Comparison of Seed-ROI Based Correlation Analysis and Independent Component Analysis in Quantification of Resting-State Brain Networks

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Introduction

Functional connectivity MRI (fcMRI) can detect low frequency BOLD oscillations in resting-state brain. These are synchronized between functionally related areas [1]. It has been shown that in multiple scleroris, a disease with axonal disconnection, this synchrony is reduced in the motor resting-state network. This synchrony reduction can lead to lateral asymmetry [2]. In most fcMRI studies, a seed ROI covering part of the relevant network is defined in a conventional fMRI experiment. This ROI is then used to define a reference signal time course (STC) in the resting-state data. Correlations to this STC indicate functional connectivity. An alternative approach to detect resting-state networks is independent component analysis (ICA) [3]. In our study, we investigated the stability and the comparability of the two different methods. Therefore, we determined the lateral asymmetry in motor resting-state network for two volunteers in six independent sessions over eight weeks.

Methods

In our study, two healthy volunteers (both male, right handed, 39y) were scanned in six sessions at intervals of a minimum of six days. All measurements were done on a 3.0 T head scanner (Magnetom Allegra, Siemens Medical, Erlangen, Germany). In each session, one fMRI experiment and two resting-state fcMRI scans were performed. In the three experiments, series of GE-EPI (BW =2kHz/Px) T2*w images parallel to the inferior borders of the corpus callosum were scanned with an identical spatial resolution of 3.5x3.5x4 mm^3. The primary motor areas (M1) were detected by a block-design fMRI paradigm. In the active periods, the subjects were advised to move their right hand with a frequency of roughly 1 Hz; the range of motion was guided in a wooden frame. Five baseline periods altered with five active periods. Each period consisted of ten volumes. Per volume, 25 slices were acquired. Two different resting-state measurements were performed in each session. In one fcMRI experiment, 1100 volumes of three slices covering the primary motor cortex were scanned with a short TR of 0.25 s. In the other fcMRI measurement, 300 volumes with a longer TR of 1s were acquired so that cardiac signal could possibly alias into a lower frequency band. In this experiment, 15 slices were acquired comprising the three slices scanned in the "short TR" fcMRI run. The order of the two fcMRI experiments was altered randomly in the six sessions to prevent systematic effects of tiredness. Data evaluation using AFNI [4] was performed for each subject and each session separately. The analysis included slice timing and motion correction, spatial smoothing with a Gaussian filter (FWHM = 7.5 mm), intensity normalization and realignment to the fMRI images.

After the pre-processing, the resting-state data were analyzed in two different ways: In the Seed-ROI based method, the resting-state data sets were low-pass filtered in time (cut-off frequency 0.08 Hz). Based on the motor task fMRI experiment, the 27 most significant activated voxels in left M1 were determined for the three slices scanned in both fcMRI runs. This activation defined ROI was then projected to the two resting-state data sets and the average STC was calculated for each set. A multiple linear regression (MLR) was performed for each resting-state voxel to the averaged STC of left M1. In the MLR, the whole brain STC and the calculated motion parameters were treated as regressors of no interest. For the fcMRI scan with long TR, the STC of the ventricles was an additional regressor of no interest to minimize cardiac aliasing. The resulting correlation maps were then transformed to z-scores of the standard normal distribution [5]. The number of significant correlated voxels over the 99% confidence level was determined for the three slices scanned in both fcMRI runs.

In the second analysis, the data sets were analyzed using MELODIC, an implementation of probabilistic independent component analysis (PICA) [6] in FSL [7]. The crucial point in ICA is the determination of the implicit dimensionality of the data set i.e. the number of independent components. Therefore, different algorithms for dimensionality estimation are implemented in MELODIC and were used in this work. The estimated dimensionality was considered as correct, if an independent component had been found which encompasses bilateral M1 and has a reasonable power spectrum. The relevant statistical maps were thresholded using mixture modeling ($p>0.5$) [6].

The resulting maps of both analyses were further evaluated for the three slices scanned in both fcMRI runs. First, the asymmetry in bilateral M1 was calculated as the ratio of significant voxels of one hemisphere vs. the number of voxels of the other (value between 0 and 1). Then, a mean asymmetry ratio was determined for each TR and each analysis technique. Second, for each type of analysis, each TR and each subject, a frequency of occurrence map of significant voxels over the six sessions was calculated.

Results

For subject 1, the mean asymmetry ratio in the TR = 0.25s experiment was 0.87±0.08 (Seed-ROI) and 0.87± 0.14 (ICA), for the TR = 1s experiment 0.93±0.08 (Seed-ROI) and 0.82±0.17 (ICA). The mean asymmetry ratio for subject 2 (TR = 0.25s) was 0.79±0.20 (Seed-ROI); 0.68±0.18 (ICA) and (TR = 1s) 0.76±0.14; 0.51±0.13 (Seed-ROI; ICA) (see Fig.1). The frequency of occurrence map for subject 1 is shown in figure 2. For subject 1, 20 % of all ever significant voxels were detected in all six sessions for the Seed-ROI method in the 0.25s scan and 28% in the 1s scan. The corresponding values for the ICA method were 18% and 9% (0.25s/1s). For subject 2, 3% and 10% (0.25s/1s) of all voxels were significant in all six sessions. For the ICA, the corresponding values were 10% (0.25s) and 1% (1s). The apparently higher frequency of occurrence in the Seed-ROI method for TR = 1s compared to 0.25s is due to the higher sampling efficiency concerning to the temporal filtering.

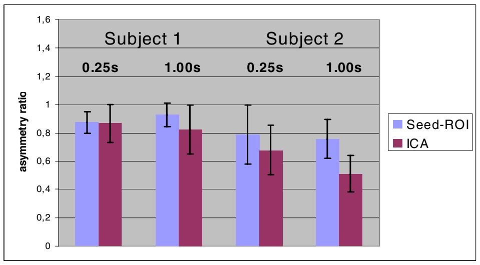

Fig. 1: mean asymmetry ratio over the six sessions.

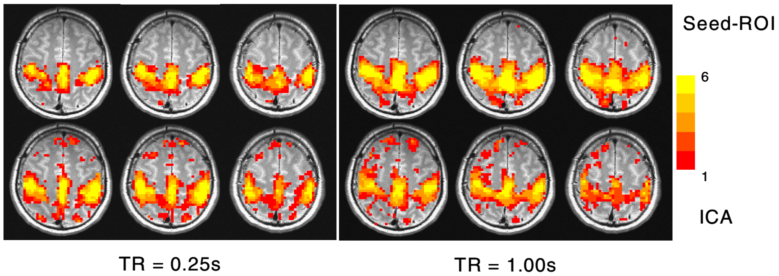

Fig. 2: Frequency of occurrence map for subject 1.

Discussion

In our study, we used two different analysis methods to detect the motor resting-state network. The quantification of statistical significance is different in both methods, hence the definition of a comparable threshold is not straightforward. However, both methods provide comparable results and errors for the lateral asymmetry of both subjects under investigation, which was stable and reproducible throughout. The ICA method can reliably detect components with high variance (e.g. cardiac pulsation in CSF, motion residuals) but sometimes has problems to detect weaker components like the resting-state network signal. This should be considered in pathological conditions as it might be an issue when reduced connectivity is present.

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