MULTIVARIATE ANALYSIS OF THE DEFAULT-MODE NETWORK IN HEALTHY SUBJECTS AT REST.

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Introduction

Several methods have been applied to analyze the low-frequency fluctuations of resting state (RS) fMRI data. Among these approaches, the functional connectivity (FC) analysis uses a seed region to obtain FC cross-correlation (CC) maps with every other time series of the brain; the Regional Homogeneity (ReHo) approach measures the coherence of one time series with those of its nearest neighbours; the measurement of the amplitude of low-frequency fluctuations (ALFF) decomposes fMRI data into independent spatial components with an associated time course, and is particularly useful for analysing fMRI data at rest, because no model is required for data decomposition. Up to now, all these methods have been applied in separate studies. Aim of this study was to combine all these approaches in a multivariate analysis, to assess how the information derived from each method correlates with that of the others in healthy subjects, focussing in particular on the default-mode network (DMN).

Methods

RS functional MRI data were acquired from 49 healthy controls (male/female=25/24, mean age=23.1 years, range=20-29 years) using a 3T scanner. After data pre-processing (realignment, normalization, smoothing and band-pass filtering between 0.01 and 0.08 Hz), ReHo and ALFF maps were obtained from each subject by using REST toolbox (http://resting-fmri.sourceforge.net). FC maps were derived using as seed region the posterior cingulate cortex (PCC). Finally, ICA was run using Group ICA of FMRI Toolbox (GIFT) (4). This latter method produced 45 spatially independent maps. Among the RS components with potential functional relevance, the DMN was detected by visual inspection. SPM2 was used to assess the spatial extent of within-group RS maps and to perform conjunction analysis among modalities. Voxel-by-voxel correlations between maps derived from each modality were assessed by using Biological Parametric Mapping (BPM) (5). Finally, the average CC value derived from FC, the ReHo and ALFF mean values, as well as the percentage signal change of RS fluctuations derived from ICA of each significant SPM cluster of the DMN were extracted and correlated by using the Spearman Rank Correlation Coefficient.

Results

RS maps of the DMN were obtained by using FC, ReHo and ICA analysis, although they had a different spatial extent at the same statistical threshold. Figure 1 shows the results of the conjunction analysis among these three modalities (p<0.05, FWE corrected). One the contrary, it was not possible to detect a spatial pattern resembling the DMN on the ALFF maps. The spatial pattern of the DMN obtained with FC was correlated at a voxel-by-voxel level with that derived from ICA and ReHo (Figure 2), especially in proximity of the seed region of the FC map (PCC) (p<0.05, FWE corrected). The average values ReHo and ALFF within the main clusters of the DMN were significantly correlated for each of the reported clusters (r ranging from 0.35 to 0.82, p from 0.01 to 0.0001), whereas ICA percentage signal change had a greater correlation with the average CC value (especially in clusters located in the proximity of the seed region) than with average ALFF and ReHo.

Conclusions

Three of the four applied methods were able to find a spatial pattern resembling the DMN, which was consistent across approaches. At a regional level, however, the information given from all approaches was only partially correlated, probably because the information given from each of them is derived from different characteristics of RS fluctuations (inter-regional coherence from FC and ICA, intra-regional coherence from ReHo, amplitude of regional activity from ALFF). Therefore, the combined used of all these methods in a multivariate analysis might be useful to have a more global description of the RS networks, rather than handling with one analysis modality at a time, and to reach a greater power to compare RS network characteristics between healthy subjects and patients with neurological diseases.

References