Measures of Resting-State BOLD Connectivity Exhibit an Inverse Dependence on Baseline CBF

A. L. RACK-GOMER[1], J. LIAU[1], AND T. T. LIU[1,2]

[1]BIOENGINEERING, UNIVERSITY OF CALIFORNIA SAN DIEGO, LA JOLLA, CALIFORNIA, UNITED STATES, [2]RADIOLOGY, UNIVERSITY OF CALIFORNIA SAN DIEGO, LA JOLLA, CALIFORNIA, UNITED STATES

INTRODUCTION

Measures of resting-state functional connectivity, defined as the correlation between spontaneous low-frequency fluctuations in the blood oxygenation level dependent (BOLD) signal, are showing increasing potential for the study of cognitive disease. A growing number of studies have found that resting-state functional connectivity is reduced in disorders such as Alzheimer's disease and epilepsy [1,2]. In these studies, a decrease in BOLD connectivity is often interpreted as an impairment of the neural connections between related brain regions. However, this interpretation can be complicated by the dependence of the BOLD signal on both neural and vascular factors. Prior work with the task-related BOLD signal has shown that the amplitude of the BOLD response to a stimulus exhibits an inverse dependence on baseline cerebral blood flow (CBF) [3,4]. The goal of this study was to assess the relationship between resting-state BOLD connectivity measures and baseline CBF in the motor cortex.

METHODS

Nine healthy volunteers were scanned on a GE Signa 3T whole body system with an eight channel receive coil. The imaging procedure consisted of a (1) high resolution anatomical scan, (2) bilateral finger tapping block design run, (3) CBF baseline and quantification scans, and (4) two five-minute resting-state BOLD scans. Functional data were collected over six oblique 6-mm thick slices prescribed through the primary motor cortex with an in-plane resolution of 3.75x3.75mm. The finger tapping scan and a CBF baseline scan were acquired with a PICORE QUIPSS II arterial spin labeling (ASL) sequence with dual echo spiral readout (TR = 2s, TI1/TI2 = 600/1500 ms, TE1/TE2 = 9.2/30 ms, and flip angle = 90°). The two resting-state BOLD scans were acquired using BOLD-weighted imaging with spiral readout (TE = 30 ms, TR = 500 ms, and flip angle = 45°). Pre-processing steps for the functional data included motion correction, physiological noise correction using cardiac and respiratory data collected during the scan, and removal of constant and linear trends. BOLD activation maps were generated using a general linear model analysis of the second echo data from the finger tapping scan. Regions of interest (ROIs) for the left and right motor cortices were defined from these activation maps. Baseline CBF images were calculated from the CBF baseline scan and converted to physiological units using a CSF reference scan. Average baseline CBF values were extracted from each subject's motor cortex.

The time series data from the BOLD-sensitive resting runs were low-pass filtered (cutoff frequency of 0.08Hz) and used to measure functional connectivity in the motor cortex. One metric of connectivity, referred to as the mean z-score, was obtained by extracting the average time course from the left motor ROI and correlating with all voxel time courses within the right motor ROI. The resulting correlation coefficients were converted to an approximately normal distribution of z-scores and the mean value over the ROI was calculated. A second metric, referred to as the percent overlap, was computed using the approach first described by Biswal et al. [5]. To summarize, the percentages of voxels in the left or right motor ROIs that were significantly ($p<0.001$) correlated with all voxel time courses in the same ROI were calculated and referred to as Left:Left or Right:Right percent overlap, respectively. Similarly, the percent of voxels significantly correlated with all voxels in the opposite ROI was calculated and referred to as Right:Left percent overlap.

RESULTS

The graphs in Figure 1 show the measures of resting-state BOLD connectivity versus baseline CBF for all subjects. The linear fit (green line) and correlation coefficients are also shown. The correlation was found to be negative and significant ($p< 0.02$) for all BOLD connectivity metrics: (a) mean z-score, (b) Right:Left percent overlap, (c) Right:Right percent overlap, and (d) Left:Left percent overlap.

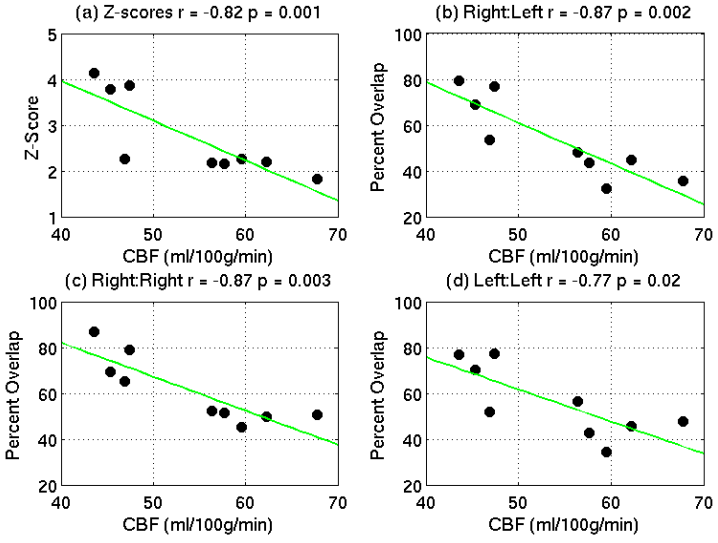

Figure 1. Measures of BOLD connectivity versus baseline CBF: (a) mean Z-score in right motor cortex using left motor cortex seed region, (b-d) percent overlap for (b) right:left correlations, (c) right:right correlations, and (d) left:left correlations.

DISCUSSION

We have shown that resting-state BOLD connectivity measures exhibit a significant inverse dependence on baseline CBF in the motor cortex. These results suggest that measures of baseline CBF have the potential to explain a significant portion of the inter-subject variability in resting-state BOLD connectivity. Furthermore, this finding highlights the importance of considering both neural and vascular factors in the assessment of differences in resting-state BOLD connectivity.

REFERENCES

[1] Greicius et al. PNAS 101:4637-42, 2004.
[2] Lui et al. JMRI 27**:**1214-20, 2008.
[3] Cohen et al. JCBFM 22**:**1042-53, 2002. [4] Liau et al. ISMRM, p. 854, 2008. [5] Biswal et al. MRM 34:537-541, 1995.