Voxel-wise fMRI group analysis using fractional volume of gray matter as a covariant

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Introduction

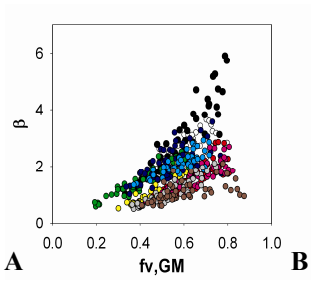
Blood oxygenation level dependent (BOLD) contrast has been widely used in fMRI study to investigate brain functionality. Since cerebral blood volume (CBV) and flow (CBF), the change of which are the main sources of BOLD contrast (called β here), are abundant in gray matter (GM) rather than white matter (WM) and the neuronal activation is mainly linked to postsysnaptic activity, GM is presumed to be a main source of fMRI contrast. Due to relatively large voxel size typically used in human BOLD studies (≥ 27 mm^3), the partial or fractional volume (fv) of GM in a voxel is unavoidable. As such, β may not proportionally reflect the strength of neuronal activity, due to the variation of tissue compositions over voxels. In a previous study, we presented that the fractional volume of GM ($f_{v,GM}$) in the activated voxels was highly correlated to β in individual fMRI analysis [1] (also shown in Fig1). In this study, we propose a method of fMRI group analysis using voxel-wise regression with $f_{v,GM}$ as a covariant.

Methods

FRActional Signal mapping from InvErsion Recovery (FRASIER): FRASIER provides volume fractions of GM, WM, and cerebrospinal fluid (CSF), based on a recently developed fast T_1 mapping method using inversion recovery Look-Locker echo-planar-imaging at a steady state (IR LL-EPI SS) [2]. The detailed technical information is described in the reference [3].

MRI experiment: Ten healthy subjects were scanned using a single-shot IR LL-EPI SS sequence for FRASIER under NIDA IRB approval: non-selective IR, TR/TE=400/13 ms, α=16°, matrix=64x64, and 15 slices, and total running time = 1 min including the preparation time of 10 s. A visual stimulation paradigm with 8 Hz flashing checkerboard (30s on and off) was used in a BOLD experiment acquired with TR/TE=3s/27ms, matrix=64x64, 39 slices, and total running time = 5:32. The center slice locations of IR LL-EPI SS and fMRI images were aligned so that the direct voxel-wise comparison between the two scans was feasible because the FRASIER method used the same gradient-echo EPI kernel as the fMRI acquisition (similar geometric distortions).

Data and statistical analysis: fv mapping was obtained using house-built source codes in Matlab. For fMRI data, β maps (parameter of predictor fitting) were obtained from individual subjects using *3dDeconvolve* function built in AFNI [4] and considering the hemodynamic response. To facilitate group analysis, individual data (β and f_v maps) were spatially normalized to the standard Talairach space with a resampled resolution of 3×3×3 mm^3. Using *3dttest++*, t-test was performed with voxel-wise covariates from $f_{v,GM}$ map.



subj	β = α × fv,GM α	r2
1	4.15	0.72
2	4.97	0.63
3	2.30	0.59
4	3.60	0.79
5	2.42	0.63
6	3.59	0.43
7	2.37	0.56
8	3.50	0.61
9	2.03	0.69
10	1.74	0.28

Fig 1. (A) Voxel-wise comparisons between β and $f_{v,GM}$ of the activated voxels. Different color dots represent individual subjects (N = 10). Table B) shows that $f_{v,GM}$ is highly correlated to β in the activated ROIs.

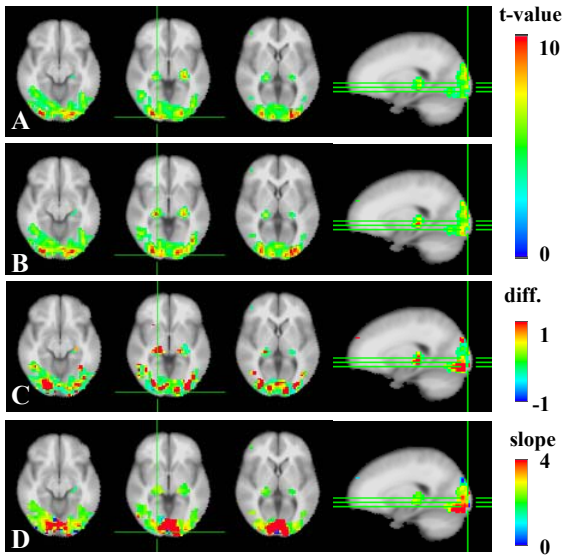


Fig 2. (A) Group t-test results (t>3.685) (B) Group t-test covarying for $f_{v,GM}$ map (t>3.685), (C) difference of t-score in the activated ROI (B-A), and (D) the slope of β with respect to $f_{v,GM}$ in the activated ROI.

Results and Discussion

This study shows mainly three findings:

1. Consistent functional activation is observed between conventional t-test and the t-test with $f_{v,GM}$ as a covariant.
2. The size of the activated ROI and average t-score in the activated ROI are increased when using the covariate t-test with the same threshold (t>3.685)
3. Different slopes of β with respect to $f_{v,GM}$ in the activated ROI are observed in V1, V2, V3 and Thalamus in the activated ROIs

Fig.2 demonstrates the activated ROI using two different analysis: a conventional t-test, shown in Fig. 2A, and the t-test covarying voxel-wise $f_{v,GM}$, shown in Fig. 2B. It is observed that areas encompassing visual cortex and lateral geniculum nucleus (LGN) are consistently activated using both methods. However, the t-test with $f_{v,GM}$ as a covariant shows larger activated ROI than conventional t-test at the same threshold (t>3.685).

The numbers of voxels in the activated ROI in Fig. 2A and 2B are 2849 and 3027, respectively, and 2768 voxels are overlapped in the two methods. Fig. 2C shows the difference of t-score (Fig.2B – 2A), indicating that t-score is increased, shown as warm color. Average t-score in a commonly activated ROI is calculated as 5.5 in conventional t-test and 6.2 in the t-test with $f_{v,GM}$ as a covariant.

Finally, Fig. 2D and Tab.1 show that the different slopes of β versus $f_{v,GM}$ are observed in V1, V2, ,V3, and LGN areas, and higher slope of β versus $f_{v,GM}$ is observed in V1 than other areas. This slop difference would not be observed in conventional β maps (not shown here). This finding indicates that the slope, or BOLD contrast change per GM, might be region dependent, and it would be interesting to further examine the anatomical and task dependency of the slope of β versus $f_{v,GM}$.

	Activated ROI (t>3.685)			
Slope	V1	V2	V3	LGN
(β to $f_{v,GM}$)	6.55±5.54	2.54±3.47	1.08±1.29	0.31±0.56

Tab. I. The slope of β with respect to $f_{v,GM}$ in the activated ROI.

Acknowledgements

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