Combining ICA and GLM: A Hybrid Approach to FMRI Analysis

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Introduction

Independent Component Analysis (ICA) [1] has recently been applied to FMRI data as an exploratory data analysis technique to find spatially independent patterns of activation in the brain [4]. While it has been shown that exploratory methods can produce time courses that are highly correlated to a task reference function, the extracted spatial component maps do not always easily lend themselves to neurophysiological interpretation. In a hybrid approach to FMRI analysis, we employ ICA to blindly estimate the haemodynamic response function of a complex FMRI experiment. The task related time courses are then used as the stimulus reference function within a GLM-based statistical analysis.

Data

We applied Independent Component Analysis to $T = 400$ ($TR = 3s$) FMRI volumes of v=64×64×21 voxels obtained on a 3T scanner from an experiment comprising 14 bursts of painful heat ($3s$ per burst) with an approx. $60s$ interstimulus interval (jittered to onset of slice collection) followed by simple visual checkerboard stimulus (AB design) as reported in [7].

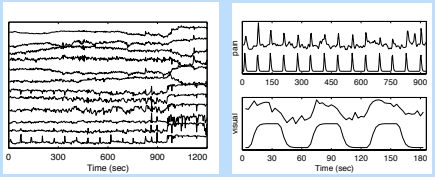
Independent Component Analysis

The three spatial dimensions were concatenated to form a $T \times v$ data matrix $\boldsymbol{X}$ of size 400×15400, where voxels outside the brain have been excluded from further analysis. The spatially independent components were calculated by maximizing negentropy as a measure of non-Gaussianity [3].
First, the data matrix $\boldsymbol{X}$ was centred and whitened using eigenvalue-decomposition. The new matrix $\boldsymbol{X}'$ was then decomposed into a $k \times v$ matrix $\boldsymbol{C}$ of spatially independent component maps and a $t \times k$ matrix $\boldsymbol{M}$ of associated time courses such that

$$\boldsymbol{X}' = \boldsymbol{M}\boldsymbol{C}.$$

The mixing matrix $\boldsymbol{M}$ was estimated using a fixed-point technique that, unlike ICA estimation based on the maximum entropy, is not required to specify the shape of the cumulative distribution function of the unknown sources. After convergence, the rows of $\boldsymbol{C}$ contain spatially independent volumes and the columns of $\boldsymbol{M}$ the corresponding (unconstrained) time courses of activation for each volume in $\boldsymbol{M}$.

Extracting the reference function



(a) (b)

Figure 1: Time courses extracted via ICA.

In an initial run, 40 independent components were extracted from the full data set. Figure 1 a) shows 12 of the corresponding time series. All of the sequences suggest a change in experimental design at $t = 930$. Note that one of the sequences picks out a spike train corresponding to the pain stimuli. The visual paradigm, however, is not well represented. For further analysis the dataset was divided into $T = 340$ scans (pain stimuli) and $T = 60$ scans (visual stimuli). From the new data sets 60 and 100 ICs were extracted respectively. In both cases, exactly one time course matched the experimental setup (see figure 1 b)). These two sequences have then been used as a task reference function in a GLM-based analysis.

GLM Analysis

Analysis was carried out using FEAT, the FMRIB Easy Analysis Tool [www.fmrib.ox.ac.uk/fsl]. The following pre-statistics processing was applied; motion correction using the SPM realign procedure with adjustment for movement; spatial smoothing using a Gaussian kernel of FWHM $6mm$; global (volumetric) multiplicative mean intensity renormalization; Gaussian lowpass filtering FWHM 2.8s; nonlinear highpass filtering (Gaussian-weighted LSF straight line fitting, with $\sigma = 45.0s$). Statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction.
A Z (Gaussianised T) statistic image was thresholded using clusters determined by $Z > 3.0$ and a cluster significance threshold of $P = 0.01$ [2].

Temporal accuracy

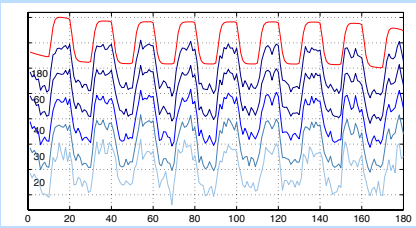


Figure 2: Experimental paradigm (red) and extracted IC time courses (blue).

ICA time courses have generally been compared to hypothesized time courses using simple correlation (e.g. [4] used a correlation threshold of 0.4 for the associated time courses). It has been argued that while the spatial decomposition results in plausible activation pattern, the temporal modes of the decomposition are 'noisy' and do not correspond well to the generally smooth hypothesized time courses. In [5], combinations of IC time courses are used to overcome this problem by projecting the reference function into the subspace spanned by a set of different IC time courses of largest correlation. Alternatively, [6] have suggested using additional regularisation terms to constrain the IC time courses to be smooth.
To demonstrate the ability of ICA to accurately represent the experimental paradigm, synthetic FMRI data based on a Null data set of 180 scans, where a volunteer was scanned without any experimental paradigm, was created. The time courses of 561 voxels within a spatially confined region were then modulated in a multiplicative way so as not to bias the analysis toward linear ICA decomposition. An artificial 'activation' time course (figure 2, top) was scaled to mean 1±2.5% and voxel time courses were then modified according to this activation sequence, resulting in 1.8% signal strength (averaged over the 561 voxels).

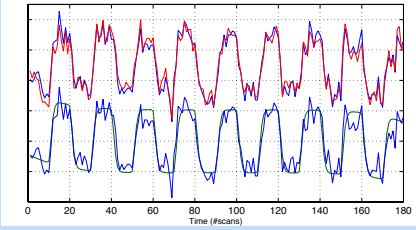


Figure 3: IC time course (red); 'activation' time course (green) and projected 'activation' (blue)

Figure 2 shows the 'activation' sequence together with IC time courses obtained after reducing the dimensionality of the data to 180,60,40,30 and 20 dimensions (top to bottom) using PCA.
Note, that even though the IC time courses appear to be 'noisy', this noise structure is consistent. As an explanation, figure 3 shows the fit between the IC time course (red) found after PCA reduction to 20 dimensions (where more than 99.92% of the variability in the data was retained) and the experimental paradigm (green) projected into the same subspace (blue). The 'noise' in the IC time courses is not due to suboptimal IC estimation but in fact accurately approximates the experimental paradigm in a lower dimensional signal subspace.

Results

Figures 4 and 5 show the thresholded Z statistic images for the pain (first 340 scans) and the visual (last 60) experiments, respectively. In both cases, the activation found when using the estimated haemodynamic response (bottom rows) is located within gray matter. Key regions of the pain matrix of activation (thalamus, basal ganglia, insula and sensory cortex) are better detected using the estimated HRF extracted by ICA (figure 4 bottom). This is similarly reflected in the visual cortex activation (figure 5).

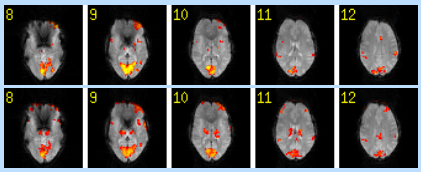


Figure 4: Pain stimuli

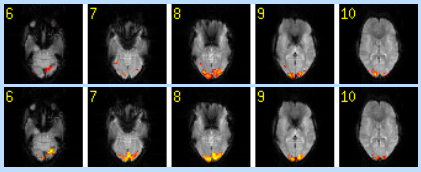


Figure 5: Visual stimuli

Conclusions

Both for the pain and the visual part of the experiment, independent component analysis allowed for the extraction of a task reference function that better highlighted activation within the pain matrix and the visual cortex respectively, particularly in areas with low signal to noise ratio of activation, such as the thalamus.
Combining model-free estimation of the HRF with model-based statistical analysis appears to be a promising tool for FMRI analysis.

Acknowledgements

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References

[1] P. Comon. Independent component analysis – a new concept? *Signal Processing*, 36:287–314, 1994.

[2] K.J. Friston, K.J. Worsley, R.S.J. Frackowiak, J.C. Mazziotta, and A.C. Evans. Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping*, 1:214–220, 1994.

[3] A. Hyvärinen. Fast and robust fixed-point algorithms for independent component analysis. *IEEE Transactions on Neural Networks*, 1999.

[4] M. J. McKeown, S. Makeig, G. G. Brown, T. P. Jung, S. S. Kindermann, A. J. Bell, and T. J. Sejnowski. Analysis of fMRI data by blind separation into independent spatial components. *Human Brain Mapping*, 6(3):160–88, 1998.

[5] M.J. McKeown. Detection of consistently task-related activations in fMRI data with hybrid independent component analysis. *NeuroImage*, 11:24–35, 2000.

[6] J.V. Stone, J. Porrill, C. Büchel, and K. Friston. Spatial, temporal, and spatiotemporal independent component analysis of fMRI data. In *Spatial-temporal Modelling and its Applications, Department of Statistics, University of Leeds*, 1999.

[7] I. Tracey, et. al. Pharmacological modulation of the central pain response. ISMRM 8th International Meeting, April 2000.

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