IMPACT: Image-Based Physiological Artifacts Estimation and Correction Technique for Functional MRI

Kai-Hsiang Chuang and Jyh-Horng Chen*

Functional MRI (fMRI) signal variation induced by respiratory and cardiac motion affects the activation signal and limits the accuracy of analysis. Current physiological motion correction methods require either synchronization with external monitoring of respiration and heartbeat, specialized pulse sequence design, or k-space data. The Image-based Physiological Artifacts estimation and Correction Technique (IMPACT), which is free from these constraints, is described. When images are acquired fast enough to sample physiological motion without aliasing, respiratory and cardiac signals can be directly estimated from magnitude images. Physiological artifacts are removed by reordering images according to the estimated respiratory and cardiac phases and then subtracting the Fourier-fitted variation from magnitude images. Compared with the k-space-based method, this method can efficiently and effectively reduce the overall signal fluctuation in the brain and increase the activated area. With this new technique, physiological artifacts can be reduced using traditional fMRI pulse sequences, and existing data can be corrected and reanalyzed without additional experiments. Magn Reson Med 46:344–353, 2001. © 2001 Wiley-Liss, Inc.

Key words: functional MRI; physiological noise; retrospective motion correction; image processing; motion artifact

Based on blood oxygenation level-dependent (BOLD) contrast, functional MRI (fMRI) has become a powerful method to map the working brain (1,2). However, the tiny signal change coming from neural activation is vulnerable to various kinds of artifacts, especially gross head motion (3) and physiological motion, such as respiration and heartbeat (4,5). Physiological motion, which increases the signal variation even when the head does not move, will decrease the statistical significance in fMRI analysis and contaminate the hemodynamic response function (HRF) in event-related experiments. Thus it will decrease the signal sensitivity and spatial specificity in fMRI (6). Respiratory artifact is caused by the variation of magnetic field distribution in the brain (7). It is found to produce both global changes in phase image and localized variations in magnitude image, especially near ventricles. In addition, regions closer to the chest are more severely affected. Cardiac motion, which causes pulsation in arteries, veins, and cerebrospinal fluid, affects both the magnitude and phase image in regions near vessels and ventricles (8). Therefore, deeper cortical structures, which are usually closer to ventricles or the chest, are susceptible to these artifacts. Moreover, as we move to high-field systems for more BOLD contrast, these artifacts increase with field strength (7).

Several techniques have been proposed to minimize physiological noises, including navigator echo (9), retrospective gating (6,10), digital filtering (11), k-space-based estimation and correction (12,13), pulse sequence gating (14), and motion-ordered data acquisition (15). Although these techniques are effective, they are still inconvenient to apply in many situations. The problem of the navigator correction method is that insertion of the navigator echo delays the data acquisition window. The artifacts produced by the T* effect, which is more critical in high field, then become worse. Besides, the navigator and image data are not collected at the same time, so the estimation and correction of motion need some kind of extrapolation. Retrospective gating requires precise synchronization of the fMRI data acquisition with externally recorded physiological cycles. This limits its utilization in usual clinical environments. Digital filtering also requires externally recorded physiological cycles to find the frequency bands to be filtered. Moreover, when the spectrum of functional activation overlaps with physiological fluctuation, this method cannot remove the artifacts without affecting the functional signal. Estimation and correction of noises from k-space can only be applied to conventional gradient-echo imaging sequences or an echo-planar imaging (EPI) sequence with a repetition time (TR) short enough to catch physiological cycles. In addition, this method requires k-space data, which are not readily available in many institutions. The problem of pulse sequence gating is that it makes the acquisition time longer or variable. It is also difficult to remove respiratory and cardiac motion simultaneously. Physiological motion-ordered data acquisition requires synchronization with externally recorded physiological cycles and well-adjusted acquisition timing of each slice.

The requirements of external monitoring of physiological activities, specialized pulse sequence design, and/or k-space data for correction, limit the application of these methods in many institutions, especially clinical environments. Here we describe an image-based method—Image-based Physiological Artifacts estimation and Correction Technique (IMPACT)—to retrospectively estimate and correct signal fluctuation induced by respiration and heartbeat. It is reported that when images are acquired fast enough to avoid aliasing of the cardiac cycle, physiological signals can be estimated from the center k-space point and the projection along the readout direction (12). Thus the information on motion could also be estimated from the magnitude image. Using this information, both physiological noises can be removed without external recording of physiological cycles, k-space data, or modification of existing pulse sequences. This method is demonstrated by

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visual fMRI data acquired with short-TR EPI and compared with the \( k \)-space correction method proposed by Hu et al. (6).

**METHODS**

There are some assumptions in this method. First, respiration and cardiac pulsation are assumed to be quasiperiodical. Because both kinds of motion are the most prominent periodic signal sources in the brain, the periodicity should be observed in the signal time-course of most brain regions. Hence, the respiratory and cardiac frequencies can be estimated by the frequency components that most pixel time-courses contain. Then the respiratory and cardiac signals can be estimated from the pixel time-courses that contain strong physiological fluctuations. The other assumption is the induced fluctuation acts like additive noise to the time-series signal. Because the signal-to-noise ratio (SNR) is very low in higher \( k \)-space, only part of the \( k \)-space will be corrected by the \( k \)-space–based correction methods. Subtracting the noises in image space will be more effective and efficient (10). Therefore, reordering the images according to the estimated respiratory and cardiac phases and subtracting the fitted physiological signal changes from each pixel time-course will correct both artifacts.

**Estimation of Physiological Signals**

First, each pixel time-course in the brain is normalized by its mean value:

\[
A_i(x, y) = \frac{I_i(x, y) - \bar{I}(x, y)}{I(x, y)}, \quad i = 1, \ldots, N \tag{1}
\]

where \( I_i(x, y) \) is the image of the \( i \)-th scan,

\[
\bar{I}(x, y) = \frac{1}{N} \sum_{i=1}^{N} I_i(x, y),
\]

and \( N \) is the total number of scans. Then the dominant frequency components in the respiratory and cardiac frequency ranges are identified from the spectrum of each pixel. The respiratory frequency range is from 0.1 to 0.5 Hz, corresponding to respiration rates varying from 6 to 30 cycles/min; the cardiac frequency range is from 0.75 to 1.5 Hz, corresponding to heart rates varying from 45 to 90 beats/min. These values, chosen to incorporate normal breathing and pulse rates, were adjustable to allow for cases with very high or very low rates. To find the frequency components that appeared most in the brain, two histograms of dominant frequency components in the respiratory and cardiac frequency ranges were generated. The corresponding physiological frequency was determined by the frequency with the largest pixel number in the histogram. Because high-frequency harmonics in a respiratory signal are not significant, the fundamental frequency is easily identified. Although cardiac signal has many significant harmonics, they are not as strong as the fundamental frequency. Hence, the cardiac frequency could also be identified without ambiguity.

To estimate respiratory and cardiac signals, we looked for the pixels that contain strong physiological fluctuations. The pixels with dominant frequency components around the identified physiological frequencies were selected and their relative powers were computed to determine the amount of physiological fluctuations. This relative power was calculated by dividing the power within 0.1 Hz, which was the width of the usual frequency peak, centered at the dominant frequency by the power within the respiratory or cardiac frequency range mentioned in the previous paragraph. Although a more complicated algorithm can estimate the relative power more accurately, this simple method was sufficient to provide effective and efficient estimation. Then the physiological signals were obtained by band-pass filtering the pixel time-courses with the highest respiratory or cardiac power. Because the respiratory signal, which resides in the low frequency range, is easily affected by interference from other signal and noise sources, it was estimated by filtering the averaged time-courses of 100 pixels with the highest relative powers. The filter we used was a fourth-order band-pass Butterworth digital filter to provide sharp cut-off. Because the cardiac signal is less affected by interference from other signals, it was estimated by filtering the pixel time-course with the highest relative power. Empirically, a first-order filter was sufficient to provide good results. The filter pass-bands were chosen to completely incorporate the main peak in the spectrum of respiration or heartbeat. The pass-band for respiration was from 0.1 Hz to the identified respiratory frequency plus 0.075 Hz, which was approximately half the width of the usual respiratory frequency peak. If the identified respiratory frequency was closer to 0.1 Hz, the lower cut-off frequency was set to a lower value. The pass-band for the cardiac signal was determined empirically. We found that pass-band with approximately four times the width of the cardiac frequency peak, i.e., usually about \( \pm 0.35 \) Hz, centered at the identified cardiac frequency could produce better results.

**Correction of Physiological Noises**

To correct the physiological artifacts, we used a method similar to that proposed by Hu et al. (6) but applied it in image space. In this method, images were reordered into normalized respiratory and cardiac cycles by their relative phases (denoted as \( \theta_i \), where \( i \) represents the \( i \)-th image) within the corresponding physiological period:

\[
\theta_i = \frac{i - T_s(j)}{T_s(j+1) - T_s(j)} \tag{2}
\]

where \( T_s(j) \) and \( T_s(j+1) \) were the starting and ending points of the \( j \)-th physiological cycle, respectively. The starting and ending points were defined by the peaks of the identified physiological signals. From the reordered data, the effects of physiological motion were estimated by fitting to a second-order Fourier series:

\[
F(\theta) = A_0 + \sum_{n=1}^{2} A_n \cos(2n\pi\theta) + \sum_{n=1}^{2} B_n \sin(2n\pi\theta) \tag{3}
\]
where $A_0$, $A_m$, and $B_n$ were coefficients to be fitted. The physiological fluctuations were corrected by subtracting the estimated fluctuations from the time-course signal of each pixel.

**Simulation**

To evaluate the performance of IMPACT in the presence of functional activation, five kinds of functional responses with different alternating times were simulated. Four of them were block designs with stimulating/rest times of 30, 20, 15, and 10 s, corresponding to alternating frequencies of 1/60, 1/40, 1/30, and 1/20 Hz, respectively. The other was an event-related design with 1 s of stimulation and 4 s of rest, i.e., an alternating frequency of 1/5 Hz. Thus, the spectrum of functional activation didn’t overlap with respiratory or cardiac frequency in the four kinds of block design conditions, whereas the one in the event-related design condition overlapped significantly with respiration. All of the simulated responses were modeled by the HRF in SPM99 software (16) and the activation signal changes were varied from 1%, 2%, ..., to 5%. The simulated responses were superimposed on pixel time-courses chosen from one volunteer’s data that were heavily contaminated by respiratory or cardiac fluctuation. After processing by IMPACT, the correlation with the original HRF was calculated to evaluate the effectiveness.

**MRI Experiments**

All experiments were conducted on a Bruker MedSpec 3T whole-body system (Ettlingen, Germany) with a birdcage head coil. Ten healthy volunteers (eight men and two women; ages 20–35 years) were studied, and consents were obtained before the experiments. To minimize gross head motion, foam pads were used to immobilize the subjects’ heads during the scan. $T_1$-weighted inversion recovery rapid acquisition with relaxation enhancement (RARE) images were acquired to localize anatomic locations. To simulate functional studies, single-slice gradient-echo EPI was acquired repeatedly for 2 min (400 time frames), with TR = 250 ms, echo time (TE) = 40 ms, matrix size = 128 $\times$ 128 or 64 $\times$ 64, field of view (FOV) = 25 $\times$ 25 cm, and slice thickness = 5 mm. Four volunteers were also scanned with TR = 200 and 150 ms to evaluate the effect of different TRs. Axial slices crossing and at different levels above and below the calcarine sulcus, and sagittal slices crossing the midline were acquired to evaluate the effectiveness of the proposed method at different positions. To validate the estimated physiological cycles, respiratory and cardiac motion in the eight men was monitored simultaneously by a pressure belt and electrocardiogram (ECG) leads. The physiological signals were digitized by an analog-to-digital card (model PCL-818HG, Advantech, Taipei, Taiwan, R.O.C.) on a personal computer with a sampling rate of 100 Hz. The respiratory signal was filtered by a low-pass digital filter with cut-off frequency at 0.5 Hz. The cardiac signal was filtered by a band-pass digital filter with the pass-band from 0.75 to 3 Hz.

Four of the men also participated in visual fMRI studies. Visual stimulation was delivered by a pair of red light-emitting diode goggles flashing at 8 Hz. The paradigm was a block design consisting of two off-periods and one on-period. Each period lasted 30 s. Additional 10-s dummy scans were also acquired in the beginning of each run. Four hundred single-slice EPI images were acquired with TR = 250 ms, TE = 35 ms, matrix size = 64 $\times$ 64, slice thickness = 4 mm, and FOV = 22 $\times$ 22 cm. A sagittal slice crossing the midline or an oblique axial slice crossing the calcarine sulcus was acquired.

**Data Analysis**

Images of the first 40 scans were discarded before further processing to make sure that the MR signal had reached steady state. IMPACT was applied to the reconstructed magnitude images. The k-space correction method using externally monitored respiratory and cardiac cycles was applied to the magnitude and phase of the k-space data before reconstruction (6). Functional activation maps were obtained by cross-correlation analysis with the correlation coefficient threshold = 0.5 (17). Root mean square (RMS) errors of the intervals between peaks of the estimated physiological signals and the monitored ones were calculated. The percent error of the estimated timing was defined by dividing the RMS error by the mean physiological period. To evaluate the effectiveness of the correction, we calculated the coefficient of variation (CV) of each pixel in the brain. The CV was calculated by dividing the standard deviation (SD) by the mean of the pixel time-course. The difference of the CV after correction was mapped to visualize the effect of correction at different regions in the brain. The mean and SD of the CV values in the brain were also calculated to evaluate the overall effectiveness.

**RESULTS**

Figure 1 shows the histogram of the dominant frequency components of one subject. Within the respiratory frequency range, it is apparent that most pixels show a strong frequency component near 0.156 Hz (Fig. 1a); within the cardiac frequency range, most pixels contain a frequency component of 1.03 Hz (Fig. 1b). The estimated respiratory signal waveform based on the identified respiratory frequency and the monitored respiratory signals are shown in Fig. 2a. Figure 2b shows the estimated and monitored results of the cardiac signal. Although the waveform and phase of the estimated signals are not exactly the same as the monitored signals, the relative timings of the signal peaks are quite close. The spectrums of the estimated and monitored respiratory/cardiac signals are shown in Fig. 2c and d. The main peaks in the spectrums of the estimated and monitored signals are the same, whereas some differences can be found in some minor frequency components, especially for the cardiac signal. This minor difference would not affect the performance of correction inasmuch as the most important value to be estimated is the cardiac phase rather than exact ECG timing and waveform. The result confirms that the estimated physiological frequencies are correct and the estimated signals are very close to the actual physiological cycles.

Figure 3a and b shows the result of Fourier fitting after reordering the time-course signals of two pixels significantly affected by cardiac and respiratory motion into the
normalized cardiac/respiratory phases, respectively. The signal change induced by cardiac motion is not fitted very well because the sample number within one cardiac cycle is low. When we compared the results after correcting the physiological fluctuations by IMPACT (Fig. 3c and d) and $k$-space correction (Fig. 3e and f), we found that the effectiveness of both methods in correcting respiration-induced signal variation is similar. Nevertheless, the cardiac-related signal variation corrected by IMPACT is not as good as the $k$-space method owing to the inherent limitations of insufficient sampling. However, the spectrums of both pixel time-courses show that the physiological artifacts are removed successfully (Fig. 4).

From the change of the CV after correction by the $k$-space–based method and IMPACT, it can be seen that signal fluctuation in most parts of the brain is reduced (Fig. 5). Signal variations near the ventricles, sulci, and vessels are decreased significantly. Although the $k$-space–based method is more powerful in correcting artifacts around some portions of the cortical areas and in ventricles, the signal variations in some other parts of the brain are increased. On the contrary, fluctuations of almost all pixels are decreased by IMPACT. Table 1 compares the mean and SD of the CV values in the brains of 10 subjects before and after correction. IMPACT reduces the overall variation with a smaller or comparable mean and SD compared to the $k$-space–based method. In addition, even when the $k$-space correction method is inapplicable owing to the lack of physiological monitoring data, IMPACT still works well.

IMPACT improved the correlation with actual HRF in all simulated paradigm design conditions and signal change levels. The improvement was greater for smaller signal changes. This showed that reduction of physiological fluctuation could produce more accurate HRF estimation and improve the statistical significance in analysis. Thus activated regions with smaller signal changes could be detected.

FIG. 1. The histogram of dominant frequency components of one subject within the (a) respiratory and (b) cardiac frequency ranges. The frequency components that most pixels contain represent the respiratory and cardiac frequency, respectively.

FIG. 2. The comparison of the estimated and monitored (a) respiratory and (b) cardiac signals of the same subject in Fig. 1. The signal variations are similar, with slight differences in waveform and phase. The spectrums of (c) respiratory and (d) cardiac signals show that the main frequencies of the estimated signals are the same as the actual ones.
The activation maps of two subjects from the visual fMRI studies are shown in Fig. 6. Both IMPACT and k-space correction increased the activated area in similar regions. The changes in the activated area of four volunteers are listed in Table 2. The activated pixel number increased from 7% to 28%, which is comparable with the k-space correction method. Furthermore, compared with correcting only respiratory fluctuation, reduction of cardiac fluctuation is more influential on the activated area. This implies that cardiac motion is a very important physiological noise source affecting visual fMRI activation.

**DISCUSSION**

An image-based postprocessing method for correcting physiological artifacts in fMRI without the need for physiological signal monitoring, k-space data, or modification of existing pulse sequences has been proposed and demonstrated. This method can easily be applied to functional data acquired by existing ultrafast imaging sequences, such as EPI or spiral scan, and even to previously acquired data. Because processing is done in image space, it can be utilized in institutions in which k-space data are not easily

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**FIG. 3.** The time-course signals of two pixels contaminated more by (a) respiratory and (b) cardiac motion, respectively, are reordered into unit cycles according to the estimated cardiac and respiratory phases, respectively. The solid lines represent the Fourier fitting curves of the physiological fluctuations. (c, d) The signal variations after subtracting the fitted fluctuation from the signals to remove the effect of respiratory and cardiac motion. (e, f) The signal variations of the same pixels after correction by the k-space–based method. The effectiveness of both methods in correcting respiratory fluctuation is similar. The k-space correction method is superior in correcting cardiac-related variations because of the high sampling rate of the ECG recording.
accessible. The only requirement is that the scan time between consecutive frames (i.e., TR) should be short enough to sample respiratory and cardiac motion without aliasing.

The other advantage of this method is that the processing time is very short compared to the \( k \)-space correction method. Because \( k \)-space correction needs to process phase and magnitude of the whole \( k \)-space, the amount of data and calculation is much greater than processing in image space. Furthermore, inasmuch as IMPACT only considers the pixels in the brain, only a fraction of the original image is processed. Thus processing time can be reduced even more.

Compared with IMPACT, the \( k \)-space–based method can reduce more fluctuation in some regions, such as the ventricles, because its information on respiratory and cardiac phases is much more accurate. However, the \( k \)-space–based method also increases signal variation in some portions of the brain. This is because only part of the \( k \)-space is changed and correlation in image space is introduced. Correction in image space avoids this problem and can improve the signal stability of almost every pixel in the brain.

Although the waveforms and the phases of the estimated signals are not exactly the same as the signals monitored by the pressure belt and ECG leads, the recorded and the estimated cycles are close. Because the correction is done by reordering the images into a normalized respiratory/cardiac phase, the relative, rather than the exact, timing of an image within a respiratory/cardiac cycle is the key to successful correction of the artifacts. If the relative timing deviates significantly, the correction will be of only slight, or even no effect. In our study, the RMS errors of the estimated cycles with respect to the actual ones were usu-

FIG. 4. The spectrums of the time-courses of pixels in Fig. 3 (a and c) before and (b and d) after correcting by IMPACT and the \( k \)-space–based method. IMPACT successfully removes the signal variations induced by cardiac and respiratory motion. Although the cardiac-induced signal variation is not fitted very well owing to insufficient sampling of cardiac cycles, the fluctuation is still suppressed significantly.

FIG. 5. The mapping of changes in the CV after correcting by (b) the \( k \)-space–based method and (c) IMPACT. Overall signal variations are reduced (blue colors), especially in ventricles and around sulci. Although the \( k \)-space–based method can reduce more signal fluctuation in some regions near the cortex and in ventricles, variations in some other regions are increased. On the contrary, fluctuations of almost all pixels are decreased by IMPACT. The mean and SD of the CV values in the brain are listed as subject 1 in Table 1. a: The averaged EPI image. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
ally less than 7.5%, which is enough to produce good results. In some cases, the relative respiratory phase can be detected more precisely using the trough instead of the ridge. Usually we identify the respiratory phase using both kinds of peaks and choose the phase that reduces signal fluctuation more.

Because the waveform of the estimated respiratory signal is still not the same as the monitored one, respiration depth could not be easily determined. Thus, the effect of respiration depth on signal fluctuation is not considered in this method. However, the respiratory-related signal variation can generally be reduced in our experiments. Although the reduction will be less in regions dominated by respiratory fluctuations, the difference is slight. For example, the SD of the pixel in Fig. 3a is reduced by 31.0% using IMPACT, compared with 34.2% using the method that incorporates respiration depth in the correction (10).

Changing various parameters in the estimation, such as frequency ranges, filter bandwidths, and filter type, could improve the quality of the estimated physiological cycles. When estimating respiratory cycle, we found that if the higher cut-off frequency could be high enough to cover the first deep point beyond the respiratory frequency peak, the resulting fluctuation would be smaller. If low-frequency fluctuations were strong, increasing the lower limit of the respiratory frequency range could improve the accuracy of the respiratory frequency estimation. Empirically, the optimal pass-band for estimating the cardiac cycle was about four times the width of the cardiac frequency peak measured from the baseline. The filter type

<table>
<thead>
<tr>
<th>Subject</th>
<th>Original</th>
<th>k-Space–based method</th>
<th>IMPACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0816 ± 0.0284</td>
<td>0.0789 (−3.31%) ± 0.0298</td>
<td>0.0790 (−3.19%) ± 0.0259</td>
</tr>
<tr>
<td>2</td>
<td>0.0996 ± 0.0436</td>
<td>0.0988 (−0.803%) ± 0.0433</td>
<td>0.0980 (−1.61%) ± 0.0431</td>
</tr>
<tr>
<td>3</td>
<td>0.0881 ± 0.0307</td>
<td>0.0874 (−0.795%) ± 0.0303</td>
<td>0.0870 (−1.25%) ± 0.0304</td>
</tr>
<tr>
<td>4</td>
<td>0.0601 ± 0.0380</td>
<td>0.0569 (−5.32%) ± 0.0345</td>
<td>0.0567 (−5.66%) ± 0.0345</td>
</tr>
<tr>
<td>5</td>
<td>0.171 ± 0.107</td>
<td>N/A</td>
<td>0.169 (−1.17%) ± 0.106</td>
</tr>
<tr>
<td>6</td>
<td>0.114 ± 0.0468</td>
<td>N/A</td>
<td>0.111 (−2.63%) ± 0.0451</td>
</tr>
<tr>
<td>7</td>
<td>0.0406 ± 0.0157</td>
<td>0.0393 (−3.20%) ± 0.0151</td>
<td>0.0393 (−3.20%) ± 0.0151</td>
</tr>
<tr>
<td>8</td>
<td>0.0284 ± 0.0122</td>
<td>0.0273 (−3.87%) ± 0.0110</td>
<td>0.0273 (−3.87%) ± 0.0112</td>
</tr>
<tr>
<td>9</td>
<td>0.119 ± 0.0644</td>
<td>0.114 (−4.20%) ± 0.0375</td>
<td>0.114 (−4.20%) ± 0.0546</td>
</tr>
<tr>
<td>10</td>
<td>0.0380 ± 0.0200</td>
<td>0.0317 (−16.6%) ± 0.0139</td>
<td>0.0326 (−14.2%) ± 0.0154</td>
</tr>
</tbody>
</table>

The numbers in the parenthesis are the percent changes compared with the original ones.

N/A, not available.

FIG. 6. Visual cortex activation maps of two subjects: (a) subject 9 and (b) subject 10 in Table 2. The activation maps of original data, after correcting by the k-space–based method, by IMPACT, and the $T_1$-weighted high-resolution RARE images are labeled as 1, 2, 3, and 4, respectively. Both correction methods increased the activated areas and the regions were very close. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]
could also be changed. Considering that respiratory and cardiac signals are not stationary, wavelet-based filtering may perform better than traditional filters. However, unless the physiological cycle of the subject varies significantly, these fine adjustments are usually not necessary because the gain in performance is small.

Another issue is related to the requirements of a short TR. Although the periodicity of respiration and heartbeat would not change even when their signals are aliased, estimating their corresponding frequencies from the aliased time-course signal is still difficult. This is because (other than physiological fluctuations) an fMRI temporal signal may contain functional activation, low-frequency fluctuation (18), thermal noise, and system drift. Most of them reside in the low-frequency region and could not be easily discriminated from the aliased physiological signals. Thus the TR should be short enough to avoid aliasing.

Because one cardiac cycle is only sampled at 4–6 points when TR equals 250 ms (compared to 80–90 points using an ECG recording), the cardiac phase cannot be estimated quite as accurately, as can be seen in Fig. 3b. The Fourier fitting under this condition did not fit the cardiac-related variation very well and the fluctuation reduction was not as good as that of respiration. This could explain why the performance of IMPACT is inferior to the method based on recorded physiological cycles. Although using a shorter TR could improve the sampling for the cardiac signal and would in turn reduce more cardiac-related signal fluctuation, the resulting decreased SNR and increased variability would compromise the overall performance. Therefore, this could not always improve the performance.

The slice position and subject differences do not seem to make the estimation of respiratory/cardiac frequency and signal invalid. For slice positions that are more affected by physiological motion, such as sagittal views or axial views closer to the chest, the estimation is more precise and there is more improvement in signal stability. However, two conditions could influence the estimation of the respiratory signal. One is that when the respiration rate is very low (close to or less than 0.1 Hz), the estimated signal would be affected by interference from other low-frequency fluctuations in the brain. Because the precision of the estimated cycles would be degraded, the reduction of respiratory fluctuation would be less, depending on the degree of interference. In one of our study’s cases (not shown here) in which about a quarter of the respiratory energy was less than 0.1 Hz, the reduction of mean CV in the brain was about 10% less than the result using a down-sampled monitoring signal for correction. This slight decline in performance shows that, to some extent, this method still works fine. But when the subject’s respiration rate is extremely low, a more elaborate method should be developed to remove the interference from low-frequency fluctuations.

The other condition is that when the respiration rate and depth vary significantly during the data acquisition, the spectrum of the respiratory signal will be broadened. Then the respiratory frequency estimated from the histogram of dominant frequency components may not correspond to the actual one. Figure 7 shows the estimated and monitored respiratory signals and their power spectra.

**Table 2**
The Increases of the Activated Areas After Processing by IMPACT and the k-Space–Based Correction Method

<table>
<thead>
<tr>
<th>Subject</th>
<th>IMPACT</th>
<th>k-Space–based method</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>7.14% (0%)</td>
<td>9.52%</td>
</tr>
<tr>
<td>8</td>
<td>12.9% (3.33%)</td>
<td>6.45%</td>
</tr>
<tr>
<td>9</td>
<td>28.6% (9.52%)</td>
<td>26.2%</td>
</tr>
<tr>
<td>10</td>
<td>11.7% (3.33%)</td>
<td>13.3%</td>
</tr>
</tbody>
</table>

The numbers in the parenthesis are the changes of the activated areas without correcting cardiac fluctuation.
tored respiratory signal and spectrum from one study of subject 3. The main peak (around 0.26 Hz) in the spectrum of the estimated signal, which deviates from the main peak (around 0.19 Hz) of the monitored data, is only coincident with the second highest peak of the monitored data (Fig 7b). Considering the respiratory signal is estimated by averaging the time courses with large power around the identified frequency, the effect of inaccurate frequency estimation could be reduced by the incorporation of other frequency components. Comparing the estimated and the monitored respiratory signals in Fig. 7a, we can see that there are only a few differences in the cycles. After correction, the reduction of the mean of the CV in the brain is 1.84%, which is less than the 1.86% reduction if we use the down-sampled monitored signal for correction. The tiny difference shows that IMPACT is quite robust in this condition.

The last consideration concerns the effectiveness of physiological noise reduction in the presence of functional activation. In the usual fMRI paradigm design, the overlap of the spectrums of hemodynamic response and physiological motion is minimized. It may not seem necessary to remove physiological noises—and even if it is needed, applying a band-pass filter would seem to be sufficient. In fact, whether from the simulation or human experimental data, the reduced signal variation can increase the statistical significance in analysis. Furthermore, removing the physiological fluctuations can help us obtain a more accurate HRF estimation, which is very important for event-related fMRI analyses. Indeed, a digital filter is more powerful than the approach we adopted in removing physiological noises because it can suppress all the frequency components in the stop-band. However, when the spectrums of HRF and physiological motion overlap, a filter will remove not only the noises but also the signal. Figure 8 shows the result of applying a notch filter to the simulated data with the spectrum of functional activation overlapping with respiration. Although we have narrowed the stop-band to cut the “artifact” precisely, the actual response is still affected. Data confronting this problem includes event-related designs with short intertrial intervals, or block- and event-related designs acquired with a TR longer than 500 ms, in which physiological fluctuations begin to alias into the low-frequency range. Using the method proposed here only removes the fluctuations synchronized with respiratory and cardiac cycles. Of course, if the functional activation were synchronized with respiration or heartbeat, none of the existing postprocessing methods would be effective. We would have to eliminate the artifacts during image acquisition.

CONCLUSIONS
In this work, a new method for removing physiological signal variations in fMRI is described. Experimental results show that this method can reduce overall signal fluctuation and increase functional sensitivity without the need for external monitoring of physiological motion, k-space data, or modification of existing pulse sequences. Consequently, physiological noises can conveniently be removed from magnitude images and this technique can easily be applied in institutions in which k-space data are not readily available. Even previously acquired data can be processed and reanalyzed without additional experiments. For subjects whose respiration rate is very low or variable, a more elaborate method is under investigation to improve the estimation of respiratory cycles.

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