Movement-related effects in fMRI time-series

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Running Title Movement artifacts in fMRI

Abstract

This paper concerns the spatial and intensity transformations that are required to adjust for the confounding effects of subject movement during fMRI activation studies. We present an approach that models, and removes, movement-related artefacts from fMRI time-series. This approach is predicated on the observation that movement-related effects are extant *even after perfect realignment.* These effects can be divided into those that are some function of position of the object in the frame of reference of the scanner, and a component that is due to *movement in previous scans.* This second component depends on the history of excitation experienced by spins in a small volume and consequent differences in local saturation. The spin excitation history will itself be a function of previous positions. This suggests an autoregression-moving average model for the effects of previous displacements on the current signal. We describe such a model and the adjustments for movement-related components that ensue. Our empirical analyses suggest that (in extreme situations) over 90% of fMRI signal can be attributed to movement, and that this artifactual component can be successfully removed.

Key words: Realignment, fMRI, Movement artifacts, Autoregression-moving average models.

Introduction

This paper is about realigning and adjusting functional MRI time-series to remove the confounding effects of subject movement. The main issue, considered in this paper, is that movement-related changes are a complex function of position and scan to scan movement, or past positions. Our results suggest that simply realigning the images is not a sufficient correction for movement effects. The aim of this work was to develop an approach that was simple, computationally expedient and capable of removing all movement artefacts.

The usual strategy in functional MRI is to collect a sequence of multi-slice images of the brain every one to three seconds. Changes in signal intensity, that are related to changes in a stimulus or task, are used to infer something about functional anatomy. However changes in signal intensity can also arise from head motion and this represents one of the most serious confounds in fMRI studies. Despite restraints on head movement willing and cooperative subjects still show displacements of up to a millimetre or so. With very young, old, ill or disturbed subjects head restraints may not be appropriate. In such circumstances head movements of several millimetres are not uncommon. Previous approaches to this problem are based on the assumption that simply moving the images back into register, *post-hoc*, is sufficient to 'undo' the effects of movement. We now re-evaluate this assumption.

Time-dependent changes in a fMRI signal, at a given point in the brain, have many components. This paper is concerned with movement-related components. These components can arise from:

♣ *Differences in the position of the object in the scanner* Spatial variation in sensitivity will render the signal a function of the object's position at the time of scanning. This spatial variability can include large scale field inhomogeneity or can be expressed at a much finer scale. An important example of the latter is found in slice-selective irradiation, used for example in multi-slice acquisition. The degree to which spins are excited in any small volume of the object will depend on an interaction between the local magnetic field and the Fourier transform of the slice-selective pulse. For example the excitation of spins in a small region on the edge of a slice will be exquisitely sensitive to small displacements in and out of that slice. In other words signal intensity will be a strong function of position relative to the volume excited or the scanner's frame of reference.

♣ *Differences due to the history of the position of the object.* If the number of excited spins is a function of position in the scanner it follows that the number of excited spins (and implicitly the signal) will also be a function of position in previous scans. This dependency is due to changes in saturation of spin magnetization, that is a function of the number of spins excited in the previous scan. This excitation will in turn be a function of position and so, by induction, a function of all previous positions. In summary the current signal is a function of current position and the spin excitation history. The spin excitation history is in turn determined by the history of past movements. This effect will manifest if the recovery of magnetization in the z direction is incomplete by the time the next slice-selective pulse arrives (i.e. if TR is comparable to T_1 which is certainly the case for many fMRI studies). In general movement within the plane of the slice will not change the set of spins excited and should not contribute to this effect.

In summary changes in the observed signal from a small volume of brain are functions of both position and past positions. This is a problem because *even with perfect spatial realignment movement-related changes could still be present*. We have already reported a method for estimating the position of an image, relative to a reference image, using a simple least squares analysis. This analysis obtains after linearising the problem with first order Taylor expansions. In this paper we use these estimates to first *realign* the scans and then remove time-dependent components of the signal that are considered movement-related. This second step uses a least squares *adjustment*

The paper is presented in three parts. The first part introduces the theory and operational equations and includes a summary of our previous work pertaining to realignment. The realignment problem represents that simplest case of a more general problem of finding the spatial and intensity transformations that best match one image process with another [see ref 1 for discussion of a general nonlinear framework]. The first part concludes with a method for removing movement-related effects The second part uses variance partitioning and eigenimage analysis of real fMRI data to demonstrate that the effects above are seen empirically, and can account for substantial amounts of the observed variance. The final part demonstrates the efficacy of the proposed method in terms of simple image subtraction.

Theory

In this section we deal with estimating movement parameters, autoregression-moving average models for the effects of movement on signal and how to remove movement-related components from the time-series. In brief movement parameters are estimated, that are then used to (i) *realign* the images and (ii) mathematically *adjust* the voxel values to discount movement-related components

Estimating movement parameters

Consider the problem of realigning one image so that it matches another. If the object image $\Omega(\mathbf{x})$ and the reference image $\tau(\mathbf{x})$ are similar then they are related by a rigid body, six-parameter, affine spatial transformation $\mathbf{q}(\mathbf{x},\gamma)$. $\mathbf{q}(\mathbf{x},\gamma)$ is a vector function of position in space $\mathbf{x}$, defined by the six parameters of a rigid body transformation $\gamma = [\gamma_1 .....\gamma_6]$, where:

$$ß.\tau(\mathbf{x}) \approx \Omega(\mathbf{q}(\mathbf{x},\gamma)) \qquad (1)$$

and ß is a scaling constant. The images are assumed to be good lattice representations of continuously differentiable deterministic scalar functions $\Omega(\mathbf{x})$ and $\tau(\mathbf{x})$. The problem of realignment reduces to finding the spatial transformation $\mathbf{q}(\mathbf{x},\gamma)$ or, equivalently, the six parameters constituting the elements of γ. At first glance Eq. (1) may appear so ill posed as to make any explicit solution impossible. However, if we assume that the images are smooth (or that they can be rendered smooth) then a first order approximation of Eq. (1) can be constructed in which γ has a least squares solution. Let $\mathbf{q}(\mathbf{x},\gamma)$ be expanded in terms of six vector functions $\partial\mathbf{q}(\mathbf{x},\gamma)/\partial\gamma_k$ of $\mathbf{x}$, approximating the k (= 6) components of a rigid body transformation. These are usually taken to be translations in x, y and z and rotations about x (pitch), y (roll) and z (yaw) (2).

$$\mathbf{q}(\mathbf{x},\gamma) \approx \mathbf{x} + \sum_k \gamma_k\partial\mathbf{q}(\mathbf{x},\gamma)/\partial\gamma_k \qquad (2)$$

By Eq. (1)
$$ß.\tau(\mathbf{x}) \approx \Omega(\mathbf{x} + \sum_k \gamma_k\partial\mathbf{q}(\mathbf{x},\gamma)/\partial\gamma_k) \qquad (3)$$

If $\Omega(\mathbf{x})$ is smooth the effects of the small transformations $\gamma_k\partial\mathbf{q}(\mathbf{x},\gamma)/\partial\gamma_k$ will not interact to a significant degree and we can expand the right hand side of Eq. (3) using Taylor's theorem where, ignoring high order terms:

$$ß.\tau(\mathbf{x}) \approx \Omega(\mathbf{x}) + \sum_k \gamma_k\nabla_x\Omega(\mathbf{x}) \,.\, \partial\mathbf{q}(\mathbf{x},\gamma)/\partial\gamma_k$$

$$\approx \quad \Omega(\mathbf{x}) \quad + \quad \sum_k \gamma_k \partial\Omega(\mathbf{q}(\mathbf{x},\gamma))/\partial\gamma_k \qquad (4)$$

Eq. (4) is asymptotically true for small γ_k and reasonably true for larger γ_k if $\Omega(\mathbf{x})$ is smooth. Intuitively Eq. (4) states that the difference between a scaled reference and an object image can be expressed as the sum of the changes in the object image, expected with each component of the displacement, times the amount of that component [see also reference (2)]. Given the 'good lattice' assumption Eq. (4) can be expressed in matrix notation

$$\Omega \quad \approx \quad \mathbf{G}.[b \;\; \gamma]^T$$

where

$$\mathbf{G} \quad \approx \quad [\tau \quad -\partial\Omega/\partial\gamma] \qquad (5)$$

τ and Ω are column vectors with one element per voxel. The element of $\partial\Omega/\partial\gamma$ in the jth row of the kth column = $\partial\Omega(\mathbf{q}(\mathbf{x}_j,\gamma))/\partial\gamma_k$ where $\mathbf{x}_j$ corresponds of the position of jth voxel. In practice it is easy to compute the six columns of $\partial\Omega/\partial\gamma$ by simply applying small translations and rotations to $\Omega(\mathbf{x})$ and measuring the changes in voxel values. b is an estimate of ß. The six elements of the row vector γ correspond to the estimated translations and rotations that constitute the estimated movement. The vector γ is estimated in a least squares sense by:

$$[b \;\; \gamma]^T \;=\; (\mathbf{G}^T.\mathbf{G})^{-1}.\mathbf{G}^T.\,\Omega \qquad (6)$$

These movement parameters can be estimated for each volume image and used to 'realign' the time-series. We have addressed the validity and efficiency of these estimates (1) and have found them to be sensitive to movements in the order of 100µm. It should be noted that the above expressions only hold when the movements involved are small relative to the smoothness of the images. This is not a problem because the images are usually smoothed prior to the estimation (see below and discussion).

Usually, after realignment we would proceed to the analysis proper. However as noted in the introduction there are likely to be signal components that are a function of the positions of the current and previous scans. Let γ_i represent the movement or position parameter estimates for scan i (relative to the first scan). The model we adopt here partitions the signal X_i from a given voxel into two orthogonal components. The first component is the one that we are interested in X^*_i and the second is designated a movement-related artefact that is some function of γ_i for the present and previous scans, say $f(\gamma_i, \gamma_{i-1}, ...)$

$$X_i \quad = \quad X^*_i + f(\gamma_i, \gamma_{i-1}, ...)$$

By signal we mean the observed voxel value in scan i, such that the time-series from a single voxel can be denoted by the column vector $\mathbf{X} = [X_1.......X_I]^T$, for I scans. By the time-series with elements X^*_i we imply a variance component of $\mathbf{X}$ that is orthogonal to those components that can be construed as movement-related effects.

The form of position-dependent effects - $f(\gamma_i, \gamma_{i-1}, ...)$

In the following we concentrate on the form of $f(\gamma_i, \gamma_{i-1}, ...)$, i.e. the form of the signal dependency on positions relative to some initial reference scan. The nature of this dependency is complicated: In slice-selective techniques the proportion of spins excited will vary as a function of position (and time). The signal will therefore be a reasonably strong function of the position at the time of scan i. However the saturation of spin magnetization will also affect the signal. This saturation will be a function of the number of spins excited in the previous scan i - 1 and therefore a function of position at the time of the previous scan. By induction, the signal is a function of the history of position at the time of all previous scans. This suggests an autoregression model for the dependence of signal X_i on position; however this autoregression is not simple. Consider the following model:

Let the z component of bulk magnetization be denoted by $M_z(t)$, where $M_z(i.TR - 0)$ and $M_z(i.TR + 0)$ are the longitudinal magnetizations just before and after the ith excitation respectively. TR is the repeat time. Let μ_i represent the proportional reduction in $M_z(t)$ following excitation, where this reduction is a measure of the relative degree of excitation elicited by the r.f. pulse. Assuming first order longitudinal relaxation (3) and that the excitation time is very short compared to T_1:

$$M_z(i.TR + 0) = (1 - \mu_i).M_z(i.TR - 0) \quad \text{if } t = i.TR$$

$$\text{and} \quad dM_z(t)/dt = (M_0 - M_z(t))/T_1 \quad \text{otherwise} \tag{7}$$

M_0 is the equilibrium magnetization. The degree of excitation μ_i can change from scan to scan and we model this as $\mu_i = \mu + \Delta_i$. Δ_i represents the small scan to scan changes in excitation and is a function of position relative to the first scan i.e $\Delta_i = g(\gamma_i)$. The observed signal will reflect the transverse magnetization that ensues after excitation (i.e. the number of spins flipped into the xy plane) and will be a function of the relative excitation and the longitudinal magnetization just before excitation. We model this signal as $S_i = h(\mu_i).M_z(i.TR - 0)$, where, taking a first order Taylor expansion $S_i \approx [h(\mu) + \Delta_i.\partial h/\partial\mu].M_z(i.TR - 0)$. Both $h(\mu)$ and $\partial h/\partial\mu$ are positive. Clearly one could a assume specific form for $h(\mu)$, however this is not necessary for what follows.

A simulated example of the evolution of $M_z(t)$ is presented in Figure 1 (upper panel) using a TR of 3 seconds, a T_1 of 5.77 seconds and modeling μ_i as a process of random Gaussian variables, with an mean of 0.6 and standard deviation of 0.1. This figure tries to make the point that after a large proportion of the magnetization $M_z(t)$ has been removed by slice-selective excitation, the ensuing scan encounters a greater degree of saturation and is likely to have a smaller signal. In general this means that a high signal in scan i will be associated with a lower signal in the ensuing scan (i + 1). This illustrated by the recursion plot (over 1024 scans) in the lower panel of Figure 1. For simplicity we assumed $h(\mu) = \mu$ and $\partial h/\partial\mu = 1$, giving $S_i = \mu_i.M_z(i.TR - 0)$. It can be seen that, although the effect is small, there is a negative correlation between the signal in the current scan and in the subsequent scan.

A precise relationship between S_i and μ_i obtains on considering simple longitudinal relaxation [Eq. (7)]. Let $M_{zi} = M_z(i.TR - 0)$.

$$M_{zi} \quad = \quad M_0 \ - \ k.[M_0 \ - \ M_{zi-1}(1 \ - \ \mu_{i-1})] \qquad (8)$$

where $k = \exp(-TR/T_1)$ and can be thought of as the proportion of spins that have recovered. The importance of this complicated [geometric] autoregression equation is that M_{zi} is a function of M_{zi-1} and μ_{i-1}. After repeated substitution to eliminate the M_{zi-1} terms, M_{zi} can be expressed in terms of μ_i, μ_{i-1}, μ_{i-2},.....:

$$M_{zi} \quad = \quad M_0\,(1 - k) \sum_{m=0}^{\infty} k^m \prod_{v=1}^{m} (1 - \mu_{i-v})$$

where the empty product at m = 0 is replaced by 1 (the usual convention). This equation can, with some considerable arithmetic, be expanded in terms of Δ_i, the small changes about μ. Ignoring high order terms (involving Δ_i), a moving average representation for the signal can be derived, with the form:

$$S_i \approx c_0 + c_1.\Delta_i + c_2.\Delta_{i-1} + c_3.\Delta_{i-2} + \ldots\ldots\ldots$$

where	c_0	=	$h(\mu)\, M_0\, (1 - k) / \{1 - k(1 - \mu)\}$	$>$	0	
	c_1	=	$\partial h/\partial\mu\; c_0 / h(\mu)$	$>$	0	
and	c_{1+i}	=	$- c_0\, k^i (1 - \mu)^{i-1}$	$<$	0	(9)

It is seen that the series of coefficients converge rapidly. The coefficient for the current scan in positive and large, whereas the coefficient for previous scans are negative and decrease rapidly. c_0 represents the signal that would be obtained if the small changes were all zero [this can be verified by substitution into Eq. (8), noting that when $\Delta_i = 0$, $S_i = h(\mu).M_{zi}$]. c_1 becomes smaller as the degree of spin excitation increases. For example spins in the centre of the excited volume, where μ is likely to be very high, will be less sensitive to small changes in excitation (or position). Conversely spins on the edge of an excited volume may have a small μ, and will be very sensitive to these effects. The c_{1+i} show a similar dependency in the sense that when μ is small, the values of these coefficients 'tail off' more slowly. The negativity of c_2 is intuitively sensible given that the signal in scan i is negatively correlated with the signal in scan i - 1 (Figure 1 lower panel).

Figure 2 shows an example of this model using a simulation. We simulated $M_z(t)$ over 128 scans with a repeat time of 3 seconds and a T_1 of 5.77 seconds (upper panel in Figure 2). The scan to scan differences in excitation Δ_i were modelled as a process of random Gaussian variables with standard deviation 0.1 and a mean of zero. The mean excitation μ was 0.6. The line in the second panel corresponds to $\mu_i = \mu + \Delta_i$. The coefficients c_1, c_2 .... were computed using Eq. (9) and are displayed as a function of scan number. The signal S_i (solid line in the right lower panel) was computed by assuming $h(\mu) = \mu$ and $\partial h/\partial\mu = 1$ and is predicted very well by the moving average approximation of Eq. (9) (dotted line). In the example shown only the first three terms were used suggesting only the current change in excitation and that of the previous scan are sufficient to predict movement-related changes in signal.

On the basis of the theoretical analysis presented here we propose the following form for the signal components due to movement $f(\gamma_i, \gamma_{i-1}, ...)$:

$$
\begin{aligned}
f(\gamma_i, \gamma_{i-1}, ...) &= p.(S_i - c_0) \approx p.c_1.\Delta_i + p.c_2.\Delta_{i-1} \\
&\approx p_1.g(\gamma_i) + p_2.g(\gamma_{i-1}) \qquad (10)
\end{aligned}
$$

where p is a constant of proportionality and $(S_i - c_0)$ represents the changes in signal about c_0, the signal in the absence of movement.

Adjusting for movement-related effects

The relationship between changes in excitation and position i.e. $g(\gamma_i)$ will clearly vary from point to point and will be a function of the local magnetic field and the frequency structure of the r.f. pulse. The former will change with position relative to the scanner (the latter will not). We model g(.) with a sum of second order polynomials, where the sum is over the components of the displacement.

$$g(\gamma_i) = \sum \{ u_k.\gamma_{ki} + v_k.\gamma_{ki}^2 \}$$

giving, from Eq.(10)

$$f(\gamma_i, \gamma_{i-1}) = \sum \{ p_1u_k.\gamma_{ki} + p_1v_k.\gamma_{ki}^2 + p_2u_k.\gamma_{ki-1} + p_2v_k.\gamma_{ki-1}^2 \}$$

or in matrix notation

$$f(\gamma_i, \gamma_{i-1}) = \mathbf{Q.p} \qquad (11)$$

where:

$$\mathbf{Q} = [\gamma_1;....\gamma_I;\ \ \gamma_1{}^2;....\gamma_I{}^2;\ \ \gamma_0;....\gamma_{I-1};\ \ \gamma_0{}^2;....\gamma_{I-1}{}^2]$$

$$\mathbf{p} = [p_1u_1,...p_1u_6,\ \ p_1v_1,...p_1v_6,\ \ p_2u_1,...p_2u_6,\ \ p_2v_1,...p_2v_6]^T$$

p is a vector of the coefficients of the polynomial expansion. γ_i [$\gamma_i{}^2$] are the vectors of position parameters [squared] relative to the reference scan, arranged so that each column of **Q** contains one parameter at time or scan i or i - 1 (';' means stack matrices or vectors on top of each other). γ_0 = [0 0 0 0 0 0].

Recall that we are modeling the signal of interest and movement-related confounds as independent components. This orthogonality constraint requires that $\mathbf{Q}^T.\mathbf{X}^* = 0$ and so, from Eq. (11):

$$\mathbf{X} = \mathbf{X}^* + \mathbf{Q.p}$$

$$\mathbf{Q}^T.\mathbf{X} = \mathbf{Q}^T.\mathbf{Q.p}$$

giving

$$\mathbf{X}^* = \mathbf{X} - \mathbf{Q}.(\mathbf{Q}^T.\mathbf{Q})^{-1}.\mathbf{Q}^T.\mathbf{X} \qquad (12)$$

As noted above **X** is a column vector of voxel values for each of the I scans. Similarly for **X***. **X*** is a column vector of *adjusted* fMRI values for the voxel in question, that is completely orthogonal to the movement artifacts modelled in terms of the movement estimates **Q**. Clearly the form of these equations means that, in practice, they can be solved for all voxels simultaneously.

In the remaining sections we assess the validity of the assumptions used above by showing movement-related effects can be very prominent and are substantially attenuated by the adjustment procedure described.

An application to real data

There are many ways of testing for the effect of position, and past changes in position, that persist after realignment. We have chosen to use variance partitioning and an eigenimage analysis to provide anecdotal but compelling evidence for these effects. The first set of data were chosen because they contained marked movement artefacts and the second set because they are more representative of standard fMRI activations studies.

The fMRI data - patient study

100 T_{2^*} weighted volume images (128x64x7 voxels) were obtained from a single male subject using a GE/ANMR 1.5T system equipped with Advanced NMR EPI capabilities. The volumes consisted of 7 sequential transverse sections and were acquired every three seconds. Voxel size was 3x3x7 mm voxels, with 0.5mm slice separation. The subject was scanned under two conditions. The baseline (darkness) and activation (photic stimulation) conditions were presented in blocks of 10, with 10 baseline, 10 activation, 10 baseline and so on. The subject was a 64 year old patient with a parieto-occipital infarct and a paranoid psychosis. He found it difficult to remain very still during the scanning session.

6 movement parameters ($\mathbf{q}_i$) were estimated for each of the 100 volumes using Eq. (6) with the first scan as the reference volume image (τ). For this estimation step the images were smoothed with an isotropic Gaussian kernel of 8mm FWHM. The results of this analysis are shown in Figure 3. The subject did very well up until the 72nd scan, when there was a pronounced roll, yaw and lateral shift (y translation) of the head. At the greatest excursion the head was some 10mm and 6 degrees away from its starting position. After this marked movement the subject returned slowly towards his initial position. Because the head conforms roughly to a sphere, it is possible to rotate the head in the scanner without much evidence of translational movement. This is seen in the

current parameter estimates where for the first 70 scans or so there is a progressive roll and yaw (up to about two degrees) with very little translation of the head's centre. The parameters shown in Figure 3 were used to realign the images for subsequent analysis and processing.

Each volume image was thresholded at 0.8 of the whole volume mean. Only voxels surviving this threshold for all the volume images were retained for further analysis. Following realignment the data were mean corrected to give a data matrix **X** with 100 rows (one for each scan) and 12577 columns (one for each voxel).

Variance partitioning

Because of the orthogonality between adjusted signal and the estimate of movement related effects, the total sum of squares (for one voxel) of the signal can be partitioned into non-movement $\mathbf{X}^{*T}\mathbf{X}^*$ and movement effects $\mathbf{p}.\mathbf{Q}^T.\mathbf{Q}.\mathbf{p}$, where:

$$\mathbf{X}^T\mathbf{X} = \mathbf{X}^{*T}\mathbf{X}^* + \mathbf{p}.\mathbf{Q}^T.\mathbf{Q}.\mathbf{p} \quad (13)$$

Similarly by splitting **Q** into two orthogonal matrices we can separate the effects of position in the current scan from the historical effects (position in the previous scan). i.e.

$$\mathbf{X}^T\mathbf{X} = \mathbf{X}^{*T}\mathbf{X}^* + \mathbf{pc}.\mathbf{Qc}^T.\mathbf{Qc}.\mathbf{pc} + \mathbf{ph}.\mathbf{Qh}^T.\mathbf{Qh}.\mathbf{ph}$$

where $\mathbf{pc} = (\mathbf{Qc}^T.\mathbf{Qc})^{-1}.\mathbf{Qc}^T.\mathbf{X}$

$\mathbf{ph} = (\mathbf{Qh}^T.\mathbf{Qh})^{-1}.\mathbf{Qh}^T.\mathbf{X}$

and $\mathbf{Qc} = [\mathbf{q}_1;\ldots.\mathbf{q}_I;\ \mathbf{q}_1{}^2;\ldots.\mathbf{q}_I{}^2]$

$$\mathbf{Qh} = \mathbf{Q} - \mathbf{Qc}.(\mathbf{Qc}^T.\mathbf{Qc})^{-1}.\mathbf{Qc}^T.\mathbf{Q} \quad (14)$$

$\mathbf{X}^T\mathbf{X}$ is the total sum of squares. $\mathbf{X}^{*T}\mathbf{X}^*$ is the sum of squares of the adjusted data. $\mathbf{pc.Qc}^T\mathbf{.Qc.pc}$ represents the sum of squares due to estimated movement effects attributable to the current scan and $\mathbf{ph.Qh}^T\mathbf{.Qh.ph}$ is the corresponding term for the previous scan.

These sums of squares were calculated for every voxel and summed over voxels. The values obtained were remarkable. The estimated movement effects attributable to the current scan accounted for 89.04% of the total sum of squares. The effects due to position in previous scans accounted for a third of the remaining variances (3.98% of the total). Only 6.98% of the variance remained to constitute the adjusted signal. These are extreme values (we deliberately chose a 'bad' data set) but demonstrate the potentially confounding effects of movement that can persist after realignment.

Eigenimage analysis

Eigenimage analysis of functional imaging time-series was developed for PET activation studies (4). It has subsequently proved fruitful in the analysis of fMRI time series [see Friston et al (5) for a description of how to compute eigenimages using singular value decomposition or SVD]. Eigenimage analysis simply partitions a spatially extended time-series into a set of orthogonal *spatial modes* or eigenimages that show independent temporal activity. The first eigenimage accounts for the greatest amount of variance and the second for the greatest amount that is left (and so on).

In the current data the effects of movement were very pronounced. The first eigenimage is shown in Figure 4 (upper panel). The lower panel in Figure 4 shows the time course of this eigenimage. The time-dependent expression of this mode $\mathbf{X}\varepsilon$ suggests that it can be largely explained by roll (compare the solid line in the lower panel of Figure 4 and the estimate of roll in Figure 3). Note that this eigenimage accounts for more than half the variance (57.2%) observed in this study. The dotted line in the lower panel of Figure 4 was the predicted time-course of movement-related signal based on the movement parameters i.e.

$$f(\gamma_i, \gamma_{i-1}) = \mathbf{Q}.\mathbf{p}\varepsilon$$

where

$$\mathbf{p}\varepsilon = (\mathbf{Q}^T.\mathbf{Q})^{-1}.\mathbf{Q}^T.\mathbf{X}\varepsilon$$

To demonstrate that there are real biological components that are not correlated with movement-related effect, the sixth eigenimage and its associated expression are presented in Figure 5. This component is clearly due to some (aliased) biorhythm and appeared to be most prominent in the venous sinuses. In this instance the best fitting movement-related prediction fails to account for the observed changes until after the 72nd scan (the broken line in the lower panel of Figure 5).

The estimated $f(\gamma_i, \gamma_{i-1})$

The coefficients $\mathbf{p}\varepsilon$ in the previous section represent an estimate of $f(\gamma_i, \gamma_{i-1})$ according to Eq. (11). This empirical estimate should show certain features based upon theoretical predictions. The key feature is that any effect of displacement in the present scan should have a smaller and opposite effect when expressed in the previous scan. An example of this is seen in Figure 6 which depicts $f(\gamma_i, \gamma_{i-1})$ as a function of z displacement in scan i and scan i - 1. This estimate was based on $\mathbf{p}\varepsilon$. It can be seen that changes in signal are a strong function of z position in the current scan and a weaker function of position in the previous scan. Furthermore the effect of position in the present and previous scans are opposite in nature, giving a saddle-like form for $f(\gamma_{3i}, \gamma_{3i-1})$. One might interpret this function as follows: There is a signal component in the first eigenimage that arises from spins that are 'between' slices. Movement in either direction, into regions that are subject to more excitation, increases the signal from these spins. However if the spins have been in regions with more excitation in the previous scan (i -1), the signal will be reduced. This reduction being mediated by an incomplete recovery from saturation.

Because these movement-related effects depend on movement in and out of the (transverse) slices one might expect estimated signal changes to be strong functions of z translation, pitch and roll and weak functions of translations in z and y and yaw. This is exactly what we observed. Figure 7 shows the estimate of $f(\gamma_i, \gamma_{i-1})$ as functions of translation and rotation in scan i. The solid lines (z translation - upper panel, pitch and roll - lower panel) are strong nonlinear functions of position whereas the dotted lines (x and y translation - upper panel, yaw - lower panel) are weaker functions of position (relative to the reference scan).

An analysis of normal subjects participating in fMRI activation studies

The data presented above represent an extreme case with pronounced movement artifacts. To demonstrate that these effects can be prevalent in normal cooperative subjects, we analyzed three further data sets from fMRI activation studies [Study 1 - a verbal fluency study (100 scans), study 2 - a motor sequencing study (120 scans) and study 3 - a paced finger movement study (120 scans)]. The data were acquired as described above and subject to the same analyzes. In general all three subjects remained remarkably still, with less than a millimetre and less than a degree excursion from the reference scan. Positional drifts were not correlated with changes in task or conditions and there were no systematic features from subject to subject (see Figure 8). The sum of squares (pooled over voxels) attributable to movement in the current or past scans were calculated according to Eq. (13). Despite the fact that the subjects remained very still, a considerable proportion of the variance could be designated movement artifact, namely 48%, 38% and 31% for the three studies respectively. The results are typical of those obtained in our laboratory where we routinely use these methods for image realignment and adjustment.

Adjusting the fMRI time-series

The data from the patient were adjusted according to Eq. (12). The efficacy of this adjustment was assessed by comparing two images that showed a marked relative displacement (the 64th and 78th volume images). The two images were compared by simple subtraction. The results of this analysis are presented in Figure 9. The upper row shows a slice through the original volumes before realignment. Marked yaw is immediately apparent. The bottom row of images show that same two slices after both have realigned to the first image. The 78th slice is presented after realignment and after realignment plus adjustment. The middle row depicts difference images comparing the 64th and 78th scans. The original difference (left) is somewhat attenuated by conventional realignment (centre). The key point to note is that the 'adjustment' for movement-related effects (current) is considerably better than realignment alone. Note that we did not align the 78th scan to the 64th, but both the 78th and 64th to the first scan. Using the realignment and adjustment procedure we were able to demonstrate significant activation in the striate cortex that had previously eluded us.

Discussion

We have presented an approach for removing the confounding effects of movement-related artifacts in fMRI time-series. This approach is predicated on the conjecture that residual effects remain even after perfect realignment. These effects can be divided into those that depend on absolute position in the image space (relative to the scanner) and a component that is due to the history of past displacements or changes in position from scan to scan. This second component depends on the history of excitation experienced by spins in a small volume and consequent differences in local saturation. The spin excitation history will itself be a function of previous movements. An autoregression-moving average model for the effects of previous displacements on the current signal has been proposed. On the basis of this model we concluded that is was important to include not just information about the position at the time of scanning but also the position at the time of the previous scan. We have described how this information can be used to adjust for the movement-related components that ensue. Our empirical analyses suggest that over 30-90% of the fMRI signal can be attributed to movement, and that this artifactual component can be successfully removed.

The proposed approach takes the following form:

♣ Estimate the movement parameters by comparing each scan in the time series to a reference scan. This is effected by expressing the difference between the scan in question, and the reference scan, as the sum of all partial derivatives of the image, with respect to each movement component, times the amount of each component. Estimates of the latter are obtained using least squares..

♣ Realign the time-series using the parameter estimates above.

♣ Adjust the values of each voxel by removing any component that is correlated with a function of movement estimates, obtained at the time of the current scan and the previous scan. We have used the linear sum of a second order polynomial for each parameter estimate.

Limitations

Some limitations of the technique relate to the 'reasonableness' of the first order approximation in Eq. (3), which holds only when the spatial displacements are small relative to smoothness. In a sense this is not a fundamental limitation because (i) the images can always be made sufficiently smooth or (ii) the procedure can be applied iteratively as a highly constrained least squares search. In general the relative displacements between any two images should be less than their smoothness, or resolution. We recommend that the data be convolved with a Gaussian filter before the movement parameters are estimated (clearly the realignment and adjustment procedures can be applied to the original unsmoothed data). In the examples above we have used a Gaussian kernel of 8mm FWHM to ensure that movements of up to several millimetres could be properly estimated (see ref 1 for a fuller discussion and simulation results).

Another potential limitation is the length of the time-series used. It is important to note that if the number of scans is less than the columns of **Q** (movement-related effects to be removed) the resulting adjusted data (**X***) will be (nearly) zero. This is because the dimension of the data would be less than that of the potential confounds. This is not typically a problem for fMRI but does preclude the use of this sort of technique in PET.

If any component of activation-dependent or task-related changes are correlated with an estimated movement effect, this component will be removed. Although this may be seen as 'throwing the baby out with the bathwater', we would prefer to think that it provides absolute protection against false attribution of signal changes in the context of activation-related movement artifacts (6).

Implication for fMRI activation studies

The analysis presented in this paper is not intended to undermine the results of previous activation studies using fMRI. What we are saying is that true activations (that may be detectable in the absence of a correction for movement) may be characterized with greatly increased sensitivity if movement-related effects are first removed. Artifactual 'activations' will only ensue when the movement effects are correlated with changes in task or condition. In our experience this is not the case. However movement-related effects can confound the analyses of activation studies in another way: Movement-related variance will be modelled (in any statistical model) as error variance when testing for a particular time-dependent response. As a consequence the statistical quotients will be much smaller than if this movement component had been removed. In short, if activations are detected before correcting for movement, then they are likely to be real (assuming that they are orthogonal to movement effects), however a re-analysis using the techniques described in this paper should increase the significance and extent of these activations, and possibly reveal some that were not seen before.

Conclusion

In conclusion we hope to have presented a reasonable solution to a fairly simple problem: How to remove movement-related artifacts from fMRI time-series, quickly, automatically and with some degree of validity.

Note Many of the algorithms presented in this paper have been implemented in MATLAB (MathWorks Inc, Sherborn MA, USA). These ASCII files (interpreted by MATLAB) are available from the authors as part of the SPM software.

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Legends for Figures

Figure 1

Schematic showing the results of a simple simulation of the effects of movement on successive signal intensities. Upper panel: This is the time course of longitudinal magnetization $M_z(t)$, assuming a repeat time of 3 seconds and a T_1 of 5.77 seconds. Equilibrium magnetization is set to 1. The decrease in $M_z(t)$ following each scan varies in a random fashion from scan to scan, emulating differential excitation due to movement. The overall impact of this variability is a variance in signal [proportional to the decrements in $M_z(t)$] that depends on both the current degree of excitation and the degree of excitation in the previous scan. Lower panel: Recursion plot of simulated signal [decrease in $M_z(t)$ at the time of each scan] from scans i and i + 1. This figure demonstrates that a high signal in one scan results in a generally lower signal in the ensuing scan.

Figure 2

Results of a simulation to demonstrate the first-order moving average approximation of changes in signal intensity. For simplicity we assume that the spins are excited one every TR. This moving average, of a stochastic process of small changes in the relative excitation of spins, closely approximates the simulated signal changes.. Upper panel: Simulated $M_z(t)$ as a function of time over 128 scans with a repeat time of 3 seconds. M_0, the equilibrium magnetization was set at 1 and the T_1 was 5.77 seconds. Second panel: The proportional reduction in $M_z(t)$, as a function of scans. This proportion $\mu_i = (\mu + \Delta_i)$ was modelled as a random Gaussian process Δ_i with standard deviation 0.1 and a mean of 0, plus a constant $\mu = 0.6$. Lower left panel: The moving average coefficients based on Eq. (9) in the main text.. Lower right panel: The simulated signal S_i (solid line) and that predicted (broken line) by a moving average of the process Δ_i

Figure 3

Estimated movement parameters from a real time series of 100 fMRI volume images. Above: x, y and z translation. Below: Rotations as estimated by the least squares approach. Note the substantial movements after the 72th image.

Figure 4

Eigenimage analysis of the fMRI time series referred to in the previous figure *following realignment.* Above: positive and negative parts of the first spatial mode or eigenimage following SVD. The grayscale is arbitrary and the images have been scaled to their maximum. The display format is standard and corresponds to maximum intensity projections of the data providing views of the brain from the front, than left and from below. Below: Time dependent expression of this spatial mode. The broken line corresponds to estimated movement effects as described in the main text. It can be seen that this mode is, almost entirely, explained by movement effects.

Figure 5

As for the previous figure (Figure 3) but showing the sixth eigenimage. In this instance the eigenimage cannot be explained by movement artefacts and includes an orthogonal biological component.

Figure 6

The estimated signal change as a function of z displacement (from the first scan) in the present (i) and previous scans (i - 1). Note that the effects of position are opposite in sign although similar in form.

Figure 7

Estimates of signal changes as functions of movement parameters. These functions are expressed in terms of translation (upper panel) and rotations (lower panel) using component movements in, and only in, the current scan. The solid lines (z translations, pitch and roll) are string functions of movement when compared to the dotted lines (x and y translation and yaw).

Figure 8

Estimated movement parameters for three normal subjects during fMRI activation studies. The format is the same as that used in Figure 3. a - study 1, b - study 2 and c - study 3.

Figure 9

Comparing the efficacy of realignment and realignment with adjustment as described in the main text. Upper row: Two transverse slices through the 64th and 78th volume images before any processing. Middle row: Differences between the the two slices in the upper row before any processing (left), after realignment (centre) and after realignment with adjustment (right. Lower row: The two slices in the top row following realignment and adjustment.