

Model-free Group Analysis Shows Altered BOLD Networks in Dementia

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Introduction

FMRI research in Alzheimer's disease (AD) and mild cognitive impairment (MCI) typically is aimed at determining regional changes in brain function linked to disease state or progression. In common FMRI analyses a model of the expected BOLD-response is created and its magnitude estimated using a general linear model (GLM) analysis. This crucially depends on the suitability of the model at the individual subject level as well as on the assumptions about normality of both within and between group distributions.

Exploratory data analysis techniques such as independent component analysis (ICA) do not depend on these assumptions and are able to detect unknown, yet structured spatiotemporal processes in neuroimaging data^{1,2}. Until recently, application of such model-free methods has been limited to the analysis of single sessions. Tensorial probabilistic ICA (T-PICA) is a model free technique that can be used to analyze multiple subjects and groups, extracting signals of interest in the spatial, temporal and also subject domain of FMRI data³. In this study we applied T-PICA to further analyze data we reported on previously using model-based techniques^{4,5}. Our aim was to study whether (1) the T-PICA technique shows spatial activation maps comparable to previous model-based analyses; (2) this technique shows significant group differences between dementia and controls in any spatiotemporal mode; (3) T-PICA is more sensitive to detect group differences than the model-based approach.

Methods

Eighteen AD, 28 MCI patients and 41 healthy elderly controls performed an on/off face encoding task during FMRI scanning^{4,5}. Preprocessing of the FMRI data was done with FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl)⁶. FMRI scans of each individual were transformed to standard space. Next, data were decomposed into space/time/subject components characterizing structured signals in these domains using the model-free T-PICA technique³. Final maps were thresholded using an alternative hypothesis test based on fitting a Gaussian/Gamma mixture model to the distribution of voxel intensities within spatial maps and a posterior probability threshold of $p > 0.5$ ⁷. For each component, the values in the subject domain were compared within the GLM framework to analyze group differences, including age and gender as additional covariates. The same data were analyzed using the standard model-based FMRI GLM analysis. The results of the model free and model based techniques were compared statistically.

Results and Conclusion

The T-PICA technique showed various networks of activation with the task. These networks were associated with cognitive processing (A), motor activation (B), and visual processing (C and D) (see figure 1). Deactivation was found in the so called default mode network^{8,9}, which included posterior cingulate cortex, medial frontal regions and parietal cortex (E and F in figure 1). In total 6 of the networks showed a significantly decreased response in patients using T-PICA ($p < 0.05$) (all shown in figure 1). There were no networks showing an increased response in patients. For the networks C and D in figure 1, the T-PICA technique was significantly more sensitive to detect group differences than the standard model-based technique ($p < 0.05$).

We conclude that T-PICA is a promising tool to identify and detect differences in (de)activated brain networks in elderly controls and dementia patients. The technique is more sensitive than the commonly applied model-based method. Consistent with other research, current findings show that both networks of activation and deactivation show decreased reactivity in dementia.

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References

- (1) Beckmann CF, et al. IEEE Trans Med Imaging. 2004;23:137-152;
- (2) McKeown MJ, et al. Hum Brain Mapp. 1998;6:160-188;
- (3) Beckmann CF, et al. Neuroimage. 2005;25:294-311;
- (4) Rombouts SA, et al. Neuroimage. 2005;26:1078-1085;
- (5) Rombouts SA, et al. Hum Brain Mapp. 2005;
- (6) Smith SM, et al. Neuroimage. 2004;23 Suppl 1:S208-219;
- (7) Beckmann CF, et al. 9th Int. Conf. on Functional Mapping of the Human Brain, Neuroimage Vol. 19(2), 2003:S985;
- (8) Raichle ME, et al. PNAS USA 2001;98:676-682;
- (9) Greicius MD, et al. PNAS USA. 2003;100:253-258.

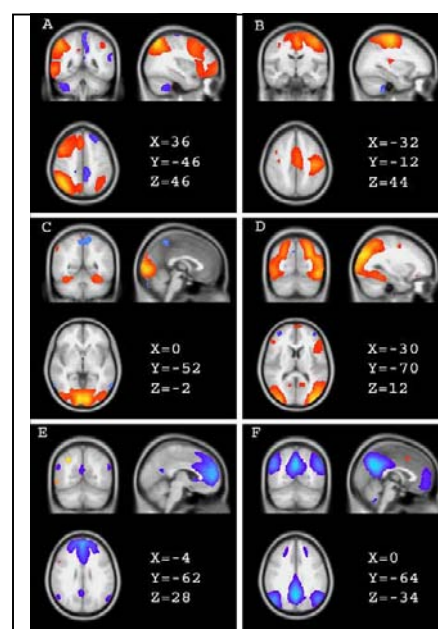


Figure 1: spatial modes of the T-PICA analysis. Networks A-F show a significantly diminished BOLD response in patients. Red-yellow: activation positively correlated with the paradigm. Blue: signal negatively correlated with the paradigm ("deactivation"). The coordinates refer to mm distance from the anterior commissure in MNI space and images are shown in radiological convention.