Temporal Correlations in Low Frequency BOLD Fluctuations
Reveal Functional Networks

Mark J. Lowe, Mario Dzemidzic, Joseph T. Lurito, Vincent P. Mathews, Micheal D. Phillips
Department of Radiology, Indiana University School of Medicine, Indianapolis, IN

Introduction

It has been demonstrated that very low frequency temporal fluctuations in rapidly sampled blood oxygenation level dependent (BOLD) weighted echoplanar imaging data are phase-locked between many right and left-hemisphere symmetric functional cortices such as precentral gyrus (i.e. motor cortex) in human subjects at rest (1, 2). It has been postulated by the authors that these correlations in low-frequency fluctuations are a reflection of functional connectivity. It has also been shown that resting-state acquisitions are, in fact, timeseries acquisitions in which the subject is asked to refrain from overt activity. The "state" of the brain is otherwise uncontrolled. A recent experiment by Fransson et al showed residual effects of BOLD signal lasting several tens of seconds after very brief neuronal stimulation (3). Thus, a possible explanation of the a posteriori observations of low-frequency temporal correlation between functionally connected anatomic regions is that uncontrolled brain activity excites these connected regions and subsequent filtering isolates the long-term effects from higher frequency noise fluctuations, which are non-specific to function (e.g. cardiac and respiratory-related BOLD fluctuations).

As a further test of this, we designed an experiment in which subjects continuously performed a cognitive task, which excites a network of brain regions. The task is performed at a rate of 0.4Hz. The data are then filtered to remove fluctuations above 0.08Hz (corresponding to a period of 12.5 seconds). If low frequency fluctuations are a measure of functional connectivity, then the correlations between brain regions in the filtered data should reflect the network of brain regions involved in the task.

Methods

All scans were performed on a 1.5T GE Excelsior speed MRI scanner (GE Medical Systems, Waukegan, WI). BOLD-weighted data using gradient-recalled echo echo planar imaging (GE-EPI) were acquired in axial orientation on the same subject with the following parameters: echo time=50ms, matrix=64 x 64, field-of-view=24cm x 24cm, receiver bandwidth=125kHz, slice thickness=7mm. Two experiments were performed on each of three subjects. Head motion was controlled through use of a bite-bar affixed to the birdcage RF coil.

In the first experiment 14 axial slices were chosen with an interslice gap of 2mm covering the entire cerebral cortex. A flip angle of 90 degrees and a repetition time of 2 seconds were used. A spatial, 2-back working memory task was performed, interleaved in 48 second blocks with a simple motor task (see Casey et al (4) for a description of the working memory and motor tasks). All visual stimuli were presented using an MRI-compatible visual presentation system (Silent Vision, Avotec, Jensen Beach, FL, USA). The paradigm was executed for a total of 432 seconds, comprising 4 memory epochs and 5 motor epochs. The data were analyzed using the least-squares method described in Lowe et al. (5). The result is a map of Student’s t which reflects the significance of involvement in the working memory paradigm. The first experiment was used to identify a single axial slice through the region of dorsolateral prefrontal cortex (DLPFC) involved in the spatial working memory task for each subject. In the second experiment for each subject one axial slice was chosen through the DLPFC region selected from the first experiment. Two studies were performed during this experiment.

Study 1: imaging: repetition time: 250ms, repetitions: 1200, task: working memory
Study 2: imaging: repetition time: 250ms, repetitions: 1200, task: motor

A region of interest based on the location of DLPFC determined from the first experiment is chosen for each subject. In all cases the ROI is 1cm x 1cm x 7mm in size. All timeseries are digitally filtered using a finite impulse response filter to remove fluctuations above 0.08Hz. The cross-correlations for each pixel are calculated and a correction to a normalized Student’s t distribution is performed (the digital filtering and normalization procedure is described in Lowe et al. (2)). The result is a corrected Student’s t (tcorr) map for each study.

Results and Discussion

Figure 1a shows the T2-weighted anatomy used to identify the DLPFC region of interest from the 14-slice working memory fMRI experiment. Figure 1b shows a grayscale map of the corrected Student’s t values which reflects the degree of correlation to the low-frequency fluctuations in the ROI (black box) during continuous performance of the 2-back working memory paradigm. Figure 1c shows the grayscale map for the correlations to low-frequency fluctuations in the ROI during continuous finger tapping.

Figure 1

A comparison of Fig 1b and 1c shows that the regions of high correlation (bright pixels) to DLPFC change when shifting from one task to another. The regions of highest correlation to DLPFC in the working memory study include regions known from previous studies (4) to be involved in spatial working memory. The regions of highest correlation to DLPFC during finger tapping include known motor regions such as pre- and postcentral gyrus.

Conclusion

We have shown that regions with high correlation in low-frequency BOLD fluctuations depend on the functional state of the brain regions being sampled.

References