack of this kind of studies in the MS context. Furthermore, our study raises the importance of this processing step in functional connectivity studies, where one wants to study functionally connected networks throughout the brain that are correlated only due to the stimulation or cognitive processing, in task-based fMRI, or due their intrinsic functional organization, not because of head motion.

We decided to compare these approaches, however there are other techniques that can be implemented. External optical tracking systems that constantly measure the position of the head or the use of dedicated sequences with navigators echoes or active markers (Maknojia et al. 2019; Caballero-Gaudes and Reynolds 2017) are such examples. Data driven approaches can also be used, namely algorithms such as Principal Component Analysis

(PCA) or Independent Components Analysis (ICA), which first decompose the data into a set of components, then the corrected fMRI data is obtained by removing the contribution of motion-related components (Caballero-Gaudes and Reynolds 2017; Liu 2016). Yet, we focused on study the number of MPs that would better characterize the head shifts to be regressed out from fMRI data and on comparing modelling vs interpolation methods to tackle the motion outliers' effects since these are the most used in the literature, and as such, are of greater relevance.

5 CONCLUSIONS

In this paper, we aimed at applying different techniques to tackle head motion in fMRI data in order to reach a consensus on the best strategies to use. We compared common approaches to correct head motion effects such as motion regression, motion censoring and data interpolation. Our results pave the way towards finding an optimal motion correction strategy, which is required to improve the accuracy of fMRI analyses, crucially in clinical studies with patient populations, and are an encouragement to test comprehensively different approaches.

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