REVIEW

Head Motion and Correction Methods in Resting-state Functional MRI

Masami Goto^{1*}, Osamu Abe², Tosiaki Miyati³, Hidenori Yamasue⁴, Tsutomu Gomi¹, and Tohoru Takeda¹

¹School of Allied Health Sciences, Kitasato University, Kitasato,
1-15-1 Minami-ku, Sagamihara, Kanagawa 252-0373, Japan
²Department of Radiology, Nihon University School of Medicine
³Graduate School of Medical Science, Kanazawa University
⁴Department of Neuropsychiatry, Graduate School of Medicine, University of Tokyo
(Received June 2, 2015; Accepted October 28, 2015; published online December 22, 2015)

Resting-state functional magnetic resonance imaging (RS-fMRI) is used to investigate brain functional connectivity at rest. However, noise from human physiological motion is an unresolved problem associated with this technique. Following the unexpected previous result that group differences in head motion between control and patient groups caused group differences in the resting-state network with RS-fMRI, we reviewed the effects of human physiological noise caused by subject motion, especially motion of the head, on functional connectivity at rest detected with RS-fMRI. The aim of the present study was to review head motion artifact with RS-fMRI, individual and patient population differences in head motion, and correction methods for head motion artifact with RS-fMRI. Numerous reports have described new methods [e.g., scrubbing, regional displacement interaction (RDI)] for motion correction on RS-fMRI, many of which have been successful in reducing this negative influence. However, the influence of head motion could not be entirely excluded by any of these published techniques. Therefore, in performing RS-fMRI studies, head motion of the participants should be quantified with measurement technique (e.g., framewise displacement). Development of a more effective correction method would improve the accuracy of RS-fMRI analysis.

Keywords: functional, head motion, motion correction, magnetic resonance imaging, resting-state

Introduction

Resting-state functional magnetic resonance imaging (RS-fMRI) is used to investigate brain functional connectivity in attention-deficit/hyperactivity disorder (ADHD), bipolar disorder, multiple sclerosis, major depression, epilepsy, preclinical Alzheimer's disease, and Parkinson's disease, as follows:

i. ADHD¹: most studies have been consistent in supporting three interrelated themes: cognitive control—default mode network (DMN) anticorrelations are attenuated in ADHD; connectivity within the DMN itself is reduced in ADHD; and connectivity patterns, at least based on the DMN and cognitive control—DMN anticorrelations,

- ii. Bipolar disorder²: most studies have supported the theory of cortico-limbic regulation and have suggested that connectivity is more complex than a simple increase or decrease in connectivity between cortico-limbic networks, on the basis that different subregions of one brain area may have different connectivities with other brain areas. Nonetheless, the findings are preliminary, sometimes even contradictory, and do not allow a complete understanding of connectivity in bipolar disorder.
- iii. Multiple sclerosis³: many studies have shown that the increased resting-state network connectivities of the dorsal fronto-parietal network, the right ventral fronto-parietal network, and the prefronto-insular network are correlated negatively with the multiple sclerosis functional composite score.

reveal parallel structural MRI findings in ADHD that suggest delayed neuro maturation.

^{*}Corresponding author, Phone: +81-42-778-9617, Fax: +81-42-778-9628; E-mail: car6_pa2_rw@yahoo.co.jp

- iv. Major depression⁴: one of the most robust patterns that has emerged from many studies is the abnormal involvement of the cortico-limbic mood-regulating circuit in major depression. In addition, in depressed patients, structures in the limbic area that have abnormal activation include the medial thalamus, which is thought to be involved in emotional perception and in the amygdala.
- v. Epilepsy⁵: most studies have found that abnormal synchronization is widespread in medial temporal lobe epilepsy patients. For example, in addition to abnormal networks of epileptic foci, RS-fMRI studies have found decreased functional connectivity in the attentional, perceptual, and DMNs, as well as in the subcortical regions.
- vi. Preclinical Alzheimer's disease⁶: With regard to mild cognitive impairment, significantly decreased DMN connectivity has been observed in cognitively normal elderly persons with elevated brain amyloid. Furthermore, connectivity between the precuneus and hippocampus is significantly lower in individuals with amyloid plaques versus those without evidence of brain $A\beta$ plaques. This finding indicates that resting state functional disconnection had already occurred in nondemented aging in the presence of $A\beta$ plaques.
- vii. Parkinson's disease⁷: most studies have found dysfunction in multiple areas of the resting brain in individuals with Parkinson's disease. This dysfunction in resting activity extends beyond the sensorimotor network to include areas across the fronto-parietal and visual networks, as well as the DMN. In addition, resting activity within the posterior putamen may play a significant role in the motor abnormalities seen in Parkinson's disease.

There has been a rapid increase in research with RS-fMRI into clinical disease. However, there are numerous controversial issues associated with RS-fMRI, including noise from human physiological factors such as head motion, respiratory motion, arterial carbon dioxide (CO₂) concentration, blood pressure, cerebral autoregulation, and vasomotion, as follows:

- i. Head motion: head motion causes the content of each voxel to change, altering the uniformity of the magnetic field that has been shimmed for a particular head position. When head motion occurs during scanning, it alters the steady state magnetization by changing the time between excitations in those parts of tissue that have moved from one slice to the next.8
- ii. Respiratory motion: changes in the magnetic field due to respiration can cause a shift of the MR image in the phase-encoding direction, and the small amount of head motion that occurs during breathing alters the spin history in a spatially dependent manner.⁸

iii. Arterial CO₂ concentration: the CO₂ in arterial blood is a potent vasodilator, producing a global increase in cerebral blood flow, which in turn reduces the deoxyhemoglobin concentration, resulting in a longer T₂*. This change in T₂* causes blood-oxygen-level-dependent (BOLD) signal changes.8

Other possible sources of noise include blood pressure, cerebral autoregulation, and vasomotion.

Following the surprising results of previous reports that group differences in head motion between control and patient groups cause group differences in the resting-state network with RS-fMRI,9-16 we became interested in the motion of the head in particular, in human RS-fMRI studies of physiological noise. Van Dijk et al. explored the influence of head motion on RS-fMRI estimates, and reported that comparisons between groups of individuals with subtly different levels of head motion yielded difference maps that could erroneously interpreted to indicate neuronal effects.¹⁵ Head motion has been found to be responsible for decreasing long-distance correlation and increasing local correlations. 12,14,15 In addition, group differences in head motion have been reported as follows: there was significantly more motion in an elderly group compared with a young group,9 there was significantly more motion in an early adolescence (8–9 years) group compared with a youth group (15-22 years), 14 impulsivity associated with attention deficit hyperactivity disorder contributed to head motion, ¹⁷ and there was significantly more head motion in patient populations than in controls.¹⁸ Therefore, if the effects of motion artifact are greater than those of true brain activity, the RS-fMRI results might show regions of false brain activity. Our aims are to review head motion artifact with RS-fMRI, evaluate individual and patient population differences in terms of head motion, and investigate correction methods for head motion artifact with RS-fMRI.

Head motion artifact with RS-fMRI

The known affected areas and the effects of enhanced or diminished connectivity due to head motion artifact with RS-fMRI are described as follows:

i. Regions of the DMN in which artifact have been found include the medial prefrontal cortex, lateral temporal cortex, and the inferior parietal lobule. Dijk et al.¹⁵ analyzed the associations between head motion and artifact with RS-fMRI, in 10 groups categorized by the level of head motion. Group 1 included subjects with the least head motion, and group 10 included subjects with the most head motion. The mean distance of motion (standard deviation) in group 1 was 0.027 (0.002) mm, and that in group 10 was 0.100 (0.021) mm. Functional connectivity differences between group 1 and group 10 were observed throughout the

M. Goto et al.

DMN, including the medial prefrontal cortex, lateral temporal cortex, and the inferior parietal lobule. In addition, the regions showing differences in functional connectivity in the comparison between group 3 and group 8 were the same as those observed in the comparison between group 1 and group 10, although the former differences were weaker than the latter. Dijk et al. showed that differences in head motion yielded difference maps that could easily be mistaken for neuronal effects.

ii. Artifacts enhance the short-range connectivity and diminish the long-distance connectivity among network nodes. Bright et al. reported excessive correlation values across the posterior cortices near the posterior cingulate cortex seed region. 11 Satterthwaite et al. showed that the inter-node Euclidean distance among 12,720 pairwise connections was robustly related to the effect of motion, and that the effect of motion transitions from causing increased connectivity to decreased connectivity at a distance of more than 96 mm.14 In their intersubject analysis, Zeng et al. identified a correlate of head motion consisting of reduced distant functional connectivity primarily in the DMN, in individuals who had a large amount of head motion.¹⁹ Yan et al. showed that high-motion datasets exhibited more pronounced negative-motion-BOLD relationships (esp. prefrontal areas), and that low-motion datasets exhibited more pronounced positive-motion-BOLD relationships (esp. primary and supplementary motor areas).²⁰

Individual differences in head motion

The interpretation of data obtained with RS-fMRI is complicated by individual differences in head motion if the data include these effects. Meier et al. analyzed RS-fMRI data from 26 right-handed younger adults (mean age, 24.7 ± 0.9 years; range, 18-35; 12 males, 14 females) and 26 right-handed older adults (mean age, 64.7 ± 1.56 years; range, 55-85; 11 males, 15 females) obtained from the International Consortium for Brain Mapping dataset made publically available as part of the 1000 Functional Connectomes project (www.nitrc.org/projects/fcon 1000). The results show significantly more motion in the older adults compared with the younger adults (0.14 \pm 0.013 in older adults, 0.07 ± 0.005 in younger adults) based on the composite score of total motion²¹ for each subject.²² Satterthwaite et al. reported a negative correlation (r = -0.34, P = 2.2×10^{-14}) between age and in-scanner head motion in 456 individuals (mean age, 15.6 ± 3.4 years, range, 8-23 years; 199 males, 257 females). 14 As mentioned above, the effect of head motion in RS-fMRI results is influenced by the age of the participants.

Zuo et al. also showed individual differences in head motion. They analyzed the data of 234 healthy participants

in the Nathan Kline Institute–Rockland Sample,²³ and evaluated head motion in both nonlinear and linear registrations. The quality of the nonlinear registration was quantified by spatial correlation between the registered individual image and the Montreal Neurological Institute 152 standard template with the functional MRI of the brain's nonlinear image registration tool (FNIRT),²⁴ and the minimal cost of function–structure realignment using boundary-based registration (mcBBR) was used to quantify the linear registration quality.²⁵ The resulting error of nonlinear registration using FNIRT (errFNIRT) was 0.10–0.25 and the mcBBR was 0.3–0.6.²⁶

While Zuo et al. showed individual differences between inter-subjects, Power et al. evaluated head motion for the time course during the RS-fMRI data collection period. They measured head motion in 160 subjects and found an elevation of head motion during periods of motion.²⁷

Head motion in patient populations and other factors

Autism spectrum disorders (ASDs), stroke, self-reported impulsivity scores, sedation, and resting conditions as factors influencing head motion are described as follows:

- i. ASD: Tyszka et al. compared head motion between ASD and control subjects.²⁸ The participants were 19 high-functioning adults with ASD and 20 neurotypical controls with no family history of autism. Frame-to-frame Euclidean displacement (Δrff) and total frame-to-frame angular rotation ($\Delta\theta$ ff) were used to quantify head motion. No significant difference between the groups were observed in either metric, and the effect sizes were small to negligible. For frame-to-frame displacements, Δrff was 60 ± 5 um (mean \pm standard error of the mean) in controls and $75 \pm 9 \,\mu\text{m}$ in ASD subjects (P = 0.1651, unpaired t-test, equal variance). For frame-to-frame rotations, $\Delta\theta$ ff was $0.031 \pm 0.003^{\circ}$ (mean \pm standard error of the mean) in controls and $0.031 \pm 0.003^{\circ}$ in ASD subjects (P = 0.960, unpaired t-test, equal variance). Starck et al. also compared head motion between ASD and control subjects.²⁹ The participants were 30 high-functioning adolescents with ASD and 30 age- and gender-matched control subjects. Absolute (referenced to middle time-point) and relative (compared with previous time-point) estimations were used to quantify head motion. These estimates were taken as the root-mean-square values of translational and rotational movements. Relative motion was reported as 0.059 mm for control and 0.061 mm for ASD subjects (P = 0.37), and absolute motion was 0.24 mm for control and 0.37 mm for ASD subjects (P = 0.03). The group averages and group differences of the root mean square motion estimates were computed by FSL MCFLIRT.³⁰
- ii. Stroke: Seto et al. used task-based fMRI to compare head motion between stroke and control

subjects. ¹⁸ The participants were 8 stroke subjects (5 males and 3 females; average age, 58 years; range, 22–78 years) and 7 age-matched controls (2 males and 5 females; average age, 59 years; range, 25–71 years). The sample standard deviation of the head motion (with linear drift detrended) ($M_{\rm sd}$) was used to quantify head motion. The metric $M_{\rm sd}$ was defined by the formula:

$$\mathbf{M}_{sd} = \left(\frac{\sum_{i=1}^{N} (X\mathbf{i} - \mathbf{Z})^{2}}{(N-1)}\right)^{\frac{1}{2}}$$
(1)

where Xi is the head position measurement at time i, X is the mean of all the head position measurements, and N is the total number of data points. The average variance for M_{sd} across all tasks was 0.026 \mbox{mm}^2 for the stroke group and 0.007 \mbox{mm}^2 for the age-matched controls, and the stroke group produced greater head motion than the age-matched controls. In the present study, we were interested in head motion in the resting phase, but the results of Seto et al. were for motion data obtained during the task phase. However, from the M_{sd} data for the resting phase that were included in their figure 5, we found equivalent values between the stroke and control subject groups.

iii. Self-reported impulsivity scores: Kong et al. 17 showed a positive correlation between the magnitude of head motion and self-reported impulsivity scores across participants (P=0.02). Impulsivity was assessed using the Barratt impulsiveness scale, 31 and the participants were 581 college students (mean age, 20.5 years; standard deviation, 0.95; 327 females) from Beijing Normal University, Beijing, China.

- iv. Sedation: Hlinka et al.³² showed that sedation-induced low-frequency fluctuations (LFFs, 0.01–0.1 Hz) of fMRI signal increases were mediated by increased head motion in 20 healthy volunteers (age range, 18–35 years; 18 men, 2 women). Volunteers were rescanned within 5 min after they stabilized at Ramsay level 3 (patient responds to commands only)³³ as assessed (by the attending anesthesiologist) with the subject on the scanner table outside the magnet, with the head coil removed. The amount of head motion was measured by mean relative displacement (MRD).³²
- v. Resting conditions: Patriat et al.³⁴ investigated head motion in three resting conditions: with the eyes closed (EC), with the eyes open (EO), and with the gaze fixed on a cross (EF) that was back-projected onto a screen. The subjects were 25 healthy adults (mean age, 35.5 ± 17.7 years; 10 females) with no history of neurological or psychological disorders. There was no significant difference in the amount of motion among the three resting conditions, as measured by the MRD. However, the authors recommended that only one condition should be used as the resting condition.

Correction methods for head motion artifact with RS-fMRI

Correction methods for head motion artifact with RS-fMRI are summarized in Table 1. The various methods are discussed as follows:

Power et al.^{35,36} proposed the scrubbing method for correcting head motion with RS-fMRI. This preprocessing technique can be implemented after or as a

Table 1. Summary of correction methods for head motion artifact with RS-fMRI

Study	Correction technique	Characteristics
Power et al. (2012)	scrubbing method	motion-induced spikes in the RS-fMRI time series are identified and excised
Satterthwaite et al. (2013)	"improved" preprocessing method	performance of 36-parameter + single-TR spike regression on an ROI-wise basis
Spisák et al. (2014)	regional displacement interaction method	information on voxel-wise motion is incorporated into the population-level model
Xu et al. (2014)	dual-mask sICA method	separate decompositions within a brain mask and a head mask are applied to time series
Beall et al. (2014)	SLice-Oriented MOtion COrrection (SLOMOCO) method	slicewise rigid-body motion parameter estimation and subsequent correction
Behzadi et al. (2007)	anatomical CompCor method	estimation of coherent noise components in same tissues using principal component analysis
Scheinost et al. (2014)	uniform smoothing algorithm method	a uniform level of smoothness is created across the dataset
Patel et al. (2014)	wavelet despike method	modeling with wavelet-based method and removing secondary motion artifacts from data

Details of the methods are provided in the section "Correction methods for head motion artifact with RS-fMRI."

182 M. Goto et al.

part of standard RS-fMRI preprocessing.³⁷ The scrubbing method identifies motion-induced spikes in the RS-fMRI time series. These data are excised with a temporal mask, and adjacent time points are temporally concatenated. Yan et al.20 evaluated the ability of the scrubbing method to decrease the impact of motion on the BOLD signal at the individual level, in 176 adult subjects (mean age, 20.9 ± 1.9 years; 106 females). They found that scrubbing of volumes with frame-wise displacement >0.2 effectively removed negative-motion–BOLD relationships, tive-motion-BOLD relationships tended to cluster in primary and supplementary motor areas and remained even after scrubbing. Based on these findings, they concluded that positive relationships might reflect neural origins of motion, while negative relationships are likely to originate from motion artifact.

Satterthwaite et al. 12 compared differences in community structure between subjects with small and large amounts of head motion, for both standard and improved preprocessing methods with RS-fMRI. "Standard" preprocessing included 9-parameter voxelwise confound regression and a band-pass filter of 0.01-0.1 Hz; "improved" preprocessing included 36-parameter + single-TR spike regression performed on an ROI-wise basis, followed by band-pass filtering at 0.01-0.08 Hz. "9 parameters" included 6 standard motion parameters (x, y, z translations and rotations) + WM/CSF/global time courses. "36 parameters" additionally included the quadratic term for all parameters in the 18-parameter model (includes regressors from the 9-parameter model, plus the temporal derivative of each parameter across the time series). Inclusion of the quadratic term effectively removes the sign of the motion parameter and also models nonlinearities in the effect of motion on the BOLD signal. The results showed that improved preprocessing of RS-fMRI data can substantially reduce the burden of artifact induced by in-scanner head motion.

Spisák et al.³⁸ proposed the RDI method for motion correction, a novel modeling approach for second-level brain connectivity analysis, which provides the opportunity to incorporate voxel-wise motion information into the population-level model and to account for corresponding artifactual effects. The population sample consisted of 79 patients with autism spectrum disorders (age range, 7.1–39.1 years) (53 autistic disorder, 21 Asperger's disorder, 5 pervasive developmental disorder, not otherwise specified) and an age- and gender-matched group of 105 typical control subjects (age range, 6.5–31.8 years). To test the efficiency of the RDI method, the authors performed group comparisons where both motion-related artifacts and real neuronal differences were expected to be present, and compared the functional networks of autistic and control patients.

The results showed that while including RDI significantly reduced (presumably artifactual) differences between voxel-wise displacement-related subject cohorts, differences in the autism-related comparison were more or less preserved. These results suggest that the RDI method, while effectively reducing motion artifacts in group comparisons, preserves the sensitivity to neural differences. The authors concluded that the inclusion of RDI as second-level nuisance covariates is generally appropriate, especially in moderate nuisance correction methods, and may become increasingly necessary when the variable of interest is interrelated with altered subject kinetics.

Xu et al.³⁹ proposed a data-driven denoising technique including a dual-mask spatial independent component analysis (ICA) method, which involves separate decompositions within a brain mask and a head mask applied to the sagittally acquired fMRI time series of each subject. Eighteen healthy, right-handed, native English speakers (age range, 20–32 years; 7 males, 11 females) participated in this study. All participants were scanned in an fMRI experiment and 17 of them participated in a subsequent positron emission tomography (PET) experiment. When comparing narrative to pseudoword production, the results showed activations of the left Brodmann area 45/47 with the data-driven denoising technique and with PET; however, these were absent when no data-driven denoising technique was used. The authors concluded that a data-driven denoising technique can be applied in a variety of experimental paradigms for improving the reliability of fMRI measurements. The entire procedure is fully automated and has minimal impact on other features of conventional data processing.

Beall et al.40 developed SLice-Oriented MOtion COrrection (SLOMOCO) based on the theory that the volumetric parameters are related to the sum of the slice motion. SLOMOCO is not a coregistration technique, but rather a slicewise rigid-body motion parameter estimation and subsequent correction through regression using these parameters. MRI data were acquired from a total of 7 cadaver subjects (all cadavers were scanned within 8 h postmortem and before any tissue removal), and 2 males and 1 female healthy live participants (mean age, 35 years; range, 33-38 years). This study of volumetric correction performance analysis showed the linear correlation between the injected motion and SLOMOCO detected-motion parameters. Moreover, a comparison of various motion-correction methods (for image temporal variance) showed that image noise was reduced by more than half (56% reduction in the temporal standard deviation) by the best correction technique, which was second-order correction using the retrospective SLOMOCO method. Based on these results, Beall et al. concluded that SLOMOCO, a completely retrospective solution for head motion correction in BOLD-weighted MRI data, is a substantial new advance.

Behzadi et al.⁴¹ proposed that a method referred to as anatomical CompCor or aCompCor may help minimize the effects of head movement, in addition to accounting for cardiac and respiratory fluctuations. In the aComp-Cor approach, spatially coherent noise components are estimated in the same tissues using principal component analysis. A potential strength of aCompCor is that it can identify multiple nuisance signals from WM and CSF. Another benefit of aCompCor is that it does not make assumptions about the relationship between the source of noise and the resulting change in MR signal, potentially making it easier to account for delayed and non-linear effects of motion. Muschelli et al. 42 performed a comparative study of two motion-correction methods, aCompCor and the more commonly used mean tissue-based nuisance signal-regression method. The participants in their study were 130 children with typical development (mean age \pm standard deviation, 10.2 ± 1.2 years). The results showed that aCompCor attenuated the relationship between head motion and MR percent signal change, and also showed that aCompCor improved connectivity metric specificity.

Scheinost et al.⁴³ proposed the uniform smoothing algorithm method for reducing the effect of significant differences in head motion between experimental groups. The method can be used without needing to explicitly control motion. To create a uniform level of smoothness across the data set (thus minimizing group differences associated with image smoothing), each subject's functional run was smoothed with AFNI's 3d Blur to full width half maximum (FWHM) (http://afni. nimh.nih.gov/afni). In this program, a diffusion-based scheme is used to iteratively smooth the functional series until the desired level is reached. The ages of the 103 participants in this study lay within a narrow range (20–23 years; mean age, 21.5 years; standard deviation, 0.6 years) with the aim of minimizing any age-related effects on motion¹⁵ or connectivity.^{44,45} The authors then compared smoothing using the uniform smoothing algorithm with that using a Gaussian kernel with FWHM of 6 mm. The results showed that the uniform smoothing algorithm reduced the correlation of the motion time courses and the BOLD time courses, while no regions showed a significant increase in correlation of the motion time courses and the BOLD time courses. Accordingly, it was concluded that the uniform smoothing algorithm minimizes the variance of spatial smoothness across subjects, and that controlling image smoothness provides an effective way of controlling motion confounds in functional connectivity. The uniform smoothing algorithm has the advantage that by not explicitly controlling motion, it enables the

exploration of potentially real changes in functional connectivity that may lead to, or in some way be associated with, increased motion.

Patel et al. 46 proposed the wavelet despike method, which is a data-driven, wavelet-based method for modeling and removing secondary motion artifacts from fMRI data, without the need for data scrubbing. This unsupervised method detects non-stationary events caused by movement as chains of scale-invariant maximal or minimal wavelet coefficients, and despikes these from the voxel time series. Importantly, because the algorithm can identify non-stationary events across different frequencies, it is able to remove slower and prolonged motion artifacts such as spin-history type effects, as well as higher-frequency events such as step changes in signal intensity and spikes. The participants in this study were divided into three cohorts as follows: Cohort 1 was a group of 22 children with a mean age of 8.5 years; Cohort 2 was a group of 40 stimulant-dependent adults that met the DSM-IV criteria for stimulant dependence, with a mean age of 34.8 years; and Cohort 3 was a group of 45 healthy biological siblings of the Cohort 2 subjects, with a mean age of 32.3 years. The amount of signal variance retained in each gray matter time series (gray matter voxels identified by the Eickhoff-Zilles macrolabels atlas in Talairach space) after wavelet despiking was compared with that after traditional 13-parameter regression, and the effects of the denoising on resting-state networks was assessed. The two sets of maps generated were broadly similar, indicating that the wavelet despike method does not remove too much of the real signal. Moreover, the motor cortical connectivity map obtained following the wavelet despike pre-processing included anatomically predictable regions of the contralateral cerebellum and ipsilateral thalamus. but these were not demonstrated in the connectivity maps obtained following the traditional 13-parameter regression. It is often difficult to assess the relative validity of different methods for functional connectivity analysis in the absence of a gold standard or ground truth; however, the results of that study are consistent with the view that wavelet despiking does not attenuate, and may indeed enhance, the demonstration of functional connectivity between anatomically connected brain regions. The wavelet despike method outperforms other methods, based on various previously published and newly developed diagnostic measures, and importantly, requires only one additional step to standard pre-processing pipelines.

Discussion

For application to population-level analysis and group comparisons, retrospective removal of artifact

M. Goto et al.

related to head motion can be performed at five different stages of image processing³⁸: stage 1, motion correction of fMRI time-series by realignment to a reference image (using automatic co-registration approaches)⁴⁷; stage 2, censoring data to exclude periods of high motion (scrubbing, de-spiking)^{12,35}; stage 3, modeling the effect of motion-related nuisance parameters on BOLD signal [simple linear effects (e.g., translation and rotation of brain regions) were modeled by the six motion parameters (e.g., 3 translation, 3 rotation), but more complex nonlinear effects (e.g., changes in the distortion and blurring of the image due to magnetic field inhomogeneities) remain as imaging artifact]41,48,49; stage 4, temporal filtering of BOLD time courses to discard frequencies encumbered by motion artifacts; and stage 5, correcting subject-specific motion effects at the population level (descriptive summary statistics of subject-specific motion as second-level model regressors, a common choice for descriptive summary statistics is to include a measure of the average subject movement). 14,50,51 Traditional realignment-based correction approaches ensure that different time-points of the BOLD signal correspond to the same location. However, such methods do not handle voxel-level intensity confounds originating from the establishment of magnetic gradients and subsequent readout of the BOLD signal, 35,52 and automatic co-registration approaches may introduce spurious displacements in intervals of relatively low motion.⁵³

One of the most commonly used methods for dealing with motion-related artifacts is scrubbing.³⁵ also known as frame or volume censoring, 27,50 which identifies and rejects noise-contaminated images based on a set of criteria for estimating the degree of motion or amount of artifactual changes in image intensity. For example, framewise displacement (FD) is an empirical sum of the rigid-body motion between consecutive images in all directions, and DVARS is a whole-brain measure of the temporal derivative (D) of image intensity computed by obtaining the root mean square variance across voxels (VARS). Although DVARS is easily understood and applied, it has at least three apparent limitations³⁹: (1) statistical power is reduced because of the rejection of images, especially when a significant degree of motion is present in the data; (2) artifacts with potential detrimental effects, though not meeting the threshold for rejection, still exist in the remaining images; and (3) an inability to derive continuous time series may jeopardize analytical methods that depend on an unbroken temporal sequence of images (e.g., methods utilizing causality, periodicity, phase, and entropy measures).

Satterthwaite et al.¹² showed evidence for better model fit and lower effect of motion on connectivity of the 36-parameter model. The 36-parameter model had

the lowest average the Akaike information criterion (AIC) value. However, this effect was not homogeneous. AIC values declined for the low motion group when six standard motion parameters were included, but the AIC in this group did not drop when derivative and quadratic terms were added in the 18- and 36-parameter models. In contrast, in the high-motion group AIC values continued to decline at each step as more parameters were added.

Component analysis methods are often able to remove some, but not all of these secondary motion artifacts. Notably, spin-history effects can be difficult to remove. The difficulty in modeling these secondary effects on fMRI time series from the movement parameter information available, may be further complicated by a number of factors, including, but not limited to, subject movement in between frames, which may result in substantial non-linear and non-spatially-uniform effects in time series. In the case that fMRI data contain potent influence by the secondary effects, wavelet despike method may demonstrate an especially high correction effect compared with other correction methods.

Major limitation of the present study is that we cannot compare the effect for a motion correction between different types of RS-fMRI analysis, because we cannot find comparison study for it. However, we found comparison study for stability with several different types of RS-fMRI analysis methods by Li et al.,54 Li et al. used four different types of RS-fMRI analysis methods: the seed-region-based functional connectivity (SRFC), ICA-derived network-based FC (NTFC), regional homogeneity (ReHo), and the amplitude of low frequency fluctuation(ALFF). And Li et al. reported difference of stability between different types of RS-fMRI analysis methods.⁵⁴ Therefore, we infer that the effect for a motion correction is influenced by RS-fMRI analysis method, and an appropriate correction method may change depending on RS-fMRI analysis method. Second limitation of the present study is that we cannot distinguish between the head motion by the physiological (e.g., pulsation) noise and the head motion by the body motion. We think that motion evaluation method using the marker which was put at many points of the scalp may be effective for discrimination of the motions. The head motion by the body motion induces movement of the marker at irregularity, but the head motion by the physiological (e.g., pulsation, etc) noise induces the movement of the marker at regularity. Based on this theory, analysis method for separation of the head motion by the body motion and the head motion by the physiological is target of future study in our team. Third limitation of the present study is that there is no gold standard for evaluation of RS-fMRI analysis methods. Therefore, sensitivity and reproducibility are mainly used as an index of the evaluations for RS-fMRI analysis. On the other hand, there is a study determining that lower noise is the result with superior analysis method, but this index of evaluation for RS-fMRI analysis may be the evaluation method that is not correct scientifically.

Conclusion

Many previous studies (see section on "Correction methods for head motion artifact with RS-fMRI") have reported new methods for correcting the detrimental influence of head motion with RS-fMRI. Based on the findings of the reviewed articles, we think that wavelet despike method is the best correction method for head motion⁴⁶ in the RS-fMRI. However, with all these techniques, the influence of head motion is not entirely excluded from the RS-fMRI results. Therefore, when a study is performed using RS-fMRI, device (band to suppress the motion of body trunk and head) to lower the movement of the head must be used in MR data acquisition. The amount of head motion of the participants must be investigated with a motion-evaluation method (e.g., FD or DVARS). Development of a more effective correction method and improved imaging method would improve the accuracy of RS-fMRI analysis.

Acknowledgments

This study was supported by a Grant-in-Aid for Scientific Research on Innovative Areas (Comprehensive Brain Science Network) from the Ministry of Education, Science, Sports and Culture of Japan.

References

- 1. Posner J, Park C, Wang Z. Connecting the dots: a review of resting connectivity MRI studies in attention-deficit/hyperactivity disorder. Neuropsychol Rev 2014; 24:3–15.
- Vargas C, López-Jaramillo C, Vieta E. A systematic literature review of resting state network—functional MRI in bipolar disorder. J Affect Disord 2013; 150:727–735.
- Filippi M, Agosta F, Spinelli EG, Rocca MA. Imaging resting state brain function in multiple sclerosis. J Neurol 2013; 260:1709–1713.
- 4. Wang L, Hermens DF, Hickie IB, Lagopoulos J. A systematic review of resting-state functional-MRI studies in major depression. J Affect Disord 2012; 142:6–12.
- 5. Wurina, Zang YF, Zhao SG. Resting-state fMRI studies in epilepsy. Neurosci Bull 2012; 28:449–455.
- Sheline YI, Raichle ME. Resting state functional connectivity in preclinical Alzheimer's disease. Biol Psychiatry 2013; 74:340–347.
- Prodoehl J, Burciu RG, Vaillancourt DE. Resting state functional magnetic resonance imaging in Parkinson's disease. Curr Neurol Neurosci Rep 2014; 14:448.

- 8. Murphy K, Birn RM, Bandettini PA. Resting-state fMRI confounds and cleanup. Neuroimage 2013; 80:349–359.
- Song J, Desphande AS, Meier TB, et al. Agerelated differences in test-retest reliability in resting-state brain functional connectivity. PLoS One 2012;7:e49847.
- Lee MH, Smyser CD, Shimony JS. Resting-state fMRI: a review of methods and clinical applications. AJNR Am J Neuroradiol 2013;34:1866–1872.
- 11. Bright MG, Murphy K. Removing motion and physiological artifacts from intrinsic BOLD fluctuations using short echo data. Neuroimage 2013; 64:526–537.
- Satterthwaite TD, Elliott MA, Gerraty RT, et al. An improved framework for confound regression and filtering for control of motion artifact in the preprocessing of resting-state functional connectivity data. Neuroimage 2013; 64:240–256.
- Ferreira LK, Busatto GF. Resting-state functional connectivity in normal brain aging. Neurosci Biobehav Rev 2013; 37:384–400.
- Satterthwaite TD, Wolf DH, Loughead J, et al. Impact of in-scanner head motion on multiple measures of functional connectivity: relevance for studies of neurodevelopment in youth. Neuroimage 2012; 60:623–632.
- 15. Van Dijk KR, Sabuncu MR, Buckner RL. The influence of head motion on intrinsic functional connectivity MRI. Neuroimage 2012;59: 431–438.
- Detre JA. Clinical applicability of functional MRI. J Magn Reson Imaging 2006; 23:808–815.
- 17. Kong XZ, Zhen Z, Li X, et al. Individual differences in impulsivity predict head motion during magnetic resonance imaging. PLoS One 2014; 9:e104989.
- Seto E, Sela G, McIlroy WE, et al. Quantifying head motion associated with motor tasks used in fMRI. Neuroimage 2001; 14:284–297.
- 19. Zeng LL, Wang D, Fox MD, et al. Neurobiological basis of head motion in brain imaging. Proc Natl Acad Sci U S A 2014; 111:6058–6062.
- Yan CG, Cheung B, Kelly C, et al. A comprehensive assessment of regional variation in the impact of head micromovements on functional connectomics. Neuroimage 2013; 76:183–201.
- 21. Jones TB, Bandettini PA, Kenworthy L, et al. Sources of group differences in functional connectivity: an investigation applied to autism spectrum disorder. Neuroimage 2010; 49:401–414.
- 22. Meier TB, Desphande AS, Vergun S, et al. Support vector machine classification and characterization of age-related reorganization of functional brain networks. Neuroimage 2012; 60:601–613.
- 23. Nooner KB, Colcombe SJ, Tobe RH, et al. The NKI-Rockland sample: a model for accelerating the pace of discovery science in psychiatry. Front Neurosci 2012; 6:152.
- Zuo XN, Kelly C, Di Martino A, et al. Growing together and growing apart: regional and sex differences in the lifespan developmental trajectories of functional homotopy. J Neurosci 2010; 30:15034–15043.

- 25. Greve DN, Fischl B. Accurate and robust brain image alignment using boundary-based registration. Neuroimage 2009; 48:63–72.
- Zuo XN, Xing XX. Test-retest reliabilities of resting-state FMRI measurements in human brain functional connectomics: a systems neuroscience perspective. Neurosci Biobehav Rev 2014; 45:100–118.
- Power JD, Mitra A, Laumann TO, Snyder AZ, Schlaggar BL, Petersen SE. Methods to detect, characterize, and remove motion artifact in resting state fMRI. Neuroimage 2014; 84:320–341.
- Tyszka JM, Kennedy DP, Paul LK, Adolphs R. Largely typical patterns of resting-state functional connectivity in high-functioning adults with autism. Cereb Cortex 2014; 24:1894–1905.
- Starck T, Nikkinen J, Rahko J, et al. Resting state fMRI reveals a default mode dissociation between retrosplenial and medial prefrontal subnetworks in ASD despite motion scrubbing. Front Hum Neurosci 2013; 7:802.
- Jenkinson M, Bannister P, Brady M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. Neuroimage 2002; 17:825–841.
- Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt impulsiveness scale. J Clin Psychol 1995; 51:768–774.
- Hlinka J, Alexakis C, Hardman JG, Siddiqui Q, Auer DP. Is sedation-induced BOLD fMRI low-frequency fluctuation increase mediated by increased motion? MAGMA 2010; 23:367–374.
- Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974; 2:656–659.
- 34. Patriat R, Molloy EK, Meier TB, et al. The effect of resting condition on resting-state fMRI reliability and consistency: a comparison between resting with eyes open, closed, and fixated. Neuroimage 2013; 78:463–473.
- Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage 2012; 59:2142–2154.
- 36. Power JD, Cohen AL, Nelson SM, et al. Functional network organization of the human brain. Neuron 2011; 72:665–678.
- 37. Van Dijk KR, Hedden T, Venkataraman A, Evans KC, Lazar SW, Buckner RL. Intrinsic functional connectivity as a tool for human connectomics: theory, properties, and optimization. J Neurophysiol 2010; 103:297–321.
- 38. Spisák T, Jakab A, Kis SA, et al. Voxel-wise motion artifacts in population-level whole-brain connectivity analysis of resting-state FMRI. PLoS One 2014; 9:e104947.
- 39. Xu Y, Tong Y, Liu S, et al. Denoising the speaking brain: toward a robust technique for correcting artifact-contaminated fMRI data under severe motion. Neuroimage 2014; 103:33–47.

- 40. Beall EB, Lowe MJ. SimPACE: generating simulated motion corrupted BOLD data with synthetic-navigated acquisition for the development and evaluation of SLOMOCO: a new, highly effective slicewise motion correction. Neuroimage 2014; 101:21–34.
- 41. Behzadi Y, Restom K, Liau J, Liu TT. A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. Neuroimage 2007; 37:90–101.
- 42. Muschelli J, Nebel MB, Caffo BS, Barber AD, Pekar JJ, Mostofsky SH. Reduction of motion-related artifacts in resting state fMRI using aCompCor. Neuroimage 2014; 96:22–35.
- 43. Scheinost D, Papademetris X, Constable RT. The impact of image smoothness on intrinsic functional connectivity and head motion confounds. Neuroimage 2014; 95:13–21.
- 44. Fair DA, Cohen AL, Dosenbach NU, et al. The maturing architecture of the brain's default network. Proc Natl Acad Sci U S A 2008; 105:4028–4032.
- 45. Hampson M, Tokoglu F, Shen X, Scheinost D, Papademetris X, Constable RT. Intrinsic brain connectivity related to age in young and middle aged adults. PLoS One 2012; 7:e44067.
- Patel AX, Kundu P, Rubinov M, et al. A wavelet method for modeling and despiking motion artifacts from resting-state fMRI time series. Neuroimage 2014; 95:287–304.
- 47. Kim B, Boes JL, Bland PH, Chenevert TL, Meyer CR. Motion correction in fMRI via registration of individual slices into an anatomical volume. Magn Reson Med 1999; 41:964–972.
- 48. Fox MD, Zhang D, Snyder AZ, Raichle ME. The global signal and observed anticorrelated resting state brain networks. J Neurophysiol 2009; 101:3270–3283.
- Glover GH, Li TQ, Ress D. Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. Magn Reson Med 2000; 44:162–167.
- 50. Fair DA, Nigg JT, Iyer S, et al. Distinct neural signatures detected for ADHD subtypes after controlling for micro-movements in resting state functional connectivity MRI data. Front Syst Neurosci 2013; 6:80.
- 51. Jakab A, Emri M, Spisak T, et al. Autistic traits in neurotypical adults: correlates of graph theoretical functional network topology and white matter anisotropy patterns. PLoS One 2013; 8:e60982.
- 52. Friston KJ, Williams S, Howard R, Frackowiak RS, Turner R. Movement-related effects in fMRI time-series. Magn Reson Med 1996; 35:346–355.
- 53. Freire L, Mangin JF. Motion correction algorithms may create spurious brain activations in the absence of subject motion. Neuroimage 2001; 14:709–722.
- 54. Li Z, Kadivar A, Pluta J, Dunlop J, Wang Z. Test-retest stability analysis of resting brain activity revealed by blood oxygen level-dependent functional MRI. J Magn Reson Imaging 2012; 36:344–354.