The role of registration and spatial normalisation in detecting activations in functional imaging

John Ashburner & Karl Friston
Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK.

Principles of activation detection using functional MRI

The principle behind detecting activations using *functional Magnetic Resonance Imaging* (fMRI) is essentially a voxel by voxel t-test on a series of images acquired under different conditions (Friston *et al.*, 1995b; Worsley & Friston, 1995). Currently, the index of neuronal activity used for these experiments is the *Blood Oxygenation Level Dependent* (BOLD) contrast (Ogawa *et al.*, 1990). The assumption in functional neuroimaging is that an increase in neuronal activity within a brain region results in an increase in local blood flow, leading to reduced concentrations of deoxyhæmoglobin in the blood vessels. Unlike oxyhæmoglobin, deoxyhæmoglobin has a differential magnetic susceptibility in relation to the surrounding tissue. Therefore, relative decreases in deoxyhæmoglobin concentration lead to a reduction in local field inhomogeneity and a slower decay of the MR signal, resulting in higher intensities in $T2^*$ weighted images.

Image realignment

The signal changes due to any hæmodynamic response are small compared to signal changes that can result from subject motion, so prior to performing the statistical tests, it is important that the images are as closely aligned as possible. Subject head movement in the scanner can not be completely eliminated, so motion correction needs to be performed as a preprocessing step on the image data.

Most current algorithms for movement correction consider the head as a rigid object. In three dimensions, six parameters are needed to define a rigid body transformation (three translations and three rotations). The first step in the correction is image registration, which involves determining the parameter values that optimize some criteria for matching each image with a reference image. In order to be effective, the accuracy of the registration needs to be within a fraction of a voxel. Following the registration, the images are transformed by resampling according to the determined parameters, generally using a form of sinc interpolation. In the purest form of sinc interpolation, the values of every voxel in the image are needed to resample a single voxel. This is not feasible in practice, so a windowed sinc function (using only a few nearest neighbours) is generally used as an approximation.

Motion correction is especially important for paradigms where the subject may move in the scanner in a way that is correlated to the different experimental conditions (Hajnal *et al.*, 1994). Even tiny systematic differences can result in a significant signal accumulating over numerous scans. Without suitable corrections, artifacts arising from subject movement correlated with the paradigm may appear as activations. Even after the registration and transformations have been performed, it is likely that the images will still contain artifacts correlated with movement. There are a number of sources of these artifacts, including the approximations used in the sinc interpolation, aliasing effects due to gaps between the slices, ghosts in the images, slices not being acquired simultaneously (so the data no longer obeys the rules of rigid body transformations) and spin excitation history effects. Fortunately (providing that there are enough images in the series), the artifacts can largely be corrected by using an ANCOVA model to remove any signal that is correlated with functions of the movement parameters (Friston *et al.*, 1996).

A second reason why motion correction is important is that it increases sensitivity. The t-test is based on the signal change relative to the residual variance. The residual variance is computed from the sum of squared differences between the data and the linear model to which it is fitted. Movement artifacts add to this residual variance, and so reduce the sensitivity of the test to true activations.

Spatial normalisation

Sometimes it is desirable to warp images from a number of individuals into roughly the same standard space to allow signal averaging across subjects. Unlike the case for PET images, it is not necessary to combine fMRI data from a number of subjects to achieve a significant activation signal. However, since different people may have different strategies for performing tasks in the scanner, spatial normalisation of the images is useful for determining what happens generically over individuals. A further advantage of using spatially normalised images is that activation sites can be reported according to their Euclidian coordinates within a standard space (Fox, 1995). The most commonly adopted coordinate system within the brain imaging community is that described by Talairach & Toumoux (1988). The normalisation usually begins by matching the brains to a template image using an affine transformation, followed by introducing nonlinear deformations described by a number of smooth basis functions (Friston *et al.*, 1995a). Matching is only possible on a coarse scale, since there is not necessarily a one-to-one mapping of the cortical structures between different brains. Because of this, the images are smoothed prior to the statistical analysis in a multi-subject study, so that corresponding sites of activation from the different brains are superimposed.

For fMRI studies of a single subject, the sites of activation can be accurately localized by superimposing them on a high resolution structural image of the subject (typically a T1 weighted MRI). This requires the registration of the functional images with the structural image. As in the case of movement correction, this is normally performed by optimizing a set of parameters describing a rigid body transformation, but the matching criterion needs to be more complex since the images are often acquired using different MR contrasts. A further use for this registration is that a more precise spatial normalisation can be achieved by computing it from a more detailed structural image. With the functional and structural images in register, the computed warps can be applied to the functional images.

Conclusions

In summary, spatial transformations are ubiquitous and essential for the proper characterization of evoked hæmodynamic changes in fMRI, both in terms of removing unwanted variance and in terms of anatomical localization.

References

Fox, P. T. 1995. Spatial normalization origins: Objectives, applications, and alternatives. *Human brain mapping*, **3**, 161–164.

Friston, K. J., Ashburner, J., Frith, C. D., Poline, J.-B., Heather, J. D., & Frackowiak, R. S. J. 1995a. Spatial registration and normalization of images. *Human brain mapping*, **2**, 165–189.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J.-B., Frith, C. D., & Frackowiak, R. S. J. 1995b. Statistical parametric maps in functional imaging: A general linear approach. *Human brain mapping*, **2**, 189–210.

Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S. J., & Turner, R. 1996. Movement-related effects in fMRI time-series. *Magnetic resonance in medicine*, **35**, 346–355.

Hajnal, J. V., Mayers, R., Oatridge, A., Schwieso, J. E., Young, J. R., & Bydder, G. M. 1994. Artifacts due to stimulus correlated motion in functional imaging of the brain. *Magnetic resonance in medecine*, **31**, 289–291.

Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D. W. 1990. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc. natl. acad. sci.*, **89**, 9868–9872.

Talairach, J., & Tournoux. 1988. *Coplanar stereotaxic atlas of the human brain*. New York: Thieme Medical.

Worsley, K. J., & Friston, K. J. 1995. Analysis of fMRI time-series revisited - again. *Neuroimage*, **2**, 173–181.

Figure Legends

Figure 1
Typical movement parameters estimated over a series of images. The parameters are translations in three orthogonal directions and rotations about the three axes.

Figure 2
Artifacts arising from subject movement. Top row: two original images from a series. Bottom row: Difference images prior to realignment (left), after realignment (centre) and after realignment with adjustment by removal of signal that is correlated with movement (right).

Figure 3
Diagramatic illustration of steps involved in the localization of activations in fMRI. The images are corrected for movement, spatially normalised to Talairach space and smoothed with a Gaussian kernel. Finally the statistical tests are applied to determine the t-statistic using the general linear model.