Functional Connectivity after Removal of Task Related Activation using Independent Component Analysis

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Introduction

Resting state fMRI time-series data from functionally connected regions of the brain exhibit a high degree of temporal coherence of low frequency fluctuations[1] ($\leq$0.1 Hz). These synchronous fluctuations occur spontaneously by changes of local blood flow.

In this report we used independent component analysis, (ICA), to detect and remove task related activation. Then we studied the effects of activation removal on functional connectivity in activated and non-activated regions of the human brain. Functional connectivity algorithms were applied to resting state fMRI studies as well as to task related activation studies before and after the subtraction of the activation.

Theory

Independent component analysis assumes that the time-series data are related by a linear transformation to spatially independent components (sources),

$$S_{ip} = \sum_t W_{it} X_{tp}, \qquad (1)$$

where S_{ip} is the i-th source of pixel p, X_{tp} is the fMRI signal intensity of pixel p at time t where the mean signal intensity (over p) has been subtracted, and W_{it} is the linear transformation (weighting matrix). The weighting matrix is square and of full rank. The average time course of the i-th source is given by the inverse of W, i.e. W_{ti}^{-1}. The sources S_i are statistically independent of each other.

ICA (or blind source separation) as formulated by Comon[2] attempts to estimate W and S from X by minimizing the mutual information in S. Bell and Sejnowski[3] have proposed a neural network algorithm to obtain the ICA components. In this study we used a blind source separation algorithm combined with the ICA method of Bell and Sejnowski.

In a task related activation study, after estimation of the sources S_{ip} for all i, and detection of the source, m, that corresponds to the activation, we can obtain activation-free pixel timecourses by setting $S_{mp}=0$, and using

$$X_{tp} = \sum_i \left(W^{-1}\right)_{ti} S_{ip} . \qquad (2)$$

The functional connectivity between two pixels i and j is defined as the scalar product,

$$C_{ij} = \left(\underline{m_i} \cdot \underline{m_j}\right) / \left(m_i \cdot m_j\right), \qquad (3)$$

where m_i and m_j are the timecourses in vector form that denote the hemodynamic measurement at time t, from voxels i and j in the brain.

Methods

This research was performed on a 1.5T GE Horizon MRI scanner (Waukesha, WI) with high-speed gradients. The EPI scanning protocol consisted of the parameters: Flip angle 90 deg, TE 50ms, TR 2000ms, FOV 24cm x 24cm, slice thickness 7mm, gap 2mm, 18 slices, 64 x 64 imaging matrix, and 125kHz receiver bandwidth. Six healthy volunteers, between 20-40 years of age, were studied in both resting and task related activation states. Head-motion signal changes were found to be minimal in all six subjects.

For the resting state studies a series of 260 images were acquired in the coronal plane. The volunteers were instructed to refrain from any cognitive, sensory or motor activity and to keep their eyes closed during these studies.

The scan protocol for the activation studies consisted of four on-off cycles, each cycle 64 sec, 148 images total, and all other parameters were the same as for the resting state scans. The tasks performed by the volunteers included bilateral finger tapping, passive listening to narrated text and looking at a strobe light of 8Hz frequency. A single task was performed during each scan.

The activation data were used to produce Student's t-test maps. The motor, auditory and visual systems were identified and the coordinates of one pixel from each system were recorded. ICA was also performed on the data acquired during the task activation studies and the component(s) that corresponded to the activation was identified. Then, the task related component(s) was removed and activation-free timecourses were acquired for each pixel (eq. 2).

Cross correlation calculations were performed and correlation maps were produced for each selected pixel, using the task activation data before and after removal of the activation. Cross correlation maps were also produced using the resting state data. The temporal correlation analysis was performed between a 3x3 square, centered at the selected pixel, and all other pixels of the brain.

The removal of activation was first performed on a simulated dataset in order to test the effectiveness of the method. For that purpose resting state data were used and a 3% increase in signal was added in two 3x3 regions of a single slice, with four on-off cycles similar to the activation studies from the volunteers. The simulated boxcars were smoothed by a Poisson filter. The same simulation was repeated for several locations of the 3x3 regions.

In order to study the limits of our method we changed the percentage of signal increase for the simulated activation in steps of 0.1% from 0% to 3% and we applied ICA on the simulated data. Thus, we empirically determined the lowest percent signal increase, due to activation, that can be detected by ICA[4].

Results and Discussion

The Student's t maps from the simulation showed that after the removal no activation remained in the selected 3x3 regions, (Figure 1). This was verified for even very low thresholds. All the volunteer studies with regular activation also showed no residual activation, in the initially activated regions, after subtraction.

One of the two 3x3 regions that was selected as a site for simulated activation was located in the left motor cortex, (Figure 1). Before the removal this region exhibited strong correlation with the second region of simulated activation, located in the medial right temporal lobe. After removal of the activation the two sites showed no connectivity to each other, (Figure 1d).

For all the regular activation studies, based on the Student's t-test maps, one pixel from the motor cortex and one pixel from the auditory cortex were selected. Using the data from the scan in which the volunteer performed bilateral finger tapping we removed the motor activation. Then, using functional connectivity analysis we generated correlation maps from the resting state data and the motor activation data before and after the subtraction, for the motor pixel and the auditory pixel (Figure 2). A similar process was followed for auditory and visual activation. The correlation values after the removal were approximately equal to these obtained in a resting state study for the motor, auditory and visual cortices. The effectiveness of the task activation removal method is also illustrated by means of the FFT of the signal from regions with activation (Figure 3). Frequency space peaks caused by motor activation are completely removed from the spectrum of a pixel that belongs to the motor cortex, after motor activation removal using ICA.

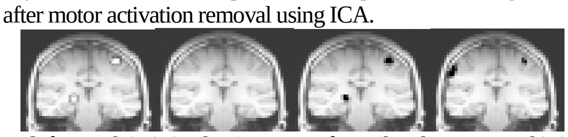

Figure 1. (left to right) a) Student's t map of <u>simulated</u> activation, b) Student's t map after removal of <u>simulated</u> activation, c) Correlation map before removal, d) Correlation map after removal.

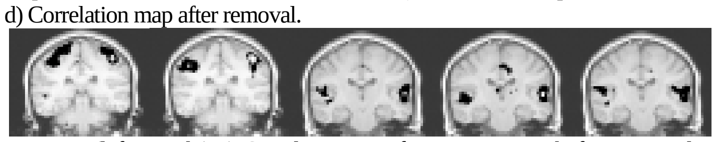

Figure 2. (left to right) a) Correlation map for motor cortex before removal of motor activation, b) Correlation map for motor cortex after removal of motor activation, c) Correlation map for auditory cortex before removal of motor activation , d) Correlation map for auditory cortex after removal of motor activation, e) Correlation map for auditory cortex using resting state data.

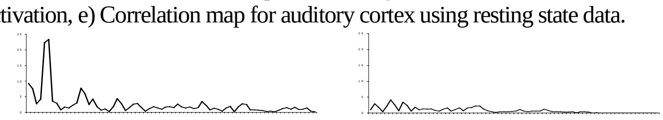

Figure 3. Frequency spectra of a pixel that belongs to the motor cortex, before (left), and after (right) the removal of motor activation using ICA.

Conclusions

It is evident from our simulations that with the parameters used in our scans ICA could detect an activation due to a signal increase of as low as 0.3%. This project has demonstrated that ICA can differentiate between task related activation and functional connectivity. Although task activation was successfully removed, connectivity due to low frequency fluctuations was present after the removal for activated as well as not activated brain regions. In addition, the cross correlation values after the removal of task activation were approximately equal to the values obtained from resting state studies.

Functional connectivity may be more effectively measured in task activation data, after activation removal, since the subject's cognitive activities can be more controlled than in the resting acquisition. The removal method can be used to measure functional connectivity when a resting state scan has not been acquired. The removal method can also be applied to event related activation studies.

References

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