Subject-Specific HRF in fMRI Data Analysis for Brain Tumor and Leukemia Survivors

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Introduction

The BOLD fMRI signal is based on hemodynamic responses secondary to neural activity; therefore characteristics of the hemodynamic response function (HRF) affect fMRI data analysis and interpretation. The canonical form of the HRF (Fig 1.) is often used to improve the sensitivity in fMRI data analysis. However, when applying fMRI in a clinical population with possibly altered hemodynamic responses, using the subject's own HRF in fMRI data analysis may be advantageous because HRF variability is greater across subjects than across brain regions within a subject[1]. Here we compare the use of the canonical- and subject-HRFs in the data analysis of an ongoing fMRI attention study in pediatric brain tumor (BT) and acute lymphoblastic leukemia (ALL) survivors. BT and ALL survivors often have attention deficits and cerebral vascular changes probably caused by radiation therapy aimed at their brains.

Methods

Subjects: Subjects included 30 healthy volunteers and 7 cancer survivors (3 ALL and 4 BT), who gave written informed consent to participate. ***MRI:*** 1.5T Siemens Symphony scanner. Single shot T2* weighted EPI (TR = 2.06sec, TE = 50 msec, FOV =192 mm, matrix =64x64, slice thickness = 5mm) was used for fMRI data acquisition. ***fMRI paradigms:*** 1) blocked design continuous performance test (CPT[2], a standard psychological test for sustained attention and inhibition, similar to go-no-go task), with 20 sec of task altered with 20 sec of rest for 6 blocks. 2) event-related visual stimulation, reversing (8hz) black and white checkerboard on for 2 sec in a 40 sec epoch and repeated 8 times. ***Data Analysis:*** SPM99 software was used. BOLD signal change to the visual stimulation at voxels at primary visual region was obtained as the subject-HRF for each survivor. Regions of interest (ROIs) for CPT activation were identified from the second level random effect analysis of the 30 volunteers' CPT activation maps. For each survivor, the canonical HRF and subject HRF was convolved with the CPT paradigm and then scaled to form a regressor for the general linear model (GLM) for SPM data analysis. The thresholds for the survivor activation map were $p = 0.001$ (uncorrected) and 5 voxels ($p < 0.01$ corrected). Activation in the ROIs was compared between the subject-HRF and canonical-HRF maps for each survivor.

Results

CPT activation involved an extended brain network including supplementary motor area (SMA), cingulate, extrastriate visual, prefrontal, and parietal areas (Fig 2). These ROIs are thought to be involved in attention and inhibition control functions required by CPT. For each survivor, the measured HRFs varied from the canonical HRF (Fig. 1), thus, the regressor used in GLM defined by the subject-HRF differed from the canonical HRF regressor. For 3 survivors (2 BT and 1 ALL), similar CPT activation was detected with the canonical HRF and the subject HRF. For another 3 survivors (1 ALL and 2 BT) some ROIs were detected only with the canonical HRF. Finally, for 1 ALL survivor, some ROIs were detected only with the subject HRF. Table 1 summarizes differences in the regional activation detected with the two data analysis approaches in these 4 subjects.

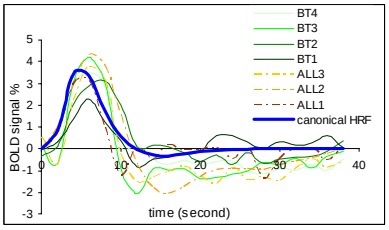

Fig 1. Measured visual HRF for each subject and the canonical HRF

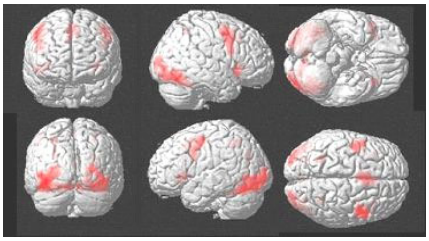

Fig 2. CPT Activation Map

Tabel 1. Differences in Activation of ROIs between the use of the Canonical and Subject HRFs

	ROI Activations	
	Canonical HRF	Subject HRF
ALL1		SMA, Visual (Right), Prefrontal (Left)
ALL2	2nd Visual (Left, more voxels)	
BT1	SMA	
BT2	Prefrontal (Left)	

Discussion and Conclusion

ROIs were detected as active with the canonical HRF for 6 out of 7 survivors, suggesting that using the canonical HRF in data analysis is generally effective in blocked design fMRI study on these patients. The differences of subject HRFs from the canonical HRF may have greater impact on event-related fMRI studies on this population. The ALL survivor, for whom important ROIs were detected only with subject HRF, illustrates the potential benefit of using a subject-specific HRF in fMRI data analysis. However, linearity of BOLD signal and small HRF variation across brain regions within a subject were assumed for using subject-HRF here, but these assumptions may not be valid with certain clinical populations. Thus, further investigation is needed to optimize data analysis with the subject-specific HRF in fMRI studies of clinical populations.

Reference

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