Title: Comparing approaches for estimating regional hemodynamic timing differences in BOLD-fMRI data

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Introduction

Resting-state fMRI (rs-fMRI) is widely used to study neuronal functional connectivity. However, the blood-oxygenation-level-dependent (BOLD) signal demonstrates variable hemodynamic delays throughout the brain that should be accounted for in rs-fMRI analysis. BOLD-fMRI signals are also strongly influenced by carbon dioxide (CO2) [1], a strong vasodilator [2]. There are varying temporal offsets between CO2 fluctuations and BOLD signal changes due to measurement delay, vascular transit times and local vasodilatory dynamics. Previous studies have proposed using this temporal offset to correct for hemodynamic delays in fMRI data [3,4]. There is also evidence that it is easier to estimate hemodynamic timings in BOLD-fMRI data with breathing tasks compared to resting-state data [5,6]. We compare two approaches for estimating relative hemodynamic timings (RHT) in BOLD-fMRI data, with and without CO2 information. These methods are compared for two scans: resting-state only and resting-state preceded by breathing tasks to induce fluctuations in CO2.

Methods

9 volunteers (6F; 26±4y) were scanned with a 3T Siemens Prisma and 64-channel head coil. A T1w scan was acquired for registration purposes. Two BOLD-weighted scans (GRE-EPI, TR/TE=1200/34ms; 2mm3; 60-slices, multi-band 4) were acquired: a rest scan preceded by a hypocapnic Cued Deep Breathing (CDB) task and a rest scan preceded by a hypercapnic Breath-Holding (BH) task. A nasal cannula and gas analyzer sampled expired CO2 levels. AFNI, FSL and MATLAB were used for analysis. fMRI scans were motion corrected and brain extracted.

Scan data were grouped into 4 segments of equal duration (Fig1): 2 segments ($BH+REST_{BH}$, $CDB+REST_{CDB}$) included a breathing task followed by rest, and 2 segments included only the rest portion from each scan ($REST_{BH}$, $REST_{CDB}$). The brain was parcellated into 104 regions using FSL's Harvard Oxford Cortical and MNI atlases transformed to functional space. We compared two methods for estimating RHT between regions. BOLD-xcorr: the average BOLD signal from each region, with motion parameters and polynomial terms removed, was upsampled to 0.3s. For each pair of regions, RHT was measured using cross correlation (max shift ±9s). CO2-BOLD-GLM: HRF-convolved end-tidal CO2 (ETCO2) traces were shifted ±15s in 0.3s increments, then down-sampled to the TR. Multiple linear regression was performed, including polynomial and motion parameters and shifted ETCO2. Voxelwise lag was identified by the ETCO2 shift of the model with the largest R-squared [7]. An average

CO2-BOLD lag was found for each atlas region; RHT was represented by the lag difference between each pair of regions.

RHT matrices were compared by taking the squared difference for each subject and averaging across subjects (mean squared error, MSE). Within-method agreement in RHT was assessed separately for segments that included breathing tasks and segments that only included rest. Between-method agreement was compared for each of the four data segments.

Results

Better agreement in RHT is visualized by lower MSE (Fig2). For the BOLD-xcorr method, RHT matrices agree more between breathing task segments, compared to between two REST segments (Fig2A). For the BOLD-CO2-GLM method, the RHT agreement is similar for both types of data segments (Fig2A). Between-method agreement was better in data segments including breathing tasks compared to REST only segments (Fig2B).

Conclusion

Resting-state data show greater variability, both within and between methods, in measurements of RHT. The addition of a breathing task, inducing larger fluctuations in ETCO2 and therefore blood flow, results in better agreement. Further work is needed to understand the influence of single subject variability, partial volume effects and small regions of interest on these RHT estimates, as well as how either RHT measure relates to variation in task-activation hemodynamics.

References

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