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Robust motion correction and outlier rejection of in vivo functional MR images of the fetal brain and placenta during maternal hyperoxia

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Abstract

Subject motion is a major challenge in functional magnetic resonance imaging studies (fMRI) of the fetal brain and placenta during maternal hyperoxia. We propose a motion correction and volume outlier rejection method for the correction of severe motion artifacts in both fetal brain and placenta. The method is optimized to the experimental design by processing different phases of acquisition separately. It also automatically excludes high-motion volumes and all the missing data are regressed from ROI-averaged signals. The results demonstrate that the proposed method is effective in enhancing motion correction in fetal fMRI without large data loss, compared to traditional motion correction methods.

Keywords

fMRI; fetal brain; placenta; motion correction; outlier rejection; hyperoxia

1. INTRODUCTION

Subject motion is a major challenge in blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) studies of the brain, and has been addressed by diverse motion correction tools based on linear image registration such as AFNI, AIR, FSL, and SPM.^{1, 2} However, these traditional tools for adult fMRI studies are not successful in achieving acceptable performance for in vivo functional imaging data of the fetal brain and placenta acquired during maternal hyperoxia, given the complex anatomy and multiple organs that involve a high degree of motion.^{3, 4}

In an experimental design that uses maternal hyperoxia to acquire in vivo fMRI data of the fetus, a high degree of fetal motion is common, which is different when compared to the adult brain that tends to move randomly in a small degree like the Brownian motion, and intermittently behaves as a spike returning immediately to the original location.⁵ According to empirical studies, fetal motion tends to be more pronounced in response to maternal hyperoxia, which increases the heterogeneity of fetal movements between two phases: resting state and induction of hyperoxia.⁶ These important differences result in the failure of conventional motion correction tools for fetal functional MRI datasets.

Furthermore, the fMRI hyperoxia data include two independently moving objects such as the fetal brain and placenta. Both have different motion; the fetal brain has a rigid body and moves actively while the placenta passively moves in a relatively small scale but can be easily affected by fetal and maternal movement. On the other hand, the traditional motion correction tools primarily infer that the fMRI image contains either just the brain or a single moving object.² Consequently, these implicit assumptions of these typical tools do not only lead to the failure in estimating motion parameters of two moving objects simultaneously, but also may give rise to lots of volumes which remain wrongly registered even after motion correction due to their high or heterogeneous motion field. Earlier studies have attempted to manually exclude such flawed high-motion volumes that were not compensated by motion correction.⁷ However, manual volume outlier rejection leads to an irrecoverable loss of data. Moreover, its reliability cannot be guaranteed since the rejection criteria is subject to the evaluator's subjective impression.

In this study, we propose an advanced motion correction and volume outlier rejection method to correct severe motion artifacts without unnecessary data loss. The method is customized to the experimental paradigm by applying preprocessing steps separately to each phase as well as to each moving object which is distinct according to its characteristic pattern of movement. It also automatically excludes misaligned volumes by considering the occurrence probability of temporal outliers triggered by object motion that jointly reflects the temporal variation of BOLD signals as well as motion-oriented image mismatching. Moreover, all the missing data are estimated from signals averaged over a region of interest (ROI) on the basis of the sinusoidal regression model with Gaussian uncertainty in order to avoid the data loss in advanced post-processing steps.

This paper is organized as follows. In section 2, the fMRI study design of maternal hyperoxia in the fetus is introduced, and the technical concepts of each step in the proposed motion correction pipeline are described in detail. In section 3, experimental results are shown and our pipeline for motion correction is compared with traditional tools. In section 4, we conclude that the proposed method is effective in enhancing the performance of motion correction in maternal hyperoxia fMRI data of the fetal brain and placenta without deleterious data loss.

2. METHOD

2.1 Data acquisition and preprocessing pipeline

We acquired interleaved echo planar imaging (EPI) sequences on a 1.5T GE MR scanner using an 8-channel receive-only surface coil from 8 healthy fetuses and 8 fetuses diagnosed with complex congenital heart disease (CHD) between 25–39 weeks of gestation. The data were acquired in either coronal or axial views with a matrix size of 128×128 and slice thickness 5–8 mm. The MR parameters were different for data acquired in the axial versus coronal plan. For axial acquisitions, MR parameters were as follows: TR of 3 seconds, 144 volumes, and 17–18 slices. For coronal acquisitions MR parameters included a TR of 2 seconds, 288 volumes, and 23–46 slices.

As shown in Fig. 1, the hyperoxia task paradigm consisted of a two-minute normoxia (so called resting state), followed by 100% oxygen which was administered via a maternal facial oxygen mask for 3 minutes, and additional 2:12 minutes of normoxia to quantify return to baseline. For coronal acquisitions, the 4-minute hyperoxia was followed by returned normoxia during 3:36 minutes.

The inhomogeneity of the radiofrequency field (B1) effect in the resulting MR images was corrected using the 4D nonparametric bias estimator (N4ITK).⁸ Each EPI sequence was then temporally divided into three phases: i) baseline, ii) hyperoxia, and iii) returning baseline. A global motion correction was carried out in each phase sequence, and each phase sequence was spatially segmented using fetal brain and placenta masks manually predefined as illustrated in Fig. 2. All six ROI phases (3 brain, 3 placenta) were processed for local motion correction using sun grid engine (SGE) parallel processing. Thereafter, significantly misaligned volume outliers were automatically detected and eliminated. In ROI-averaged time series, the missing data removed from volume outlier rejection were estimated and imputed to two ROI-averaged time series.

2.2 Motion correction

Let us consider an EPI sequence $\mathbf{X} \equiv \{X_t; t = 1, \dots, N\}$ where X_t is a volume containing both the fetal brain and placenta; $X_t(\mathbf{q})$ denotes the intensity at voxel $\mathbf{q}$ in the volume X_t . The typical approach to motion correction in fMRI data of the adult brain is to align a volume X_t to a template T using rigid or affine image registration.⁹ Without loss of generality, it can be regarded as the correction of global motion which affect the whole image regardless of object motion. The global motion may originate from a number of factors such as subject movement, respiration, and cardiovascular motion. Let $\mathbf{g}_H$ denote a vector of global motion parameters pertinent to either rigid body transform with six degrees-of-freedom (DOF) or affine transform with 12 DOF. Let a voxel $\mathbf{q}$ be mapped to the voxel $\mathbf{q}_H$ through the geometric transform H with the global motion parameter $\mathbf{g}_H$; that is, $\mathbf{q}_H = H(\mathbf{q}; \mathbf{g}_H)$. The global motion vector $\mathbf{g}_H$ can then be estimated by minimizing the cost function f as follows

$$\hat{\mathbf{g}}_H(t) = \arg \min_{\mathbf{g}_H} \sum_{\mathbf{q} \in U} f(X_t(\mathbf{q}), T(H(\mathbf{q}; \mathbf{g}_H))) \quad (1)$$

where $\mathbf{U}$ denotes the full volume including all voxels. This linear image registration has been effectively applied to correct subject motion in typical adult brain fMRI data. However, it does not correct the motion of each individual object when the data include multiple objects moving independently.

Our proposed approach to multi-object data is to employ a multi-stage motion correction framework including local motion correction (LMC) as well as global motion correction (GMC). Overall, it can be approached by delineating a set of optimal motion vectors $[\mathbf{g}_H(t), \mathbf{g}_1(t), \mathbf{g}_2(t)]$ at time t where $\mathbf{g}_1(t)$ is the fetal motion vector and $\mathbf{g}_2(t)$ is the placental motion vector. The global motion vector $\mathbf{g}_H(t)$ is first estimated based on equation (1), and then the local motion vectors $\mathbf{g}_1(t)$ and $\mathbf{g}_2(t)$ are subsequently estimated. In the LMC step, the linear image registration method is optimized to the experimental design in order to deal with challenging patterns of motion in hyperoxia fMRI data of the fetal brain and placenta. The design optimization of local motion correction is achieved using the following two strategies.

The first strategy is to split the entire EPI sequence into several phases and to apply separate and individual motion correction to each phase. As described in section 2.1, the hyperoxia task paradigm followed a single block design containing three phases: baseline, hyperoxia, and return to baseline (see Figure 1). According to the hyperoxia study design, the sequence $\mathbf{X}$ can be separated into three independent phases: baseline, hyperoxia, and return to baseline. The i -th phase sequence is defined on the set of volumes $\mathbf{X}_i \equiv \{X_t; t = z_{i-1}, \dots, z_i\}$ for $1 \leq z_{i-1} < z_i \leq N$. For example, in our fMRI data set acquired in the coronal view, the EPI sequence is split into three phase sequences $\mathbf{X}_1 = \{X_1, \dots, X_{60}\}$, $\mathbf{X}_2 = \{X_{61}, \dots, X_{180}\}$, and $\mathbf{X}_3 = \{X_{181}, \dots, X_{288}\}$. The accuracy of image registration can then be improved by using a unique template dedicated to each of these three phases; in other words, the template $T_t(\cdot)$ corresponding to the volume X_t in time t is defined as the mean volume locally averaged over the phase sequence $\mathbf{X}_i$ to which the volume X_t belongs (not over the whole sequence $\mathbf{X}$). Therefore, the intensity of a voxel $\mathbf{q}$ in the template T_t is given by

$$T_t(\mathbf{q}) \equiv \frac{1}{z_i - z_{i-1} + 1} \sum_{k=z_{i-1}}^{z_i} X_k(\mathbf{q}). \quad (2)$$

This template definition is effective in improving the performance of LMC by reducing the variance between the phase-specific template and each volume, compared to the variance between the full sequence template and each volume.

The second strategy is to deal with the local motion of each moving object separately by restricting the field of view (FOV) for image registration to a local area including one object and its surrounding regions. By contrast, the GMC step incorporates the FOV which is selected to cover the full volume⁹ as depicted in Fig. 3. To achieve this, the ROI masks for the fetal brain and placenta should be defined in each phase sequence. Let $\mathbf{R}_{k,i}$ denote the k -th ROI for the i -th sequence. Thus, we finally have six ROI masks; $[\mathbf{R}_{1,1}, \mathbf{R}_{1,2}, \mathbf{R}_{1,3}]$ for the fetal brain, and $[\mathbf{R}_{2,1}, \mathbf{R}_{2,2}, \mathbf{R}_{2,3}]$ for the placenta. These masks are then dilated by a mean filter of size 3×3 to ensure that the objects of interest are fully included inside the mask by

considering the tolerance of object movement; that is, the dilated mask is given by $\mathbf{R}'_{k,i} \equiv D(\mathbf{R}_{k,i})$ where D is the two-dimensional dilation filter.¹⁰ Then, the FOV is set as the dilated ROI mask $\mathbf{R}'_{k,i}$ to correct local motion of the k -th ROI in the i -th phase sequence. In the i -th phase sequence, the optimal motion vector $\mathbf{g}_k$ of the k -th ROI at time t can be estimated by minimizing the cost function f localized for voxels inside the ROI mask $\mathbf{R}'_{k,i}$ as follows

$$\begin{aligned}\hat{\mathbf{g}}_k(t) &= \arg \min_{\mathbf{g}_k} \sum_{\mathbf{q}_H \in \mathbf{R}'_{k,i}} f(X_t(\mathbf{q}_H), T_t(G(\mathbf{q}_H; \mathbf{g}_k))) \\ &= \arg \min_{\mathbf{g}_k} \sum_{\mathbf{q} \in \mathbf{R}'_{k,i}} f(X_t(\mathbf{q}), T_t(G(H(\mathbf{q}; \mathbf{g}_H); \mathbf{g}_k))).\end{aligned}\quad (3)$$

Note that the geometric transform G of local motion in equation (3) is jointly applied along with the global motion transform H in equation (1). This local motion correction in turn reduces the risk that the cost function in image registration gets stuck in local minima from fMRI data containing either multiple moving objects or dynamically changing surrounding tissues.

2.3 Volume outlier rejection

The motion correction may not be successful in some volumes due to severe subject movement. Those volumes remain misaligned and therefore cannot be used for post-processing. While such erroneous volumes had been manually eliminated in previous fetal fMRI studies,⁷ available tools can detect motion outlier volumes which have a low correlation coefficient with a predefined template. However, these tools are not always successful because they are based on the assumption of between-volume similarity while each volume may undergo the temporal change of intensities. We propose an automatic method to reject such misaligned volumes by considering the temporal change of BOLD intensities.

Let ρ_t denote a volume outlier score (VOS) at time t . Then, the volume outlier rejection (VOP) can be posed as the problem to obtain the missingness vector $\mathbf{m} = [m_1, \dots, m_N]$ such that $m_t = 0$ if $\rho_t < \rho_{th}$ and $m_t = 1$ otherwise where ρ_{th} denotes a threshold. Let us consider an object (either the fetal brain or placenta) moving at time t with negligible rotation. The image at time t would be separated into both an overlapped part and non-overlapped part of object regions with the template image T as shown in Fig. 4. Let $P(B)$ denote the probability of the voxel $\mathbf{q}$ belonging to the non-overlapping part (that is, background) in time t due to the object motion. Since the probability $P(B)$ has the tendency of increasing as the degree of translation increases, the average of $P(B)$ over voxels belonging to the k -th ROI can be exploited as the volume outlier score; that is, $\rho_t = \langle P(B) \rangle_{\mathbf{R}_{k,t}}$ where $\langle \cdot \rangle$ denotes averaging over all $\mathbf{q} \in \mathbf{R}_{k,t}$. The VOS is also called the *motion outlier probability* (MOP). Note that the MOP is determined separately in relation to each individual object; that is, the MOP for the fetal brain would be different from the MOP for the placenta. According to the law of large numbers,¹¹ the MOP can be approximated as follows

$$\rho_t = \frac{V_b}{V} \quad (4)$$

where V_b is the number of ROI voxels not belonging to the overlapped part in time t as shown in Figure 1, and V is the total number of voxels belonging to the predefined ROI. V_b can be estimated as long as the object motion parameters are known, however V_b is unknown in erroneous volumes whose motion parameters have been wrongly estimated.

Instead of estimating V_b based on object motion, the MOP ρ_t can be estimated on the basis of the temporal variation of BOLD signals. Let $P(O)$ denote the outlier probability which is defined as the probability of an ROI voxel $\mathbf{q}$ having an outlier of its BOLD intensity at time t ; in other words, the probability of the voxel intensity at time t being classified as an outlier by a temporal outlier scoring algorithm when a single BOLD signal corresponding to the voxel $\mathbf{q}$ is considered. Then, we have the following relationship according to the Bayes' rule:¹¹

$$P(O) \equiv P(\mathbf{q} \in O | \mathbf{g}_k) = P(O|B)P(B) + P(O|F)P(F) \quad (5)$$

where $P(B)$ and $P(F)$ denote the probabilities of a voxel $\mathbf{q}$ belonging to either background or foreground at time t respectively, $P(O|B)$ is the posterior probability of a non-overlapping voxel (that is, an ROI voxel belonging to the non-overlapping part) having a temporal outlier in its corresponding BOLD signal at time t , and $P(O|F)$ is defined for a foreground voxel (that is, an ROI voxel belonging to the overlapping part) in a similar manner as $P(O|B)$. Suppose that these posterior probabilities are almost constant over certain degrees of translation; that is, $P(O|B) = p_{ob}$ and $P(O|F) = p_{of}$. Then, the probability $P(B)$ can be calculated using the following equation:

$$P(B) \approx \frac{V_b}{V} = \frac{V_o/V - p_{of}}{p_{ob} - p_{of}} \quad (6)$$

where V_o denotes the number of ROI voxels whose BOLD signal intensities are classified as outliers. V_o , p_{ob} , and p_{of} are dependent on how the temporal outlier scores (TOS) are computed for individual voxels. After computing the TOS for each voxel, V_o can be simply computed by counting the voxels with outlier intensity. Because of the assumption on the approximate invariability of posterior probabilities, p_{of} would be lower than the smallest outlier probability over all volumes, and p_{ob} higher than the highest outlier probability.

The volume outlier rejection procedure described above can be performed in a hierarchical way as summarized in Fig. 5. First, the posterior probabilities p_{ob} and p_{of} can be assigned as certain high and small values respectively (for example, $p_{ob} = 0.95$ and $p_{of} = 0.05$). Note that the rough assignment of posterior probabilities can be compensated by controlling the threshold ρ_{th} . Second, the temporal outlier scores are calculated over all ROI voxels in each volume by using one of the existing TOS tools such as AFNI and FSL. Third, the MOP is computed for each volume by counting the number of outlier voxels in equation (6). Finally, the outlier volumes are chosen by thresholding the MOPs and rejected.

2.4 Missing data recovery

Following motion correction and volume outlier rejection, ROI-averaged time series for the fetal brain and placenta are then extracted by averaging the BOLD signals over each ROI. However, the rejection of outlier volumes is followed by data loss, that is, missing data points in ROI-averaged time series, which may in turn lead to unreliable statistical data analyses in the post-processing phase. To circumvent this, we introduce a method of imputing missing data through statistical estimation.

Let $y(t)$ be an ROI-averaged time series, and assume that it has a missing data point at time t_0 . The time series $y(t)$ can be regressed, in a similar manner as described in Ref. 12, using the sinusoidal regression model with Gaussian uncertainty; that is,

$$y(t) = \sum_{k=1}^K \alpha_k \cos(\omega_k t + \phi_k) + e(t) \quad (7)$$

where α_k is the coefficient for the k -th sinusoidal component, both ω_k and ϕ_k are frequency and phase of the k -th sinusoidal component, and $e(t)$ is the Gaussian noise component. In final, the missing data $\hat{y}(t_0)$ can be estimated by estimating the set of model parameters (α_k , ω_k , ϕ_k) and adding the Gaussian noise component with variance $\sigma^2 = \text{var}[y(t)]$ to the deterministic sinusoidal signal. The model parameters (α_k , ω_k , ϕ_k) can be estimated using one of the generic nonlinear least squares methods.¹³

3. RESULTS

To demonstrate the dependency of object motion on the task design, the statistical changes in object translation due to maternal hyperoxia are summarized in Table 1. The degree of three-dimensional translation is represented by the absolute distance of translation (ADT) defined as $D = (T_x^2 + T_y^2 + T_z^2)^{1/2}$ where (T_x, T_y, T_z) denotes the three-dimensional translation vector in the rigid-body motion transform. The average degree of fetal motion was prominently higher than the expectation in the adult brain.¹⁴ The translation of the fetal brain was significantly higher in response to hyperoxia. The increasing rate of mean ADT (from resting state to hyperoxia) was 213.5% in the fetal brain compared to 2.1% in the placenta.

The performance of the proposed method was compared to the FMRIB's linear image registration tool (FLIRT). In both the proposed method and FLIRT, similar parameters for linear image registration were applied; the cost function was based on normal correlation and the maximum search angle was set to be 20°. To analyze the effect of the motion correction methods on outlier reduction, we measured not only the ratio of outliers in structural similarity (SSIM)-associated to luminance, contrast, and structure- between each volume and a template,¹⁵ but also the ratio of temporal outliers. The former reflects outliers in spatial information while the latter reflects outliers in temporal information. Fig. 6 illustrates that both the ratio of structural outlier volumes and the ratio of temporal outlier volumes was significantly reduced using the propose method compared to the FLIRT. Fig. 7 illustrates the progressive reduction of the number of outliers in mean structural similarity in

the multi-stage motion correction pipeline. It shows that the number of SSIM outliers exponentially decreased as the global motion correction and local motion correction were applied sequentially.

After motion correction, the BOLD signals were averaged over each ROI, which produced ROI-averaged time series. Fig. 8 illustrates an example of ROI-averaged time series for the fetal brain and placenta. Some outlier volumes (shaded in Fig. 8) were automatically rejected through the proposed volume outlier rejection process. The posterior probabilities (p_{ob}, p_{of}) were set as (0.95, 0.05), and the MOP threshold ρ_{th} was set as 0.1. The TOS was computed by using the function 3dtoutcount as a part of the AFNI program which detects outliers in time series, and any signal falling outside of 1.5 times of the interquartile range (IQR) was determined to be an outlier. As shown in Fig. 8, the rejected volumes were not identical between the placenta and fetal brain because of their heterogeneous movements. Table 1 shows the statistics on rejected volumes over phases. The increase in the number of rejected volumes during maternal hyperoxia was not significant comparing to the prominent increase in fetal motion.

To verify the performance of the volume outlier rejection, we measured the voxel-wise median absolute residual variation (MARV) score, which is defined as the absolute value of mean residuals in the difference between each volume and the template,⁹ as well as the SSIM scores. Fig. 9 illustrates the distribution of MARV scores over voxels. As shown in the histogram, the average MARV score was greater than 30 before volume outlier rejection. After the VOR process, the average MARV score was significantly reduced at a value less than 10. This indicates that the difference of intensities between each volume and template was significantly reduced using volume outlier rejection. Fig. 10 shows the effects of volume outlier rejection on structural similarity between each volume and template. While some outlier volumes in SSIM scores were present before volume outlier rejection, all volumes had high SSIM scores (> 0.97) after those outlier volumes were rejected.

The missing data points produced after the rejection of outlier volumes were recovered to obtain the fully recovered time series for the fetal brain and placenta. In the sinusoidal regression model of equation (7), the number of sinusoidal components K was set to be 3. Fig. 11 illustrates the regression of ROI-averaged time series with missing data; the deterministic time courses were estimated from both the fetal brain and placenta on the basis of the sinusoidal regression model. As illustrated in Fig. 8, the change in BOLD signals was pronounced in the placenta while there were no significant changes in the fetal brain. This difference in time courses between the fetal brain and placenta was also previously described in Ref. 3.

As an example of post-processing analysis after the proposed preprocessing pipeline is applied, we performed the correlation analysis of ROI-averaged time series between the placenta and fetal brain. As shown in Fig. 12, the brain-placenta correlation coefficient increased as gestational age increased.

4. DISCUSSION AND CONCLUSION

We propose a robust preprocessing pipeline which allows us to effectively correct serious fetal motion in fMRI data of the placenta and fetal brain acquired using a hyperoxia stimulus design. This is accomplished not only by optimizing the motion correction pipeline to the applied experimental design, but also by automatically rejecting outlier volumes. We suggest a novel volume outlier score based on the motion outlier probability to improve the performance of detecting outlier volumes by considering the temporal variation of BOLD signals. In addition to the automatized volume outlier rejection, we also propose a method of recovering the missing data resulting by the VOR process in order to allow advanced time series analyses during post-preprocessing.

This multi-stage motion correction pipeline was developed based on the assumption that the fetal brain and placenta demonstrate heterogeneous motion between resting state and hyperoxia. Indeed, the statistics of estimated rigid-body motion parameters confirmed that the fetus showed increased movement in response to hyperoxia. The phase-dependent motion correction was appropriate for stimulus-based fetal fMRI while it is not generally required in stimulus-based fMRI of the adult or infant brain where the motion heterogeneity between phases is not significant. The technical limitation in the proposed motion correction method deserves mention. While the proposed method is still based on the assumption that any moving object has a rigid body to allow linear image registration, the placenta has a deformable shape which is variable during data acquisition and between subjects, which in turn may affect the reliability of motion correction. Algorithms that correct placental motion may be optimized by dealing with the variability of placental shape.

The performance of the proposed motion correction pipeline was shown to be significantly better when compared to FLIRT, which is one of typical motion correction tools based on linear image registration. The performance evaluation shows that the proposed approach decreases outlier volumes in the resulting ROI-averaged time series. Worthy of note is that the performance evaluation does not directly demonstrate the accuracy in estimating motion parameters. Therefore, the performance needs to be confirmed quantitatively using a simulation study. Regarding the performance of volume outlier rejection, we illustrate that the proposed VOR process improves the similarity in both voxel-wise time courses and spatial structure between each volume and the template. Unlike the significant increase in estimated fetal motion during hyperoxia, the number of volume outliers increased modestly during hyperoxia. This offers indirect evidence that the motion correction was successful in reducing the number of outlier volumes.

Finally, we tested the applicability of the proposed preprocessing pipeline on post-processing of fetal data. Increasing functional connectivity between the placenta and fetal brain was demonstrated through correlation analyses between ROI-averaged time series. This phenomenon was similar with the previous studies in resting state functional connectivity of the fetal brain.⁷ This preliminary analysis of hyperoxia-based fMRI data showed the feasibility of investigating the functional interaction between the fetal brain and placenta by applying the proposed preprocessing pipeline.

In summary, this work provides an important technical advancement for reliable preprocessing in stimulus-based fMRI studies of the fetal brain and placenta, and holds much promise for developing future non-invasive biomarkers for altered fetal brain-placenta circulation.

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Figure 1.

The overall pipeline for of motion correction and outlier rejection customized for the hyperoxia fMRI studies of the fetal brain and placenta; GMC (global motion correction), LMC (local motion correction), OR (outlier rejection), and MDR (missing data recovery).

Figure 2.
An example of ROI definition for the fetal brain and placenta.

Figure 3.
Fields of view in both global and local motion correction.

Figure 4. Motion-based overlapping between the predefined template ROI and updated ROI at time t . The object motion separates the predefined ROI into the non-overlapped part as shaded and the overlapped part. The area of non-overlapped part increases as the degree of object motion increases.

Figure 5.
The volume outlier rejection procedure.

Figure 6. Comparison of outliers between the proposed method and FLIRT; (a) the ratios of volume outliers and (b) the ratios of temporal outliers.

Figure 7.

The change in the number of outliers in structural similarity of the placenta in each step of the proposed preprocessing pipeline. GMC, LMC, and VOR indicate global motion correction, local motion correction, and volume outlier rejection respectively.

Figure 8.

An example of volume outlier rejection and missing data recovery at ROI-averaged BOLD time series for the fetal brain and placenta. Red data points marked with asterisks represent estimated values corresponding to missing data at rejected volumes.

Figure 9.

The change in median absolute residual variation (MARV) scores after volume outlier rejection. The left column shows the spatial distribution of voxel-wise MARV scores of the fetal brain in a slice, and the right column shows the histogram of MARV scores.

Figure 10.

The change in structural similarity between each volume and the template after volume outlier rejection.

Figure 11.
An example of regression of ROI-averaged BOLD time series with missing data.

Figure 12.
The age dependence of correlation coefficients of ROI-averaged BOLD time series between the fetal brain and placenta. ($R^2 = 0.3$)

Table 1

Statistics of rigid-body motion parameters and rejected volumes in the fetal brain and placenta.

		Baseline	Hyperoxia	Return to baseline
ADT (mm)	Fetal brain	10.31 ± 25.24	32.32 ± 100.01	9.76 ± 22.34
	Placenta	1.08 ± 0.79	1.11 ± 0.69	1.07 ± 0.69
Number of rejected volumes		1.63 ± 1.93	2.13 ± 2.31	2.19 ± 2.81