

Title: Reduction of motion artifacts in functional connectivity resulting from infrequent large motion

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Running Title: Reduction of motion artifacts due to infrequent large motion

Keywords: fMRI, connectivity, motion, infants

Abstract:

Introduction: Subject head motion is an ongoing challenge in functional MRI, particularly in the estimation of functional connectivity. Infants (1-month old) scanned during non-sedated sleep often have occasional but large movements of several millimeters separated by periods with relatively little movement. This results in residual signal changes even after image realignment, and can distort estimates of functional connectivity. A new motion correction technique, JumpCor, is introduced to reduce the effects of this motion and compared to other existing techniques. Methods: Different approaches for reducing residual motion artifacts after image realignment were compared both in actual and simulated data: JumpCor, regressing out the estimated subject motion, and regressing out the average white matter, CSF, and global signals and their temporal derivatives. Results: JumpCor significantly reduced residual motion-related signal changes resulting from infrequent large motion. Artifacts were also reduced by regressing out the estimated motion parameters. Discussion: Motion-related signal changes resulting from occasional large motion can be effectively corrected using JumpCor, and to a certain extent also by regressing out the estimated motion.

Impact Statement:

Functional MRI scans from 1-month old infants scanned during non-sedated sleep often show occasional but large head motion. Data from subjects that move this much are commonly discarded in functional connectivity studies. However, this study introduces a new motion correction technique, JumpCor, that can effectively reduce this type of motion artifact and compares this to other existing motion correction techniques. The ability to retain valuable subject data despite large motion will be highly important for the study of brain connectivity, particularly in neurodevelopmental studies where this type of motion is common.

1. Introduction:

Subject head motion is an ongoing challenge in functional MRI (fMRI), leading to an increased number of both false positive and false negative activation as well as the loss of usable data (Friston et al., 1996, Power et al., 2012, Satterthwaite et al., 2012, Van Dijk et al., 2012). This is particularly true in developmental studies, where motion is more likely to occur (Satterthwaite et al., 2013, Vanderwal et al., 2020), and for the estimation of functional connectivity, which is highly sensitive to motion (Power et al., 2012, Van Dijk et al., 2012). Our research group recently completed acquisition of fMRI data from a large cohort of infants at 1 month of age, in which infants were scanned during non-sedated sleep (Dean et al., 2018, Dean et al., 2018). During the functional MRI scans, the infants were generally motionless. However, despite our best efforts to immobilize their head and body, many of the infants had occasional large head motions of several millimeters (1mm-24mm, median 3.0mm) during the acquisition, interspersed with relatively quiet periods of very little movement (<0.2 mm frame-to-frame displacement computed as the Euclidean norm of the temporal difference in the 6 realignment parameters; Figure 1). Significant signal changes sometimes remained even after realignment and after censoring time points occurring during the motion. Prior studies often exclude participants with large or “gross” motion, that is, if any frame-to-frame displacement exceeds a predefined threshold, such as 0.55mm (Satterthwaite et al., 2012, Satterthwaite et al., 2013) or 5mm (Parkes et al., 2018). However, such a criterion would eliminate a large proportion of participants in our infant study who, in general, exhibited only a few large movements in each imaging run. This motivated the search for alternative solutions. In this study, we propose and examine different strategies to reduce this motion artifact.

Residual head-motion related signal changes remaining after image realignment can occur due to at least five different mechanisms -- errors in estimating the motion; errors due to interpolation (Grootoink et al., 2000); spin-history effects (Friston et al., 1996); B0-field changes (Jezzard et al., 1999); or movement into different parts of a non-uniform RF coil sensitivity. Spatially non-uniform sensitivity profiles are particularly common in RF coils with higher number of channels, such as the 32-channel coil used in the current study. Visual inspection of our infant fMRI data after realignment indicated that the residual signal changes were likely due to the head moving into a different part of the (nonuniform) coil sensitivity. More specifically, the images before and after large jumps showed changes in signal intensity without any change in image shape (e.g. distortions in the phase encoding direction) which would be expected from

B0-field changes. Furthermore, these signal changes were generally prolonged unlike the more transient signal changes that would be associated with spin-history effects.

The problem encountered with this large occasional motion is similar to that faced when combining data from multiple imaging runs, where the participant may have moved in between runs. We therefore adopted a similar approach to reduce the influence of large head motion, or “jumps,” that occur during the imaging run, a technique we call “JumpCor.” To evaluate JumpCor, we compared it to other motion reduction approaches.

2. Methods:

2.1 JumpCor.

A common approach to account for between-run signal changes when combining data across runs is to model a separate baseline, and optionally linear drift and lower order polynomials, for each imaging run. The idea behind JumpCor is to extend this approach to deal with large motions that occur *during* an imaging run. First, large jumps, where the volume-to-volume displacement exceeds a user-defined threshold, were identified (Fig 2). This displacement was computed using the Euclidean norm (square-root of the sum of squares) of the temporal difference of the 6 realignment parameters (“Enorm”). For most analyses presented below, a 1mm threshold was used. We also investigated the impact of changing this threshold. Next, regressors were generated for every segment between the large jumps with a value of 1 during the segment and a value of 0 outside of the segment (Figure 2). These JumpCor regressors are then used as additional nuisance regressors in a general linear model, optionally together with any other nuisance regressors that are removed in the preprocessing of resting-state fMRI data (e.g. average white matter, CSF, and possibly global signal changes). Segments consisting of only 1 time point between large movement jumps were censored.

2.2 Participants:

All study procedures were in accordance with the Institutional Review Board (IRB) policies at the University of Wisconsin - Madison, and written informed consent was obtained from each participating family. 149 mother and infant dyads took part in a longitudinal study of the association between early-life experience and infant brain development. The infant sample consisted of 77 females and 72 males who were brought to the MRI facility for imaging at approximately 1-month of age (34.1 ± 7.7 days, corrected to a 40-week gestational period). Additional sample details can be found in (Dean et al., 2018).

2.3 Imaging Procedure:

Scanning occurred during natural, non-sedated sleep (Dean et al., 2014). As previously, A MedVac vacuum immobilization bag (CFI Medical Solutions) and foam cushions were used to limit intra-scan motion (Dean et al., 2017, Dean et al., 2018). Acoustic noise from the scanner was reduced by derating gradient amplitudes and slew rates and using a sound attenuating bore insert, malleable ear plugs, and neonatal ear covers (MiniMuff; Natus Medical Inc). Electrodynamic headphones (MR Confon) played white noise during image acquisition.

MRI data were acquired on a 3T General Electric MR750 MRI scanner (Waukesha, WI) using a 32-channel receive-only RF coil (Nova Medical, Wilmington, MA). A series of sagittal T2*-weighted functional MR images were acquired using an echo-planar imaging (EPI) pulse sequence. Functional MR imaging parameters included the following: repetition time (TR): 2000ms; echo time (TE): 25ms; flip angle: 60 degrees; 36 slices; slice thickness: 3.5mm; in-plane field of view (FOV): 22.4 x 22.4 cm²; matrix: 64x64; 240 volumes for a total acquisition time of 8 minutes. Structural T2-weighted images were obtained using GE's CUBE imaging pulse sequence (TR: 2500 ms; FOV: 25.6 cm x 25.6 cm x 16.0 cm; echo train length: 65; and an acquisition time of 5 minutes and 36 seconds). To reduce the acoustic noise produced during the scan, the gradient slew rates were reduced by approximately 67% of their nominal value.

Of the 149 infants, fMRI data were missing from 11 infants, who did not sleep through the entire fMRI scan. Data from 15 infants were excluded from further analysis because large head motion resulted in a large shift and aliasing of the image in the phase encoding direction, caused by a failure of the dynamic phase correction applied by the scanner during reconstruction. Data from an additional 20 infants were excluded because they had less than 5 minutes of data left after motion censoring ($E_{norm} > 0.2\text{mm}$, see Data Analysis section below). Data from 4 more infants were excluded because the T1- and T2-weighted structural scans were un-usable; and 1 infant's data were excluded because the motion was so large that the brain moved outside the field of view. This left a final sample of 98 infants, of which 72 (73%) exhibited occasional large head movements of several mm (1-24 mm, median 3.0 mm), separated by periods with relatively little motion (Fig. 1).

2.4 Data Analysis:

All data analysis was performed using the AFNI analysis package, unless otherwise specified (Cox, 1996). The first 3 time points of the fMRI time series were removed to allow the magnetization to reach steady state, and the data were corrected for slice timing differences (3dTshift). fMRI time series data were then corrected for motion using 6-parameter (rigid-body) re-alignment with a least-square difference of signal intensity cost function (3dvolreg). Regressors to model large jumps in motion (JumpCor) were computed from the volume-to-volume motion (Enorm), as described in section 2.1 above. Data where the Enorm exceeded 0.2mm were censored and excluded from further analyses. The fMRI time series were then aligned to the T2-weighted structural scan.

A population-specific template was constructed from the infant T2-weighted images using a multivariate image registration approach with the Advanced Normalization Tools (ANTs) software suite (Avants et al., 2011, Dean et al., 2018). The T2-weighted structural scan was subsequently aligned to the group template using nonlinear warping (AFNI's auto_warp.py). The fMRI-to-structural and structural-to-template transformations were concatenated and applied to the fMRI data, and the fMRI data were resampled to 2mm isotropic resolution.

The group average T2-weighted template was segmented into white-matter, gray-matter, and CSF using the FMRIB Software Library's (FSL's) program *fast*. The group template was used for segmentation because the gray/white matter contrast-to-noise ratio in each individual subject's T2 image was too low to perform accurate segmentation. A lateral ventricle mask was defined from the CSF mask using spatial clustering. Ventricular CSF and white-matter masks were then resampled to 2mm, and the white matter mask was eroded by 1 voxel.

2.5 Motion artifact reduction strategies & evaluation:

The strategy for reducing the effects of head motion was to regress out a set of “nuisance” regressors that likely represent motion and other non-neuronal signal variations (“noise”), using AFNI's *3dTproject*. Five different sets of nuisance regressors were compared in addition to a “no nuisance regression” control: 1) JumpCor regressors; 2) average eroded white matter, ventricular CSF, realignment parameters, and their derivatives; 3) same as #2 but including the JumpCor regressors; 4) same as #2 but including the global signal; 5) same as #2 but including both the global signal and JumpCor regressors. The mean signal intensity over time was also removed from each voxel's time series as part of this nuisance regression (equivalent to adding

a constant as an additional nuisance regressor). The same time point censoring and the same transformation matrices from original to template space were used for all of these strategies. To determine the impact of different choices for the threshold of what level of motion to consider a “jump,” 5 different thresholds were evaluated (1mm, 5mm, 10mm, 15mm, 20mm). Finally, to evaluate the potential influence of spin-history effects that could result in prolonged signal changes after a jump, the above analyses were repeated by excluding an additional 5 time points (10 seconds) of data following each jump. Data were then spatially smoothed using a Gaussian kernel with a full-width at half maximum of 4mm.

Functional connectivity maps were computed by averaging the preprocessed signal over a seed region of interest and then computing the correlation of this time course with all other voxel time series (*3dDeconvolve*). Several different seed regions were evaluated: 4mm spheres placed in motor cortex, auditory cortex, visual cortex, or the posterior cingulate. The coordinates of the center of these spheres relative to the UNC 1-year brain template (Shi et al., 2011) are provided in Table 1. A constant and linear signal drift over time were included as additional nuisance regressors in this connectivity calculation. Group estimates of functional connectivity were determined using a 1-sample t-test (*3dttest++*) of the Fisher Z-transformed correlation (connectivity) maps for each seed region. The rationale for examining seed-based functional connectivity maps was that the spatial patterns of the expected functional connectivity, particularly in motor, visual, auditory, and default mode networks, are well known, and the sources of potential artifacts can be more easily identified by their impact on the spatial pattern of estimated functional connectivity (e.g. patterns matching the slice acquisition, alternating positive and negative connectivity in neighboring voxels, strong correlations at edges, etc.).

To investigate the effectiveness of different processing strategies on connectivity throughout the brain, a connectivity matrix was created by first defining 230 regions-of-interest (ROI) based on a study by (Eggebrecht et al., 2017). We then averaged the preprocessed data over these ROIs and computed all possible pairwise Pearson correlations of the ROI time series. The degree that the data are corrupted by motion, and the effectiveness of different strategies at reducing this noise, was evaluated by computing the Spearman rank correlation between the mean Enorm and the absolute value of the Fisher Z-transformed functional connectivity, across subjects, for each connection in the connectivity matrix (Satterthwaite et al., 2013, Ciric et al., 2017, Ciric et al., 2018). Multiple prior studies have used the correlation of the mean FD and the functional connectivity as a measure of potential motion artifacts (referred to as the QC-FC metric in (Ciric

et al., 2017)). A null distribution of the correlation with Enorm was obtained by randomly reshuffling the mean Enorm across subjects and then recalculating the correlation (across subjects) of this reshuffled Enorm with each connection. This was repeated for 1000 random permutations. Finally, we also examined the correlation with other summary measures of motion -- the maximum and median jump amplitudes, and the number of jumps.

To further evaluate the impact of various motion correction approaches at the individual subject level, we computed the similarity between each subject's functional connectivity matrix to the group mean connectivity matrix, for each correction. The group mean connectivity matrix for each set of nuisance regressors was obtained by averaging the Fisher-Z transformed functional connectivity matrices across all subjects. The similarity was computed as the Pearson's correlation between each subject's Fisher-Z transformed functional connectivity matrix and the group mean connectivity matrix (using AFNI's *3dcorr*).

2.6 Simulation:

To further understand the impact of different motion correction approaches on data acquired when the head moves into areas with different RF coil sensitivity, we performed a set of simulations. A brain containing functional connectivity was simulated by taking a single EPI brain volume from one of the infant's acquired data, copying it 250 times to create a 250s time series, and then superimposing a sinusoidal fluctuation (0.05 Hz, magnitude 2% of the baseline signal) that was identical in 2 different regions of interest (Fig. 6a,b). This brain volume was then translated in the anterior-posterior direction by several millimeters, for a block of time, first in one direction, then back, and then in the opposite direction, and back again (Fig. 6c). To avoid interpolation errors and focus primarily on signal changes resulting from movement into different parts of the RF coil sensitivity, the brain was translated by an integer number of voxels. Two different levels of movement were investigated: 1 voxel (3.5mm) and 3 voxels (10.5mm). For comparison, we investigated motion in both the R-L and A-P directions, as well as using estimated motion from one of the infant scans. The image volumes were then multiplied by one of 2 different coil sensitivity profile: one that was constant across space, and another that varied across space by a quadratic function (Fig. 6d). The scale of this quadratic function was chosen to roughly match the coil nonuniformity used in the imaging study. Finally, Gaussian distributed random noise with a variance of 1% of the mean signal intensity was added to the time series data. This simulated data was then corrected using rigid-body realignment, followed by either no further corrections, motion-parameter nuisance regression, or JumpCor. For comparison, the data were also realigned using the actual (input) motion, and the actual motion was regressed

from both the data realigned with the estimated and actual motion. Functional connectivity was then estimated by taking the average voxel time series from one of the ROIs with the simulated sinusoidal fluctuation (Fig. 6e) and computing the correlation with all other voxel time series (Fig. 6f-h).

3. Results:

3.1 Prevalence of head motion

Of our 98 participants, 72 (73%) exhibited occasional (1-7, median 3) large head movements (1-24mm, median 3.0mm), separated by longer periods with very little movement. Figure 1a shows a histogram of the number of large head movements (“jumps”) across subjects, and Figure 1b shows a histogram of the magnitude of the head movements, across all jumps, for all subjects. Figure 1c shows the number of subjects with at least 1 movement greater than a certain amount (the threshold used to define a “jump”).

3.2 Motion artifact reduction strategies and evaluation

The head motion from one subject illustrating occasional large jumps in motion is shown in Figure 2. The functional connectivity from a seed region in the motor cortex for this subject is shown in Figure 3, in the subject’s native space. As expected, without any image realignment, the functional connectivity shows extensive correlations (“connections”) throughout the brain, with a striped pattern in the through-slice (R-L) direction (Fig. 3a). After rigid body realignment and motion censoring (but no other nuisance regression), the functional connectivity still shows correlations across the brain, again with a striped pattern in the through-slice direction (Fig. 3b). The time course from one of the brain voxels indicates that this is likely due to residual motion-induced signal changes that were not removed by the realignment and censoring. JumpCor significantly reduced these residual signal changes, and the resulting motor cortex functional connectivity map shows the expected pattern with strong connectivity to the contralateral primary motor cortex and supplementary motor cortex (Fig. 3c).

Group connectivity maps (Fig. 4) show very little apparent motion artifact after JumpCor, as well as after all of the typical processing steps (nuisance regression of the estimated head motion and average CSF and white matter signals, with or without the global signal) without JumpCor. Similar results were obtained for group connectivity maps of the auditory cortex, visual cortex, and posterior cingulate (part of the default mode network). (Fig. S1-3)

The effects of different sets of nuisance regressors are shown in Figure 5 for the same representative subject shown in Figure 3. Regressing out either the estimated motion parameters or the JumpCor regressors significantly reduced the motion artifact (Fig. 5a-b). In contrast, artifacts remained when regressing out only the average white matter and CSF signal changes and their temporal derivatives (Fig. 5c). This was the case both with and without global signal regression (Fig. 5d). Regressing out the estimated motion together with the WM, CSF (Fig. 5e) and global signals (Fig. 5f) reduced motion related signal changes. The inclusion of the JumpCor regressors in the nuisance regression (Fig. 5g,h) further reduced the more extensive connections that appeared in the white matter when JumpCor regressors were not included (Fig. 5f, green arrow).

3.3 Simulation

The simulation first showed that, as expected, head motion disrupts the functional connectivity estimate, in this case by causing significant false positive connections (correlations) throughout the brain (Fig. 6f). Applying image realignment eliminated this motion artifact when the coil sensitivity pattern was uniform across the volume. However, the motion artifact was still present after image realignment when the coil sensitivity pattern was spatially non-uniform (Fig. 6g). Motion artifacts were reduced when the estimated head motion parameters were regressed from the data (Fig 6h). JumpCor also reduced the motion artifacts (Fig. 7d). Similar results were obtained for different levels of motion, different directions of motion (R-L, A-P) (Fig. S5), and when using estimated motion taken from one infant's scan (Fig. S6).

Closer examination of the estimated head motion parameters revealed the likely mechanism that explains why the regression of motion parameters was so effective. The simulated motion was only in one direction (anterior-posterior), and the head motion estimated from the image realignment did correctly show the largest motion to be in this direction (Fig. 8). However, the estimated head motion in the presence of a non-uniform RF coil sensitivity profile also shows small changes (approximately 0.01 to 0.5 mm) in the other motion parameters. Furthermore, these errors are not simply scaled copies of the primary movement. For example, the estimated motion in the left-right (L-R) and superior-inferior (S-I) directions show negative deviations during the simulated motion that actually occurred in the anterior direction (time points 50-100) and posterior direction (time points 150-200) (Fig. 8). In this way, the 6 motion parameters form a basis set that allows for the modeling of a wider array of signal changes (e.g., increases in signal for movement in either direction).

Functional connectivity maps obtained when aligning the data using the estimated motion are highly similar to those when the data were realigned using the actual motion. The residual motion artifact seen in Figures 6g and 7a,e (realignment without any nuisance regression) is not simply the result of errors in the re-alignment due to inaccurate estimates of the motion because realigning the data using the true (input) motion still results in artifacts (Fig. 7e). Moreover, regressing out the true motion, either from the data realigned with the true motion or estimated motion, did not correct for this artifact (Fig. 7b,f). Regressing out the estimated motion (Fig. 7c,g) or the JumpCor regressors (Fig. 7d,h) did reduce the motion artifact.

3.4 Quantitative measures of motion artifact reduction

Without any nuisance regression, most connections show a strong correlation with motion (Fig. 9a, black line). These correlations were reduced when the estimated head motion was regressed from the data (Fig 9a, magenta line). When the JumpCor regressors were regressed out of the data, the correlations were substantially reduced and more centered around zero (Fig. 9a, red line). The regression of the estimated motion, average white matter, CSF, global signals and their temporal derivatives also reduced the correlation with motion (Fig. 9a, green line). The inclusion of the JumpCor regressors in the nuisance regression showed similar results, with an additional slight decrease in (Fig. 9a, blue line). The histogram of correlation with motion after nuisance regression (JumpCor, white matter, CSF, global signals) was close to the null distribution obtained from permuting the mean Enorm values (Fig 9, gray band). Censoring an additional 5 time points (10 s) of data after each jump resulted in no difference in the association with the mean Enorm (Figure S8). Similar results were obtained when examining the correlation with the maximum jump amplitude, median jump amplitude, and number of jumps (Figure S9).

Removing jumps in motion using the JumpCor regressors resulted in a significant increase in similarity compared to not performing any nuisance regression. Regressing out the estimated head motion resulted in even higher similarity. The similarity further improved when the average white matter, CSF, global signal, and their temporal derivatives were regressed from the data. The addition of the JumpCor regressors to the estimated head motion and tissue-based regressors resulted in a significant increase in similarity ($p < 0.001$).

3.5 *The effect of different jump thresholds*

For higher thresholds (e.g. 20mm) very few jumps are identified, and the correlation of the absolute value of functional connectivity with motion is similar to that when no nuisance regression is performed. As the jump threshold is lowered, the correlation with motion decreased, until a threshold of about 5mm, with relatively little difference for smaller jump thresholds (Fig. 9b). When the average white matter, ventricular CSF, and global signals were regressed from the data, different jump thresholds had relatively little effect (Fig. 9c).

4. Discussion:

Large head motion can result in significant residual motion-related signal changes even after realignment and motion-censoring, in large part due to the head moving into different parts of the coil sensitivity profile. Our proposed correction technique, JumpCor, successfully reduces these changes when they occur infrequently during the imaging run.

Somewhat surprisingly, regressing out the estimated head motion parameters (a common preprocessing step in resting-state fMRI), also successfully reduces these motion artifacts. The reason this result is surprising is that the signal change resulting from head motion is not necessarily linearly related to the head motion, particularly if the coil sensitivity profile is spatially nonlinear and if the motion is large relative to this sensitivity profile (e.g. as illustrated in Fig. S4). Our simulations suggest that nuisance regression of the motion parameters is likely successful because the signal changes resulting from moving into a different part of the coil sensitivity affects the estimated head motion in such a way that the 6 realignment parameters form a basis set that can model a wider array of motion-induced signal changes. Therefore, nuisance regression of the 6 realignment parameters can reduce artifacts even for very large movements.

In this simulation, we examined different amounts of motion (1 voxel and 3 voxels), directions of motion (A-P, L-R), and temporal patterns of motion (A-P translation and motion estimated from one infant). In all cases, the estimated motion parameters had slight errors that provided a basis set to estimate the resulting signal changes. However, there is no way to test and examine all possible types of motion, objects, and coil sensitivity profiles, and therefore there is no way to guarantee that the regression of estimated motion parameters will always work so well. Therefore, if residual signal changes from occasional jumps in motion remain, JumpCor could be used to reduce them.

Although the motion-induced signal intensity changes are reduced by either JumpCor or motion parameter nuisance regression, our simulation shows that large movement through a nonuniform coil sensitivity can result in slight errors in the realignment. How significant is this misalignment? In our simulation, a movement of ± 10.5 mm resulted in erroneous motion estimates of up to ± 0.5 mm. Although we are often concerned with movements as low as 0.2mm in functional connectivity studies, here we have already censored time points with a $\text{Enorm} > 0.2$ mm and using either JumpCor or the regression of the estimated motion we have reduced the signal intensity changes associated with this movement. Therefore, these signal changes should not contribute to false connectivity. An alternative strategy if alignment errors are of concern is to use a realignment technique that is not as sensitive to the difference in signal intensity, such as boundary-based registration. Nevertheless, even if the realignment is accurate, signal changes resulting from moving into different parts of the coil sensitivity pattern would remain. These changes would not necessarily be reduced by regressing out the accurately estimated motion parameters (e.g. as shown in Fig. 7b,f). In this case, JumpCor could be used to reduce the residual motion-reduced signal changes.

While group functional connectivity maps (Figures 4, S1-S3) showed very little difference between including or not-including the JumpCor regressors, the effects of JumpCor were more significant at the individual subject level. JumpCor significantly increased the similarity between the individual connectivity maps and the group average, reducing between-subject variability associated with the large “jumps” in signal due to head motion.

The finding that censoring an additional 10s of data after each jump did not change the results suggests that the observed motion-related signal changes in this sample are not due to spin-history effects associated with the jumps. Furthermore, grayplots (Figs. S10-S13) show prolonged signal increases or decreases in the period between jumps (green and yellow arrows, respectively), consistent with moving into a different part of the RF coil sensitivity, but no clear transient effects after each jumps as may be expected with spin-history effects. Both JumpCor and the regression of estimated motion reduces these prolonged signal changes. The global signal changes remaining after JumpCor were not synchronized with the motion. These residual signal changes are most likely due to physiological noise (e.g. aliased respiration) since similar global fluctuations were also observed in subjects who showed relatively little head motion.

The motion threshold that should be used to define a “jump” is a tradeoff between flexibility in modeling motion and degrees of freedom. In our dataset, a threshold of 1mm reduced motion artifacts while only requiring an additional 2 to 8 degrees of freedom (1 to 7 jumps, median 3). Accounting for the degrees of freedom is important to estimate statistics correctly, and many common preprocessing approaches, such as temporal filtering, can significantly reduce the degrees of freedom. The numbers of additional JumpCor regressors are relatively small, but should be considered in the context of other processing choices, the duration of the imaging run and the total number of data points acquired. In our data, the correlation with mean Enorm decreased with lower jump thresholds, but with similar results for 1mm and 5mm thresholds (Fig. 9b). However, when the estimated motion was regressed from the data, different jump thresholds had minimal effect (Fig. 9c). This minimal effect is likely because the estimated motion parameters are already reducing the motion artifact.

The JumpCor technique presented here regressed out a constant for each segment between the jumps. In principle, one could increase the number and order of polynomials in order to account for more complex signal dynamics, such as those resulting from spin-history effects. An alternative approach to reduce the effects of large movements in the presence of non-uniform coil sensitivity is to estimate the bias fields from the acquired images and then correct for the spatial nonuniformity (Seshamani et al., 2014). Finally, an alternative strategy to reduce motion artifacts is to use prospective motion correction (Ward et al., 1998, Thesen et al., 2000, Ward et al., 2000, Todd et al., 2015). Unfortunately, this technology is not yet available on all scanners and does not correct for variations in signal intensity due to the brain moving into a different part of the coil sensitivity. Our proposed technique provides a relatively simple method to deal with this artifact when such technology is unavailable.

5. Conclusions:

Residual head motion-related signal changes in fMRI resulting from moving into a different part of the RF coil sensitivity can be successfully corrected by regressing out the estimated head motion, even when the motion is relatively large. In addition, we present an alternative correction method, JumpCor, that reduces motion artifacts resulting from large infrequent head movements (jumps). This technique significantly reduces artifacts and improves the quality of functional connectivity estimates when combined with the typical preprocessing approach (regressing out the estimated head motion and tissue based regressors). We therefore recommend that JumpCor be added to the typical nuisance regressors used to reduce noise

when large jumps in motion are present in the data. This technique, as well as the knowledge that regression of estimated motion successfully reduces motion artifacts even in the presence of very large head motion (several mm), should reduce the data loss in studies where participants exhibit this type of motion, such as sleeping infants. JumpCor could prove to be a great advantage in developmental neuroimaging studies.

Acknowledgements:

The authors wish to thank N. Schmidt, C. Frye for assistance in recruitment and data collection and the families for their participation.

Funding for this research was provided by NIH grant P50MH100031, the HealthEmotions Research Institute, and the Waisman Center.

Contributions:

R.M. Birn: Conceptualization, Investigation, Methodology, Formal analysis, Writing - original draft, Writing - review & editing. **D.C. Dean:** Conceptualization, Investigation, Formal analysis, Writing - original draft, Writing - review & editing. **W. Wooten:** Investigation, Formal analysis, Writing - review & editing. **E.M. Planalp:** Investigation, Formal analysis, Writing - review & editing. **S. Kecskemeti:** Investigation, Methodology, Writing - review & editing. **A.L. Alexander:** Conceptualization, Investigation, Writing - review & editing, Project administration, Funding acquisition. **H.H. Goldsmith:** Conceptualization, Writing - review & editing, Project administration, Funding acquisition. **R.J. Davidson:** Conceptualization, Writing - review & editing, Project administration, Funding acquisition

Disclosures:

R.M. Birn is a consultant for NOUS Imaging, Inc., a company that produces the FIRMM motion monitoring software.

R.J. Davidson is the founder, president, and serves on the board of directors for the non-profit organization, Healthy Minds Innovations, Inc.

Ethics Statement:

All study procedures were in accordance with the Institutional Review Board (IRB) policies at the University of Wisconsin - Madison, and written informed consent was obtained from each participating family.

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