Automatic classification of brain resting states using fMRI temporal signals

N. Soldati, S. Robinson, C. Persello, J. Jovicich and L. Bruzzone

A novel technique is presented for the automatic discrimination between networks of 'resting states' of the human brain and physiological fluctuations in functional magnetic resonance imaging (fMRI). The method is based on features identified via a statistical approach to group independent component analysis time courses, which may be extracted from fMRI data. This technique is entirely automatic and, unlike other approaches, uses temporal rather than spatial information. The method achieves 83% accuracy in the identification of resting state networks.

Introduction: In functional magnetic resonance imaging (fMRI), a series of images of the brain are acquired at short intervals (1–4 s) exploiting the dephasing effect that paramagnetic deoxyhaemoglobin in blood has on the MR signal. Activaton of groups of neurons in processing stimuli, implies increase in oxygen consumption, blood flow and volume, resulting in a net decrease in deoxyhaemoglobin concentration close to the activated region. This leads to an increase in the intensity of the MR signal relative to the baseline state, and provides a source of endogenous contrast, which has been used to study a vast range of sensory, cognitive and emotional brain functions over the past two decades. In addition to signal changes related to task processing, the brain also undergoes slow fluctuations in functionally-related groups of regions when subjects are at rest (not engaged in organised thought) [1]. These resting state networks (RSNs) are of interest in neuroscience because, although their role has yet to be understood, they dominate temporal fluctuations in fMRI signals and because they have been shown to differ between the normal and diseased brain in some pathologies (e.g. Alzheimer's disease). The study of RSNs in fMRI data is a typical blind source separation problem, which may be addressed with data-driven algorithms such as ICA. An extension of this technique is Group ICA (GICA) [2], in which inferences are drawn about sources that are common to all subjects considered. These may be related to RSNs, physiological noise of cardiac or respiratory origin, or other sources such as technical artefacts. The procedure yields regions of the brain showing particular signal fluctuations and associated time courses. In the literature, the detection of RSNs has mainly been based on the visual assessment of spatial maps carried out by experts, with obvious problems of subjectivity, accuracy and processing time. Although the co-localisation of RSNs and regions affected by physiological (PHY) artefacts has been reported, there have been relatively few attempts to automate the discrimination between RSNs and PHY signals, and we are not aware of any study that has tried to perform discrimination using fMRI time courses only. This Letter presents a novel automatic and unsupervised classification system that uses fMRI time courses to differentiate RSNs from PHY signals.

Proposed system: The architecture of the proposed system is shown in Fig. 1. It is made up of a preprocessing module, a feature-extraction module and a classification module. The preprocessing module exploits a GICA algorithm [2] to extract ICs from fMRI data. ICs are made up of both spatial maps (used only for validation), and time courses. For each subject j we can represent an fMRI image time-series as a spatiotemporal matrix Y of dimensions $M \times N$, where M is the number of time samples and N is the number of voxels. For the generic voxel i, which represents a location in the brain, we have the associated time course of neuronal activity $y_i(nT)$, $i = 1, \ldots, N$, where n $(n = 1, \ldots, M)$ represents a generic time sample and T is the sampling period. The time course i can be modelled as a linear combination of m unknown sources, i.e.

$$y_i(nT) = \sum_{k=1}^{m} = a_{ik} x_k(nT) \tag{1}$$

where a_{ik} is the ith element of the kth column of the mixing matrix $\boldsymbol{A}$, and $x_k(nT)$ is the time course of the kth source $(k = 1, \ldots, m)$. The task of ICA is to estimate both the unmixing matrix $\boldsymbol{A}^{-1}$ and the sources $x(nT)$ from the observed data $y(nT)$. This is done via adaptive numerical methods (e.g. Infomax [2]) based on non-Gaussianity maximisation of the source statistical distribution. One approach to GICA is to concatenate data from all subjects in a single long time series before performing ICA (after data co-registration and normalisation to a single volume space). Each IC_k obtained (i.e. source $x_k(nT)$) may be due to either RSNs or PHY. Thus each IC_k can be associated with one of two classes, ω_{RSN} and ω_{PHY} via the adoption of suitable features and a classification method. We used the Welch's method to determine frequency power spectra from the IC time courses prior to features extraction. In an exploratory step, we analysed the power spectra associated with ω_{RSN} and ω_{PHY}. ICs were manually labelled by visual inspection of the associated spatial maps. The power spectra of the ICs due to RSNs and PHY were investigated with a statistical approach, to identify whether the shapes of the spectra of the two classes were statistically different. Feature extraction was then applied to these spectra. Let $z_{kl}(f)$ be the Welch's frequency spectrum of the kth IC associated with the kth source of the lth subject $(l = 1, \ldots, L)$. For each IC_k (and so $z_k(f)$) and each quantised frequency we have a set of L sample values. Thus it is possible to apply a non-parametric statistical test (the Wilcoxon test) to evaluate the effectiveness of each quantised frequency interval in discriminating between RSNs and PHY. The Wilcoxon rank-sum test [3] is applied to each pair $IC_i \in \omega_{RSN}$ and $IC_j \in \omega_{PHY}$ $(i,j = 1, \ldots, m)$, at each quantised frequency range Δf_s so that the test$[z_i(\Delta f_s), z_j(\Delta f_s)]$ gives a value (0,1) corresponding to the failure to reject or the rejection, respectively, of the null hypothesis that the two distributions have the same medians, along with a p-value of its significance. This analysis yielded regions of significant differences between spectra. In particular, differences were established between IC $\in \omega_{RSN}$ and IC $\in \omega_{PHY}$, but also ω_{RSN} and ω_{PHY} can be divided into two subgroups, each with different characteristics (see Fig. 2). ICs $\in \omega_{RSN}$ spectra have less outlier values than those of other subgroups. This result confirms that the Welch's spectra can be used for discriminating between IC $\in \omega_{RSN}$ and IC $\in \omega_{PHY}$ in a reliable statistical way. From this observation, according to an empirical analysis, kurtosis applied to the spectra has been chosen as a discriminative feature. Given the ith IC, the kurtosis can be computed as:

$$k_i = E[Z_i(f) - \bar{z}_i(f)]^4 / \sigma_i^4 \tag{2}$$

where $E[.]$ denotes the expected value, $\bar{z_i}(f)$ is the mean value of $z_i(f)$ across all ranges of frequencies, and σ_i is the standard deviation of $z_i(f)$. The computation of the kurtosis feature on the m ICs results in a bimodal distribution, where ICs $\in \omega_{RSN}$ have lower values than ICs $\in \omega_{PHY}$. This permits the use of a linear thresholding classifier to automatically separate ω_{RSN} from ω_{PHY}. The threshold value θ was derived according to a simple yet effective iterative algorithm [4], which initialises the threshold to the mean value of the kurtosis of the m ICs and then iterates as follows:

$$\theta_k = \left(m_{f,k-1} + m_{b,k-1}\right)/2 \tag{3}$$

where $m_{af,k-1}$, $m_{b,k-1}$ are mean values of the two obtained subgroups (inferior and superior) after the thresholding. The algorithm converges when $\theta_k = \theta_{k-1}$.

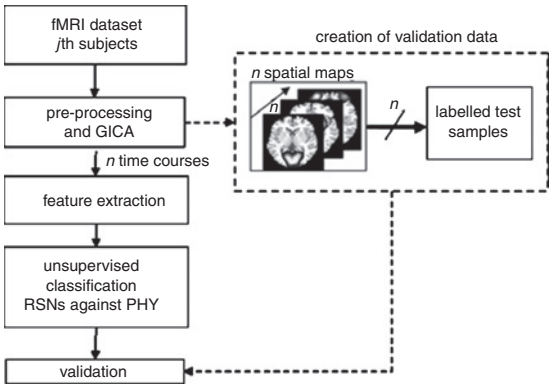

Fig. 1 *Architecture of proposed classification system*

Experimental results: Magnetic resonance images of 15 subjects (8 males), mean age 36 ± 12 years, were acquired with a 4 T Bruker Medspec scanner. Subjects were asked to close their eyes during runs and not engage in organised thought or sleep. Two runs of RS data were acquired for each subject, with whole-brain EPI with 3 × 3 × 3 mm voxels, TE/TR = 33/2200 ms and 273 time points (10 min per run). Distortion correction of EPI was performed online using the

point-spread function method. Preprocessing was carried out with FSL (www.fmrib.ox.ac.uk/fsl), performing motion correction, image registration to a common (MNI) space, and no spatial or temporal smoothing. The classification system was applied to a group including 30 RS datasets (15 subjects, two repetitions per subject). The number of ICs to be computed with GICA was set to 30. Fig. 2 presents the four main spectral shapes, with classes being identified via statistical test analysis. Results of the classification task are presented in Table 1. The accuracy of the classification system was estimated using labelled test data obtained by manually identifying the spatial map corresponding to each IC by correspondence with its appearance in the literature. Table 1 shows the overall accuracy obtained, as well as the distribution of errors between missed RSNs (false negative), which were 0 and false RSNs (false positive), which were 5. This distribution is convincing, as in this study false negatives were considered more important than false positive as the main aim of the analysis was to perform a pre-screening for identifying possible RSNs present in the data. Results from this automatic analysis were exploited for studying the properties of information sources associated with RSNs in a systematic and specific way. This has allowed temporal relationships (which imply causal relationships) between known RSNs to be identified and has contributed to the classification of an interesting IC as being an RSN, which was undocumented at the time [5].

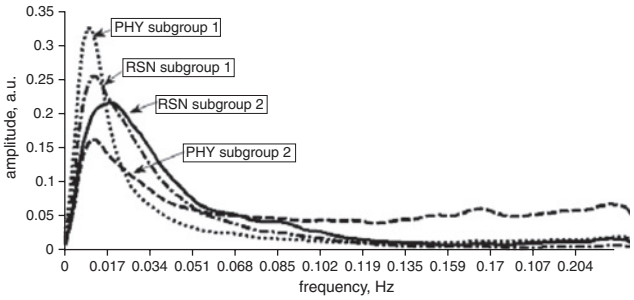

Fig. 2 *Mean spectra of four subgroups identified*

It is visible that spectra of RSN subgroups have closer metrics with respect to PHY subgroups

Table 1: Classification accuracy over all subjects (number of ICs 30)

Number of datasets	Identified RSNs	False positive	False negative	Overall accuracy (%)
30	13	5	0	83

Conclusions: A novel classification system has been proposed for the detection of RSNs in fMRI data that: (i) exploits only the information present in component time courses; (ii) is completely automatic and unsupervised; (iii) gives an 83% accuracy in the identification of RSNs when applied to 30 RS datasets; and (iv) is easy to implement and use. Results confirm both the effectiveness of the proposed system and its utility in the identification of resting state networks.

Acknowledgments: G. Basso and M. Orsini for fMRI data collection. The research was supported in part by the Fondazione Cassa di Risparmio di Trento e Rovereto.

25 July 2008
Electronics Letters online no: 20092178
doi: 10.1049/el:20092178

N. Soldati, C. Persello and L. Bruzzone (*Department of Information Engineering and Computer Science, University of Trento, Via Sommarive 14, Trento I-38050, Italy*)

E-mail: nicola.soldati@unitn.it

S. Robinson and J. Jovicich (*Center for Mind/Brain Sciences, University of Trento, Via delle Regole 101, Trento I-38060, Italy*)

N. Soldati: Also with Center for Mind/Brain Sciences, University of Trento, Via delle Regole 101, I-38060 Trento, Italy

References

1 Biswal, B.B., Yetkin, F.Z., Haughton, V.M., and Hyde, J.S: 'Functional connectivity in the motor cortex of resting human brain using echo-planar MRI', *Magn. Reson. Med.*, 1995, **34**, p. 537541
2 Calhoun, V.D., *et al.*: 'A method for making group inferences from functional MRI data using independent component analysis', *Hum Brain Mapp.*, 2001, **14**, (3), pp. 140–151
3 Wilcoxon, F.: 'Individual comparisons by ranking methods', *Biometrics*, 1945, **1**, pp. 80–83
4 Ridler, T.W., and Calvard, S.: 'Picture thresholding using an iterative selection method', *IEEE Trans. Syst. Man Cybern.*, 1978, **SMC**, (8), pp. 630–632
5 Robinson, S., Soldati, N., Basso, G., Sailer, U., Jovicich, J., Bruzzone, L., Kryspin Exner, I., Bauer, H., and Moser, E.: 'A resting state network in the basal ganglia'. Proc. 16th Annual Scientific Meeting and Exhibition of International Society for Magnetic Resonance in Medicine, Toronto, Canada, May 2008