Multimodal investigations into the pathophysiology of myoclonus-dystonia

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Robust EMG-fMRI artifact reduction for motion (FARM)

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Abstract

Objective: Current template-based artifact reduction methods are inadequate to reduce irregular volume and slice-artifacts induced by limb motion in combined (surface) EMG-fMRI (electromyography-functional magnetic resonance imaging) studies. In addition, artifacts are not removed adequately for EMG frequencies above 50 Hz. We present a new fMRI artifact reduction algorithm for motion (FARM) and compare it with standard artifact correction as implemented in fMRI artifact slicetemplate removal (FASTR).

Methods: One control subject generated motion artifacts during EMG-fMRI. Low-frequency motion artifacts and volume-artifacts were removed prior to slice-artifact correction. Slice-artifacts were phaseshifted and removed with motion adaptive templates (FARM). EMG data were also corrected applying FASTR.

Results: Time traces demonstrate that artifacts related to sudden changes in wire position are contained to shorter time periods. EMG power spectra from neck and arm muscles show that FARM has improved performance at higher frequencies.

Conclusions: High-pass filtering, volume-artifact removal, phase-shifting and adaptation of slice-templates to motion improve the quality of artifact-corrected EMG recorded during limb motion. Significance: The improved accuracy at which EMG-fMRI data can be obtained opens up new ways to directly relate self-paced movements to brain activations and to study patients suffering from movement disorders.
6.1 Introduction

The addition of electromyography (EMG) to functional magnetic resonance imaging (fMRI) gives the possibility to study limb movements during scanning and to monitor subject performance. The higher temporal resolution of the EMG can be used to add extra information to the statistical model used in fMRI experiments. Since the magnetic field of the MRI-scanner interacts with hardware containing metals, special MRI-compatible EMG equipment is required inside the scanner room as well as an algorithm for removing the gradient artifact. This artifact is generated by interactions between the electrodes and the fluctuating local gradient field according to Maxwell-Faraday law. It can be divided into periodic volume-artifacts and slice-artifacts. Their periodicity allows the construction of a template by averaging several slice-segments or volume-segments of EMG data. Different template subtraction algorithms exist for combined electro-encephalography (EEG) and fMRI\textsuperscript{[2;80;141]} . Template subtraction however requires that the shape of the artifacts remains constant, and that the onset of every slice and volume-artifact can be determined with a high accuracy.

Using combined EMG-fMRI is challenging because limb motion induces abrupt and unpredictable alterations in the shape of the slice- and volume artifacts. These shape-changes will impair the averaged templates, thus hampering artifact removal. In current EMG-fMRI studies, paradigms were limited to using static force tasks\textsuperscript{[156;206]} or to periodic blocks\textsuperscript{208}. In more recent studies on event-related EMG-fMRI\textsuperscript{[69;120;121]}, the issue of alterations in the shape of the scanner artifacts was not discussed and the allowed motion of the subjects was limited. In a single-subject study on cortical myoclonus (continuous rhythmic movements of the arms) the EMG was difficult to interpret, as the induced artifacts could possibly not be separated from real EMG activity\textsuperscript{[162]}.

Template subtraction techniques commonly used for EEG-fMRI remove less fMRI artifact for frequencies above 50 Hz\textsuperscript{[164]}. For EEG-fMRI this limitation does not pose a problem, since most important EEG frequencies are below 50 Hz\textsuperscript{[60]}. For artifact correction at higher frequencies, the synchronization between EMG amplifier and the MRI-scanner is critical. Surface EMG frequency content ranges up to 250 Hz\textsuperscript{133} and is therefore intrinsically more sensitive to high-frequency artifact components.

Here we present an fMRI artifact reduction method for motion (FARM), that can be used to remove the irregular slice- and volume artifacts from EMG data as a result of limb motion. The algorithm applied is robust against sudden movement-induced artifact changes and is designed to work without any additional hardware to synchronize EMG and fMRI clocks. EMG data were obtained from a subject that simulated different types of motion both outside and inside the scanner. Artifact correction carried out with fMRI Artifact Slice Template Removal (FASTR), a state of the art artifact subtraction algorithm for combined EEG-fMRI, was compared to the correction with the newly developed FARM method.
6.2 Methods

6.2.1 EMG-fMRI experiments

fMRI acquisition

EMG-fMRI data were obtained from a volunteer who performed a series of practiced movements during scanning. Functional images were acquired on a 3T MRI-scanner (Intera, Phillips, Best, the Netherlands) equipped with a SENSE 8-channel head receive coil. For fMRI a T2* weighted EPI sequence was used (TR=2.57 s, TE=25 ms, SENSE acceleration of 2.4, 96x96 matrix, FOV=214x214 mm², slice thickness = 2.7 mm, interslice gap = 0.3 mm, voxel size = 2.3x2.3x3 mm³) with 45 sagittal slices covering the entire brain. Slices were recorded from left to right. One slice acquisition lasted 56.1 ms. In total, 150 EPI volumes were acquired during 384s of scanning.

EMG acquisition

EMG data were recorded with an MRI compatible EEG amplifier (SD MRI 64, MicroMed, Treviso, Italy) and an MRI compatible EMG extension providing 16 Ag/AgCl electrodes usable for 8 bipolar EMG derivations. EMG was recorded at the right-hand side from the sternocleido mastoid (SCM_R), extensor carpi radiali (ECR_R) and first dorsal interosseous (FDI_R), and at the left-hand side from the sternocleido mastoid (SCM_L). The wires were twisted to minimize gradient artifacts and contained current-limiting electrodes of 12 kOhm. The skin was scrubbed with an abrasive gel and the EMG electrodes were attached to the skin using a fixing plaster and conductive electrolyte gel (see Fig. 6.1). The EMG sampling rate was 2048 Hz. Volume-onset information were transmitted by the MRI-scanner with a 5V TTL signal and inserted as volume-markers into the EMG data.

Motion and Paradigm

The experimental paradigm consisted of movements of the arm and neck which could occur normally in healthy subjects and also in common neurological movement disorders. We refer to Table 6.1 for details of the movements, the abbreviations used and the muscles that were activated. The final two movements, left-right arm swinging (LR) and up-down arm swinging (UD) are the most severe and should make EMG correction almost impossible, due to the relatively large continuous changes of the orientation of the wires. They were included to test the limits of the EMG artifact correction algorithms. A projector screen inside the MRI room indicated the motion to be performed for the duration of 25.7 seconds (10 EPI scans) before switching to the next motion. The paradigm was practiced until the subject could accurately perform each movement without using muscles that should not be activated. The EMG was recorded outside of the scanner and inside of the scanner, during EPI acquisition.

6.2.2 Movement-related gradient artifact changes

The gradient artifact is a sequence of artifact waveforms that repeats itself every EPI acquisition, containing as many slice-artifacts as there are slices in a volume, preceded by a single volume-artifact, denoted by GA_s(t) and GA_V(t). The shape
Figure 6.1: EMG electrodes, prepared on the FCR, and twisted leads. Four twisted pairs converge into a braided cable (seen below the arm) which is connected to the amplifier.

<table>
<thead>
<tr>
<th>EPI Scans</th>
<th>Abbreviation</th>
<th>Instruction / Description of movement</th>
<th>Muscles Involved (in EMG recorded before scanning)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11-20</td>
<td>N1</td>
<td>Continuous co-contraction in the neck, to simulate dystonia</td>
<td>SCM&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>21-30</td>
<td>A1</td>
<td>Continuous co-contraction in the arm, to simulate dystonia</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;, FDI&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>31-40</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>N2</td>
<td>Coughing</td>
<td>SCM&lt;sub&gt;R&lt;/sub&gt;, SCM&lt;sub&gt;L&lt;/sub&gt;</td>
</tr>
<tr>
<td>51-60</td>
<td>A2</td>
<td>Sudden jerky motion of lower arm ~5 cm, once every 4 s, to simulate tics</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>61-70</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71-80</td>
<td>N3</td>
<td>Rotational jerks in the neck, ~1-2 deg to the left, once/2 sec, to simulate myoclonus</td>
<td>SCM&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>81-90</td>
<td>A3</td>
<td>Continuous jerky movement in the fingers, ~5 deg rotation up/down, to simulate myoclonus</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;, FDI&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>91-100</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>101-110</td>
<td>A4</td>
<td>Raising/lowering of the hand, ~5 deg up/down, ~3 times/sec, to simulate tremor</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>111-120</td>
<td>A5</td>
<td>Same as A4 but with the arm lifted from the scanner table</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>121-130</td>
<td>R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>131-140</td>
<td>UD</td>
<td>Movement of the entire arm, maximum allowable movement up/down, continuous</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
<tr>
<td>141-150</td>
<td>LR</td>
<td>Movement of the entire arm, maximum allowable movement from left to right, continuous</td>
<td>ECR&lt;sub&gt;R&lt;/sub&gt;, SCM&lt;sub&gt;R&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

Table 6.1: Abbreviations and descriptions of the movements performed by the subject both inside and outside of the scanner. In the analysis of EMG data, the first volume of EMG data was omitted to allow the subject to switch to the new motion (R=Rest).
of these artifacts is determined by scanner settings such as image resolution and matrix size\(^{[4]}\). Slice-artifacts last 50-80 ms and the volume-artifact lasts 20-30 ms. The amplitude of both types of artifact is 10-20 mV, which is 20-40 times larger than amplitudes of typical EMG activity.

Motion of the limbs introduces two extra artifacts in the EMG. The first is due to movement of wires and electrodes in the main B0 field. This translates into interaction between the wires and the main magnetic field, introducing extra unpredictable components in the signal, denoted by \(MAB_0(t)\), whose frequency and amplitude depend on the trajectory and speed of the wires. If motion is fast enough, the frequency of these components can reach 25-30 Hz and the amplitude can be as high as 30 mV. Because the waveform is unpredictable, it cannot be estimated with templates. The second artifact is due to alterations in the spatial orientation of the wires, which in turn alters the shape and size of the slice and volume artifacts, as visualized in Fig. 6.2 (for slice-artifacts only). These shape changes, denoted by \(\Delta GA_s(t)\) and \(\Delta GA_V(t)\), are also unpredictable. In this case, they cannot be easily filtered out and will interfere in template construction if slice-artifacts with an uncommon shape are included in the average. The above mentioned contributions in the recorded signal are summarized as follows:

\[
S_{\text{raw}}(t) = EMG(t)+GA_s(t)+GA_V(t)+MAB_0(t)+\Delta GA_V(t)+\Delta GA_V(t) \quad (6.1)
\]

- \(S_{\text{raw}}(t)\) = raw data
- \(EMG(t)\) = contribution to Sraw from muscle activity
- \(GA_s(t)\) = slice-artifact, as estimated by the correction algorithm
- \(GA_V(t)\) = volume-artifact, as estimated by correction algorithm
- \(MAB_0(t)\) = motion artifact, interaction with main field
- \(\Delta GA_s(t)\) = deviation from normal shape of slice-artifact due to motion
- \(\Delta GA_V(t)\) = deviation from normal shape of volume-artifact due to motion

Any contributions in equation (6.1) apart from \(EMG(t)\) and \(GA_S(t)\) will impair template-based removal of the slice-artifact.

### 6.2.3 Pre-processing of EMG data

Processing of EMG data was performed using Matlab (version 7.3, The Mathworks, Matick MA). EMG data were held in the EEGLAB data format\(^{[51]}\). A schematic overview of artifact correction methods using FASTR and FARM is presented in Fig. 6.3.

Firstly, bipolar EMG data were constructed from monopolar channels. To remove artifacts due to interaction between motion and the main field (\(MAB_0(t)\) in equation (1)), the data is digitally high-pass filtered at 30 Hz using a least-square FIR (finite impulse response) filter (24 dB/Oct, created using the firls function in Matlab). We assumed that the frequency between 1-30 Hz contained most of the interaction artifact \(MAB_0(t)\). Since the EMG is a stochastic process with a frequency content of up to 250 Hz and the amplitude modulation also occurs at higher frequencies, the low-frequency EMG signal contents can be regained by rectification.

Secondly, since the MRI-scanner transmits only volume-onsets with a TTL pulse, an algorithm is used to insert slice-onset markers into the EMG data.
Figure 6.2: Fifty adjoining slice-segments of (high-pass filtered and 10x up-sampled) data $S_{raw}'(t)$, recorded from ECR$_R$ and spanning in total 2.85 s in time. Slice-onset markers have already been placed and optimized (see Section 2.6), but the slice and volume corrections have not yet been performed. Thirty slice-segments (in grey) are from EMG during rest orientation, and 20 slice-segments (in black) are from a stretch orientation of the arm.
Figure 6.3: FASTR and FARM workflows, after pre-processing of data. While FASTR adjusts marker positions msl for each slice separately (ii), FARM optimizes values for sdur and dtime (i) and directly calculate the correct marker positions in the interpolated space for the entire length of the data (ii). A phase-shift is applied to improve temporal alignment (iii). Volume-artifacts are removed (iv). During slicecorrection, FASTR uses every slice-artifact in a sliding window for averaging, while FARM uses an optimal set of slice-artifacts in larger sliding window (v). In both algorithms, principal component analysis (PCA) is used (vi). Post-processing entails low-pass filtering and down-sampling (and removal of the volume-artifact, for the FASTR workflow).
Since FASTR expects a slice-onset marker for every slice-artifact, we developed a preprocessing method that inserts slice-markers into the data and that also generates initial estimates for slice timing parameters for the FARM correction. Data is divided into volume-segments using volume-onset markers; the algorithm functions on each volume-segment individually. It uses the shape of the artifact for determining slice-markers, and as such, the channel which contained the largest artifact is used. It is assumed that the obtained timing information is equally valid for all channels of EMG data. The algorithm separates volume-segments of data into as many slice-segments as there are slices in an EPI volume, followed by a final preparation-segment, as visualized in Fig. 6.4. This separation is performed in such a way that slice-segments contain only a single slice-artifact and that preparation-segments contain the volume-artifact of a next EPI scan. The volume-artifact of the first EPI scan is omitted. Slice segments have a duration of \( s_{dur \_V} \) (slice duration for volume-segment \( V \)) and the preparation segment at the end of a volume has a duration of \( d_{time \_V} \) (delay time for volume-segment \( V \)). The value of \( d_{time \_V} \) is iterated from 0 to the closest integer near the initial estimate for \( s_{dur \_V} \). For each iteration of \( d_{time \_V} \), slice-markers are equally spaced in the remaining part of the volume-segment. The sum of the variance between slice-segments (one variance value per data-point in a slice-segment) is calculated for each iteration of \( d_{time \_V} \) using the following equation:

\[
SV = \sum_{i=1}^{N} \frac{1}{M} \sum_{j=1}^{M} \left( S_{i,j} - \frac{1}{M} \sum_{j=1}^{M} S_{i,j} \right)^2
\]  

(6.2)

\( SV \) = sum of the variance  
\( S_{i,j} \) = data value of high-pass filtered raw data (\( S'_{\text{raw}} \)) at sample \( i \) in slice-segment \( j \)  
\( i \) = sample number  
\( N \) = samples per slice-segment  
\( j \) = slice-segment number  
\( M \) = total amount of slice-segments in one volume

One value exists that minimizes this sum of the variance (see inset Fig. 6.4). In our case, the initial value for \( s_{dur \_V} \) is a reasonable upper limit for \( d_{time \_V} \). For a sequence where an amount of additional dead time exists in between the last slice-segment and the preparation segment, the maximum value should be increased even further. The algorithm generates slice-markers that have an accuracy as good as the sampling rate of the EMG system. Processing 10 minutes of EMG data (233 EPI scans) takes approximately 60 seconds of time.

Thirdly, the data are up-sampled with an interpolation factor of 10, increasing the sampling rate to 20,48 kHz (see Fig. 6.3).

### 6.2.4 Artifact reduction with FASTR

FASTR has been implemented as an extension\(^{141}\) to the EEGLAB toolset\(^{51}\) and can be obtained from: http://users.fmrib.ox.ac.uk/~rami/fmribplugin/. To fine-tune marker locations, every slice-marker is moved to earlier or later samples of the interpolated data, so as to reach a maximal correlation with the first slice-artifact of the first volume, whose slice-onset marker remains fixed (ii in Fig. 6.3). The next step consists
Figure 6.4: Volume-segment of high-pass filtered EMG data (at the original sampling rate of 2048 Hz) and illustration of the estimations of the slice- and delay times for volume $V$, $sdur_V$ and $dtime_V$, and the initial slice-markers $m_{sl}(1) \ldots m_{sl}(M)$. The number of samples in $dtime_V$ is iterated from 0 to the initial estimate for $sdur_V$. For every iteration, the sum of the variance between all slice-segments in one volume is calculated with Eq. (2). The minimal variance is reached for the optimal value for $dtime_V$ (see inset).
of subtracting slice-templates from every slice-artifact in the data (v in Fig. 6.3). Each template is calculated as the average of preceding and following slice-segments of raw data around the slice-artifact to be corrected. The size of this window is specified by the user; usually, a window size of 10-20 is used. By using a sliding window approach, the algorithm is adaptive to changes in the slice-artifact, since over time the template would adapt to new shapes. There is a trade-off between the adaptability and quality of the slice-template; by increasing the amount of slice-artifacts to include in this sliding window, the quality of the template improves but the adaptability declines. To obtain both reasonable adaptability and reasonable quality of the template, we chose to use 12 averages for this sliding window. The third step (vi in Fig. 6.3) is the analysis of the residual segments (i.e., slice-segments where the template has been subtracted) with principal component analysis (PCA). PCA is used in FASTR to obtain an optimal basis set (OBS), which is a set of principal components (PCs) that are used to estimate and subtract residual artifacts. The calculation automatically constructs an OBS of 3-8 PCs that explain 80% of the variance in the residuals. The same OBS is used in the correction of every residual segment.

### 6.2.5 Artifact reduction with FARM

The concept of the FARM artifact correction is to remove all components in the signal that could impair the slice-templates. A schematic overview of the differences between FARM and FASTR is presented in Fig. 6.3. In addition to the high-pass filter in the preprocessing, the method contains three main elements to make it more robust against sudden slice-artifact shape changes. Firstly, slice-markers are calculated mathematically with optimized values for sdur and dtime (i), and these values are used to improve the slice-alignment beyond what would be possible using the optimized slice-markers as estimated by FASTR (ii and iii). Secondly, volume-artifact correction is performed before slice-correction and consists of substituting periods of raw data where the volume-artifact overlaps with the surrounding slice-artifacts (iv). By this operation, the volume artifact is removed without interfering with the slice-artifact correction. Thirdly, in the slice-artifact correction, instead of using every slice in a relatively small sliding window, FARM uses a larger sliding window and selects only those slice-artifacts that have the highest correlation (v).

### Optimization of slice-timing parameters and phase-shifting

To align slice-artifacts, we used an idea first presented for EEG-fMRI artifact correction. The estimations of the delay time (\(dtim_{V}\)) and slice-duration (\(sdur_{V}\)), generated in the pre-processing, are averaged to produce starting estimates for \(dtime\) and \(sdur\). The final values of these timing parameters are estimated to a precision of \(\sim 1\mu s\) with unconstrained nonlinear optimization of a cost function that operates on the entire length of the interpolated data. The cost function is equal to the sum of the variance as calculated by equation (6.2), where \(M\) now equals the total number of slice-segments in the entire recording, \(S_{i,j}\) represents the upsampled filtered data, and segments are delimited with marker positions calculated by:
\[ s(i) = s_b(1) + [(i - 1)sdur + (v(i) - 1)dtime] Israte + \Delta(i) \tag{6.3} \]

- \( s(i) \): onset sample of i-th slice
- \( s_b(1) \): sample of the onset-marker of the first volume’s first slice.
- \( i \): sample number (i runs from 2 to the total number of slices in the recording)
- \( sdur \): duration of the acquisition of a single slice
- \( v(i) \): number of the current volume for \( i \)
- \( dtime \): duration of the preparation-segment
- \( I \): interpolation factor (10)
- \( srate \): sample-rate of the EMG (2048 Hz)
- \( \Delta(i) \): ‘sample-differential’ from rounding off towards an integer [-0.5 \( \leq 0.5 \)]

This cost function reaches a global minimum for the optimal values of \( sdur \) and \( dtime \), as shown in Fig. 6.5. After optimization of these parameters, the onset sample for any slice-segment re-calculated with equation (6.3). Since only a small change in \( sdur \) or \( dtime \) causes a misalignment in slices-segments that continually increases from segment to segment, it also causes a large deviation in the sum of the variance during optimization. This enables the estimation of these parameters with a very high precision, as can be seen in the supplementary data of the original paper on slice-timing parameter estimation\[80\].

Next the round-off error is used to improve slice-alignment. After data segmentation using (3), \( \Delta(i) \) is used to time-shift every slice-segment at a sub-sample scale. Each slice-segment is Fourier-transformed into the frequency domain, and multiplied by a function that introduces rotations to each frequency component that corresponds to time delay \( \Delta(i) \), before the inverse Fourier transform is applied\[80\]. This operation significantly reduces the mismatch between slice-artifacts and artifact templates due to clock asynchronies between EMG hardware and scanner. It has been shown that it is especially useful for higher frequencies in EEG data, obviating the need for additional hardware to improve the performance of the correction algorithm at higher frequencies.

**Volume Correction**

The volume artifact lasts slightly longer than the delay time (\( dtime \)) and overlaps with the surrounding slice-artifacts (see Fig. 6.6). The slice-segments within this overlap can impair the slice-template during correction of neighboring slice segments. The overlapping portion is therefore substituted with synthesized data (iv in Fig. 6.3). The synthesized data are constructed from neighboring slice artifacts that are more than 1 slice-segment away from the volume artifact. The volume artifact within the preparation period is replaced by interpolated data.

**Template Formation**

In FARM, slice-templates are formed by taking a sliding window consisting of 50 slice-artifacts. From these, 12 slice-artifacts with the highest correlation with the slice-artifact to be corrected are selected for the template. Consequently, the template for
Figure 6.5: Estimation of \textit{sdur} and \textit{dtime} using the entire length of interpolated data with unconstrained nonlinear optimization. In FARM, the cost function is equal to the sum of the variance. Supposing that there are 1150 samples within each slice-segment (as in Fig. 6.2), 1150 variances are added to obtain the cost function. Since the shape of sliceartifacts remains mostly the same, the sum of the variance (\textit{SV}) reaches a global minimum for unique values of \textit{dtime} and \textit{sdur}. 
Figure 6.6: Original signal (black) with volume-artifact and adjacent slice-artifacts. The volume-artifact is present in the preparation-segment and overlaps with the slice-artifacts in the surrounding slice-segments. In the periods where the volume-artifact overlaps, the data are substituted with synthesized data (grey). In the preparation-segment the data are interpolated preventing impaired slice-artifact removal in neighboring slices.
any slice-artifact need not be composed of neighboring slice-artifacts but can also contain slice-artifacts not directly connected in time. If the shape of the artifact would suddenly change due to motion, as is the case in Fig. 6.2, then this sub-selection will ensure that slice-artifacts after motion are not used in the slice-template to correct a slice-artifact before motion, and vice versa. It can occur that a slice-artifact has a shape that does not resemble any other slice-artifact in the window of 50. In this case, since there are still 12 slice-artifacts picked for the template, the slice-artifact itself will not be corrected optimally as there would still be a significant $\Delta G_A_s(t)$ contribution (see equation (6.1)). However, because of the selection process, this slice-artifact will also not be able to distort the templates for any other slice-artifacts. As a last step the PCA analysis for removing residual artifacts is also used in FARM, but we chose to use a fixed number of 4 principal components for the OBS.

6.2.6 Post-processing of EMG data

Data from both FASTR and FARM are down-sampled and digitally low-pass filtered at 250 Hz (12 dB/Oct). To remove the volume-artifact from FASTR-corrected data and to compare artifact-corrected data from the FASTR and FARM workflows, EMG that are less than 50 ms removed from a volume-marker is set to 0. The EMG data recorded outside is filtered with a band-pass filter between 30 Hz and 250 Hz as well as a 50 Hz notch filter to remove the power supply artifact.

6.2.7 Comparing FARM and FASTR corrected EMG data

Assessment of the entire recording of EMG data is performed only for SCM$_R$ and ECR$_R$, as either one or the other was activated by any of the movements performed. As a quality measure for the artifact correction during the entire recording, the ratio between the root means square (RMS) of uncorrected EMG periods and artifact-corrected EMG periods is calculated and compared between FASTR and FARM. The RMS will be lower if there is EMG activity and if there are uncorrected artifacts still remaining in the EMG. Finally, spectrograms from the SCM$_R$ and ECR$_R$ are calculated to assess spectral power fluctuations due to the artifact itself and to compare how much of the spectral power from the artifact is removed by FASTR and FARM.

6.3 Results

6.3.1 Comparing artifact-corrected EMG with normal EMG

The time courses for EMG outside the scanner and the FASTR and FARM-corrected data during scanning are presented in Fig. 6.7. Note that the traces from outside of the scanner and the artifact-corrected traces from during the EPI acquisition are separate measurements whereas FASTR and FARM corrected traces are identical recordings.

On comparing the EMG data outside of the scanner (left column) with the FASTR-corrected data (middle column), short bursts can be seen in the SCM$_R$ trace in R, A2 and A4, while this muscle was not activated when recording EMG outside the
CHAPTER 6. EMG-FMRI ARTIFACT CORRECTION

Figure 6.7: Artifact-corrected EMG traces of FDI$_R$, ECR$_R$, SCM$_R$ and SCM$_L$ during six movements of the experiment. Volume markers are denoted with ‘V’. Compared to data recorded outside of the scanner, the FASTR algorithm functions properly when motion is low (during R and N1). However, the SCM$_R$ has a bursting-like pattern which is present in all traces which are absent in FARM-corrected data. Furthermore, in FASTR-corrected data, bursts appear around the initiation of motion in N2 and A2 which can also cross-over to other channels, like with SCM$_L$ in N2 and FDI$_R$ in A2. Data corrected with FARM do not show extra bursts, but they still show a cross-over effect (as with the FDI$_R$ in A2). During A4, the bursting pattern as seen in the EMG outside is reproduced in the FASTR and FARM traces, although the amplitudes in ECR$_R$ are slightly larger in FASTR. In the LR condition, motion artifacts are most severe and induce artifacts in the three bottom traces of the FASTR-corrected data. These artifacts are removed in the FARM-corrected EMG data. The inset shows a 10x magnified ECR$_R$ trace in R, in which residual volume-artifact remain after FASTR correction. FDI$_R$ = first dorsal interosseus (right), ECR$_R$ = extensor carpi radialis (right), SCM$_R$ = sternocleido mastoid (right), SCM$_L$ = sternocleido mastoid (left).
6.3. RESULTS

In the FARM traces, these extra bursts are removed (right column). The bursts contain high frequencies which are not adequately removed by FASTR.

In FASTR, small extra bursts can still be seen around the times where the volume-artifact was present in the signal, as seen in Fig. 6.7 near V-markers in the SCM\textsubscript{R} trace during arm motion (A2) and in the inset in the middle column showing ECR\textsubscript{R} during rest (R). They are still quite disruptive when searching the EMG for real EMG discharges. They are generated by the sliding window in FASTR using the uncommon shape of the slice-artifacts near the volume-artifact. FARM does not introduce these extra bursts.

In muscles that should be activated in short bursts, like ECR\textsubscript{R} during A2 or the SCM\textsubscript{L} and SCM\textsubscript{R} during N2, extra EMG-like bursts are introduced prior and after the time of the movement in the FASTR trace. In FARM these extra bursts are removed. The bursts are due to FASTR using slice-artifacts in the sliding window with an uncommon shape for the correction of a regular slice-artifact whereas in the FARM traces these uncommon shapes are excluded from the artifact template.

In both artifact-corrected traces, muscles that should not be activated activate at the time of the movement, as can be seen in the A2 trace. The FDI\textsubscript{R} (and to a lower extent the SCM\textsubscript{R}) has a bursting pattern alongside the ECR\textsubscript{R}, not seen in the EMG recorded outside of the scanner. If the hand moves upwards and the ECR\textsubscript{R} is activated, the wires of both the SCM\textsubscript{R} and the FDI\textsubscript{R} will change orientation and cause a (local) slice-artifact shape that is too uncommon to correct for using the available slice-templates. Since this orientation change occurs in more than one channel, there is an apparent ‘cross-over’ of activation. Both FARM and FASTR are affected with this artifact.

The FASTR and FARM-corrected EMG traces in A4 contain bursts whose periodic pattern matches the slice-artifact. By comparing the EMG outside of the scanner with the EMG as corrected with FASTR, the amplitude of the bursting pattern in the FASTR trace is amplified. In FARM, the amplitude of the EMG during A4 better matches the amplitude of the EMG outside of the scanner.

In the motion that should introduce the most artifacts (LR), of the prepared muscles, only the SCM\textsubscript{R} and ECR\textsubscript{R} should be activated. The EMG inside, corrected with FASTR, shows that the artifact correction has completely failed. All traces are contaminated with high-frequency noise, and a tremor-like bursting pattern is introduced in the SCM\textsubscript{L} trace, making a meaningful interpretation impossible. On the other hand, the majority of these artifacts are removed by FARM.

In Fig. 6.8, spectra can be seen for the ECR\textsubscript{R} muscle during rest (R) and arm motion (A4), for EMG corrected with FAST and FARM and EMG recorded outside of the scanner. During rest, the FASTR algorithm introduces extra higher-frequency components into the EMG data between 30 Hz-250 Hz. During arm motion (A4), the power in a band between 30 Hz up to 70 Hz is increased with respect to spectral power of the EMG outside and the EMG as corrected with FARM.

### 6.3.2 RMS ratio and spectrograms

The traces of the EMG as well as the spectra are momentary evaluations of the data. To assess the full length of the recording and compare FARM with FASTR, root-mean-square (RMS)-ratios are calculated for all the periods of EMG data, presented in Fig. 6.9 for SCM\textsubscript{R} and for ECR\textsubscript{R}. The SCM\textsubscript{R} has lower RMS ratios in periods in which the scanner.

Figure 6.8: Spectra of EMG data corrected with FASTR and FARM as compared to spectra of EMG data during the practice session outside the scanner. Outside EMG data have been high-pass filtered at 30 Hz and notch-filtered at 50 Hz. Left; spectra during rest of the ECR\textsubscript{R}. Right; spectra for muscle activity of ECR\textsubscript{R} during A2. During rest FASTR introduces extra high-frequency components in the corrected signal at frequencies higher than about 50 Hz. During motion, these extra high-frequency components are masked by the heightened power of the EMG. However, extra power is generated in a band between 30 and 70 Hz. Both the high-frequency components and the increased power between 30 and 70 Hz are suppressed in the spectra of EMG data that are corrected with FARM.
Figure 6.9: RMS-ratio between uncorrected EMG and corrected EMG of SCM$_R$ and ECR$_R$ during all movements (see Table 6.1), with FASTR and FARM. RMS values are lowered by muscle activity or uncorrected artifacts. FARM RMS ratios are always higher. For tasks which require motion, the improved adaptability of the slice-template in FARM contributes most to the RMS ratio differences.

A spectral evaluation of the entire dataset for SCM$_R$ and ECR$_R$ is presented in the spectrograms in Fig. 6.10. In the uncorrected spectrograms, the spectrum of the artifact can be observed as composed of harmonics of the slice frequency (17.75 Hz), convolved with harmonics of the volume repetition frequency (0.4 Hz)$^{[122]}$, the latter causing a line broadening of the slice-frequency harmonics that obscure the task-related EMG increases in SCM$_R$. The spectrogram for the FASTR-corrected data shows that the power of the artifact has been reduced, but that harmonics are still present throughout the complete spectrum during the entire recording. These spectral harmonics are reduced in the FARM-corrected data.
Figure 6.10: Spectrograms for uncorrected EMG (left), FASTR-corrected EMG (middle) and FARM-corrected EMG (right), for both the SCM$_R$ muscle (top) and the ECR$_R$ muscle (bottom). Conditions are denoted with the abbreviations above each spectrogram. The artifact in SCM$_R$ is larger than the artifact in ECR$_R$, and totally obscures the power of the EMG. With FASTR there are still power elevations in the spectrogram at every harmonic of the slice-frequency. These are largely suppressed in the FARM spectrograms.
6.4 Discussion

The addition of EMG to fMRI presents several advantages to experiments focused on motor control. The EMG can be used to examine if subjects have actually performed the tasks as they were instructed[208] or to enable localization of brain areas that modulate (pathological) muscle activity[162;207]. So far, no artifact reduction methods specifically designed for EMG during limb movement have been presented in the literature. Up till now, standardized approaches based on the EEG-fMRI artifact correction first presented by Allen[2] have been used also for EMG artifact correction, but they are fundamentally impaired if there is motion, since they do not account for changes in the shape of the slice-artifact.

In this study, the main effects of motion on the gradient-artifacts generated by the scanner have been identified. A correction algorithm (FARM) has subsequently been constructed that largely removes residual artifacts in the EMG generated by motion. The method has an improved performance especially at higher frequencies without using hardware solutions for synchronization of EMG and MRI clocks, and increases the robustness against sudden changes in the slice-artifact.

Compared to artifact reduction schemes described in the literature, several features of FARM allow to better deal with deformations in the shape of the slice-artifact leading to more accurate artifact removal (see Figures 6.7, 6.8, 6.9 and 6.10). In our view this highlights the importance of a solution that is tailored for artifact removal in EMG data contaminated by limb motion.

High pass filtering has mostly been carried out after slice artifact removal[156;162;206;208;207]. In addition, the cutoff frequency is chosen as low as 10 Hz. Especially if motion is large, the motion-generated artifacts can have frequencies as high as 30 Hz and impair artifact correction, and therefore in FARM, high pass filtering is performed before slice-artifact removal and the frequency is set at 30 Hz.

The second difference with other methods is that FARM does not use volume templates. In the past, the standardized EEG-fMRI routine has been used in which after slice-artifact removal, a second run of volume-artifact removal is performed to clean EMG from fMRI artifacts[2]. This is acceptable if it can be assumed that the subject does not move and the wires do not change position in the fluctuating magnetic field over time. However, the use of a second template removal step, using large volume-segments, introduces an extra vulnerability in the overall algorithm to uncommon artifacts.

An essential element in artifact correction is the design of the slice template. In FASTR only neighboring slice segments are used to construct the slice template. Even in other EMG fMRI correction methods, as implemented in the original method[2] or as implemented in BrainVision Analyzer software (Brain Products, Gmbh, Munich, Germany), the slice segments that are selected are fixed in time, impairing the adaptability of the correction method to sudden changes of the slice-artifact introduced by movements.

In the EMG-fMRI studies to date, the EMG data is often reduced to one element per volume. However, one sacrifices much of the information conveyed in the EMG data. In FARM full benefit can be obtained from the high resolution temporal information of the EMG, for example in the construction of event-related designs[120].

A major issue concerning EMG is the ability to correct the signal at frequencies higher than 50 Hz. If the EMG has been measured without any additional hardware
to synchronize the EMG hardware with the MRI-scanner, all of the available correction algorithms will have a reduced performance at frequencies greater than 50 Hz. Doubling or tripling the sampling frequency to 4000 or 5000 Hz improves slightly the slice-alignment, but it is still not enough\textsuperscript{[84;122]}. Because in some cases higher frequencies (up to 70-100 Hz) in the EEG are of interest, work has been performed to improve artifact correction at these higher frequencies also for EEG, and this has led to the development of two different hardware methods. The first method, the stepping-stone technique\textsuperscript{[4]}, entails an alteration of the EPI sequence and a connection between EMG and MRI hardware to ensure that the EMG amplifier only takes samples during periods where gradient fields are constant in time, thus avoiding the slice-artifact as much as possible. The second method entails a phase-locking device that ensures that the EMG sampling is ‘hastened’ at the start of each slice-acquisition to re-align the clock of the EMG amplifier to the MRI scanner, improving the similarity of slice-artifacts\textsuperscript{[122]}. Both methods require extra MRI hardware and modifications to the EPI sequence. In current EMG-fMRI studies\textsuperscript{[156;206;208]}, it is unclear if synchronization hardware has been used. In the study on myoclonus\textsuperscript{[162]}, an additional amplifier sampled TTL pulses at 100 kHz. This improved the slice-timing onset resolution to 10 \(\mu\)s but was not as effective as the two hardware solutions described above. Probably this was the reason why a low-pass filter as low as 180 Hz was used. By using a software solution for the synchronization problem\textsuperscript{[80]}, FARM obtains a performance at higher frequencies that is comparable with existing hardware solutions.

The use of template subtraction algorithms to correct EMG data contaminated by movement artifacts could be questioned, as there are several other techniques available, like individual component analysis (ICA)\textsuperscript{[120;124]}, or combinations of template subtraction with principal component analysis (PCA) or adaptive noise cancellation (ANC)\textsuperscript{[2;141]}. However, each of these techniques uses the implicit assumption that the slice-artifact has a periodic waveform. Therefore, irregularities in this waveform will reduce performance. Furthermore, it is not clear if the components that are removed still carry some of the EMG signal\textsuperscript{[164]}. Since PCA, ICA and ANC are higher-order statistical approaches, the cause of remaining inaccuracies in the corrected EMG are more difficult to assess than with template subtraction alone. They could be due to over-fitting of components (for PCA or ICA), or filter weights that do not adjust fast enough (for ANC). By using template subtraction, as implemented in FARM, residual artifacts are known to be due to uncommon shapes in the slice artifact, and no assumptions are made.

The rationale for still using PCA analysis, also for FARM, is that the first four principal components always correlated well with the slice-templates; interpretation from the 5-th to the last component was increasingly difficult. Furthermore, in the original paper on phase-shifting\textsuperscript{[80]}, a low-pass filter of 150 Hz was used to correct for high-frequency residuals in the EEG that still remained. For EMG, frequencies up to 250 Hz are important for a meaningful interpretation. Since the use of an OBS facilitates correction of higher-frequency components\textsuperscript{[141]} we chose to add a PCA analysis at the end of the algorithm. The main difference with FARM is that PCA analysis in FASTR is essential for the algorithm to estimate shape-changes due to residual misalignment of slice-artifacts in time after slice-timing correction.

Our study has some limitations. While FARM prohibits a slice-artifact with an uncommon shape from impairing slice-correction for nearby slices, it does not yet handle the correction well if the slice-artifact itself is uncommon. This causes the
6.4. DISCUSSION

The performance of FARM to decrease for tasks where motion is both continuous and of large amplitude, as demonstrated in the bottom traces in Fig. 6.7 and spectrograms in Fig. 6.10. The second limitation is that there is still erroneous activation of other muscles at the time of the motion (cross-talk) that impairs the interpretation of the EMG, as seen in Fig. 6.7 in the middle traces (A4). One worthwhile effort would be to try to interpolate the uncommon shape of slice-artifacts, using slice-artifacts nearby that have been successfully corrected. However, due to the unpredictability of the shape-changes in the slice-artifact, the distinction between real EMG and artifact will remain difficult.

The algorithm presented here offers an improved correction for gradient artifacts in EMG at the higher frequencies and a better adaptability to uncommon slice-artifacts shapes for EMG sampled at a frequency of 2048 Hz. Although the EMG is not as clean as when measured outside the MRI, the interpretation is feasible even if uncommon artifacts are present in the EMG due to motion. Since the pitfalls encountered in EMG-fMRI artifact correction, especially related to sudden changes in artifact, are largely averted, this enables the use of EMG in the construction of event-related designs of jerks, tics or myoclonus, or to estimate the frequency of tremor using burst detection algorithms\[101\].