Hypothesis-Driven Independent Component Analysis (hICA): Incorporating Prior Knowledge about the Hemodynamic Response into ICA Analysis of FMRI Data

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Introduction

A method for incorporating prior knowledge about the expected hemodynamic response function (HRF) into Independent Component Analysis (ICA) of functional MRI (fMRI) data has been previously proposed [1] based on a deflationary version of the fastICA algorithm [2]. A variant of this method, called hypothesis-driven ICA (hICA) is proposed here based instead on the infomax ICA algorithm [3] which avoids the problems inherent with Newton iteration and the deflationary aspects of the fastICA approach. Even for very low signal strengths, where the fastICA method fails to converge to the target sources, the proposed method displays comparable performance to the standard GLM when all confounds, such as cardiac and respiratory signal, or motion artifacts, are known, and significantly outperforms the standard GLM when all confounds are not incorporated in the design matrix. The use of prior knowledge obviates many of the problems and ambiguities associated with standard ICA techniques, such as the optimal amount of data reduction, and the *a posteriori* designation of individual component maps as task-related or confound.

Theory

Assuming n voxels in the brain, and m acquired time frames, the noisy ICA model is $X = A\,S + E$ where X is the n-X-m data matrix, A is an m-X-p $(p<=m)$ mixing matrix, S is an n-X-p matrix of independent sources, and E is an n-X-m matrix of residuals. Since the noisy ICA problem is quite complicated, typically noiseless ICA techniques, such as fastICA [2] or infomax [3] are employed as an approximation, after dimensionality reduction via PCA. These techniques search for the maximum of an objective function, such as negentropy or maximum likelihood (ML), as a function of the sources $S = B\,X$ found using an unmixing matrix $B = A^{+}$. In the presence of background noise, the success of such techniques is highly dependent on the proper amount of PCA reduction [4]; in addition, some weak sources may still not be found. The performance of the ICA techniques may be improved by incorporating prior information about the form of the mixing matrix, as has been previously proposed [1]; however, the fastICA method relies on Newton iteration to find the local optima of the objective function; for weak sources, the Newton iteration may converge to a different optimum from the nearest local optimum. Thus we propose to modify the ML gradient-ascent algorithm for the case of number of sources less than number of acquired time points ($p < m$). For the full ICA model ($p = m$) the gradient update rule has been previously found [3] as $B \rightarrow B + \mu(B^{-T} + G'(BX)X^{T})$ where μ is the step size or learning rate parameter, and G is the log prior source density. In the undercomplete ICA model ($p < m$), the update rule has been derived [5] as $B \rightarrow B + \mu((B^{+})^{T} + G'(BX)X^{T})$ (replacing the inverse by the pseudoinverse). Thus, as in [1], the ICA iterations are begun with the rows in B set to the hypothesized task regressors. The gradient-ascent algorithm will converge to the local maxima of the likelihood, and avoid as well the inaccuracies associated with one-at-a-time deflationary ICA methods [4] (since errors in the first extracted component will filter into all subsequent ones).

Materials and Methods

Datasets were simulated via routines written in IDL (Research Systems Inc., Boulder, CO). 10,000 voxels and 100 time points were used. A Gaussian noise background with unity standard deviation was generated. Sources were generated by taking the square of a Gaussian distribution (keeping the original sign). Twenty confound sources were generated and normalized to unity standard deviation, while five much weaker target sources were generated and normalized to a standard deviation of 0.05. All sources were mixed into the noise background with an associated time series taken from a zero mean, unity standard deviation Gaussian distribution. The known time series were used as the starting point for hICA as well as fastICA. To simulate the effects of inaccurate prior specification, Gaussian noise with unity standard deviation was added to the known time series and the noise-corrupted time series were used as the starting point for hICA. For comparison, the simulated data was processed using standard ICA after PCA reduction to 25 components, as well as the standard GLM, using the known twenty regressors for the confound sources, and the five known time series for the target sources, in the design matrix. The GLM analysis was repeated using the noise-corrupted time series, as well as only incorporating ten out of the twenty confound regressors, in the design matrix. The simulation was repeated 100 times, for a total of 500 target sources. To gauge the relative accuracy of each method, the cross-correlation coefficients between the found sources and the target sources were calculated (for standard ICA, each target source was matched to the found source with the highest cross-correlation value).

Results and Discussion

The hICA technique converged robustly after about only 25 iterations for each dataset. Results are shown in Figure 1. The performance of the hICA method was comparable to that of the standard GLM, even with noise-corrupted time series, and much superior to standard ICA. The fastICA method failed completely to find the target sources, since the Newton iteration always converged to one of the much stronger confound sources. The importance of correctly modeling and/or inferring all confounds is seen with the significantly reduced performance of the GLM with only 10 confound regressors modeled in the design matrix. Thus, the hICA technique provides the potential of improved performance relative to conventional GLM techniques when all confounds are not known. Further research will be necessary, however, in order to develop and validate a method, such as one previously proposed in [6], to generate voxelwise statistical inferences based on the IC intensity values.

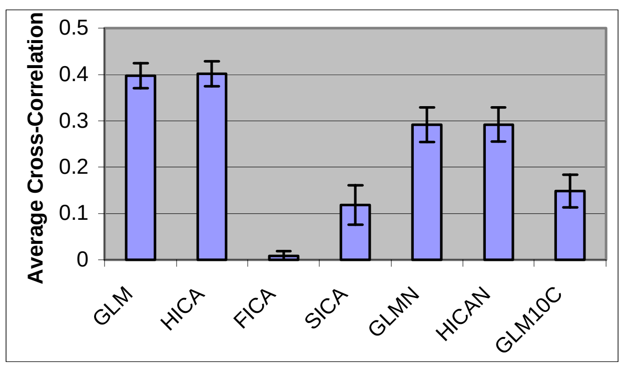

Figure 1. Comparison of various processing methods for simulated data with twenty confound sources and five target sources with 0.05 relative strength. Results are cross-correlation values (mean +/- std. dev.) between found and target sources. Processing methods: GLM = standard General Linear Model, hICA = hypothesis-driven ICA, fICA = fastICA, sICA = standard ICA, GLMN = GLM with noise-corrupted time series, hICAN = hICA with noise-corrupted time series, GLM10C = GLM with only ten of twenty confound regressors modeled in the design matrix.

Conclusion

A method for incorporating prior knowledge about the HRF is into ICA analyses is proposed. The method is robust even for very weak sources, and displays similar performance compared to standard GLM techniques. In addition to being more sensitive to the discovery of weak sources, the hICA method also avoids many of the problems found with standard ICA procedures. No data reduction was necessary, getting around the "how-many-components" problem. Since there is a one-to-one correspondence between each source and each hypothesized task regressor, no *a posteriori* designation of components as "task-related" or "confound" is needed.

References

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