Enhancement of BOLD response using carbogen modulation

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Background

Blood Oxygenation Level Dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) is a noninvasive and major technique to probe neuronal activation of brain using hemodynamic responses. By assuming no significant change of cerebral metabolism during mild hypercapnia, the carbogen inhalation was proposed to improve sensitivity of fMRI studies by modulating vascular autoregulation. Therefore the fMRI visual studies with and without CO_2 modulation were performed to demonstrate the dynamic coupling between CO_2 modulation and BOLD signal changes.

Materials and Methods

1. fMRI: Nine right handed normal subjects (male : female = 5 : 4 ; 24± 2 years old) with written consent were participated in this study. Written consent was approved by the Institutional Ethics and Radiation Safety Committees of Taipei Veterans General Hospital. Gradient echo echo planar imaging (EPI) sequence was conducted using a Bruker 3T MR system (MedSpec S300, Germany) for fMRI scans. 245 volume scans (including 5 dummy scans) were obtained with repetition time (TR)=2000 msec, echo time (TE)=50 msec, in-plane matrix=64*64 pixels, field of view=230*230 mm^2, slice thickness=5 mm and interslice gap=1 mm. Twenty axial slices were acquired to cover the whole brain for one volume.

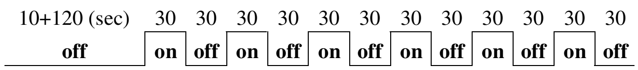

Figure 1 Blocked- Paradigm of visual fMRI studies

2. Visual fMRI and CO_2 ***delivery:*** A red cross was displayed the first 130 sec for baseline condition. The paradigm of block-designed fMRI was constructed by **on**-periods of 8Hz flickering black/white checkerboard and **off**-periods of a red cross alternatively every 30 seconds as **Figure 1**. Video display was synchronized with MRI by TTL triggering signals. With head fixation by a vacuum pad, medical grade carbogens (volume/volume, 5% CO_2, 20% O_2 and 75% N_2) and air was delivered from individual tanks and central supply, respectively, with correction of humidity. Gas inhalation and exchange were obtained by a medical grade non-rebreathing mask with high flow rate (10 liters/minute) and manual control during MRI studies using a home-made switching system. Two sessions of visual fMRI tasks were obtained with and without CO_2 modulation. Air was supplied all the time and 5% CO_2 was switched on for **on**-periods only for visual task with CO_2 modulation.

3. Data Analysis: Optimal hemodynamic response of fMRI sessions was estimated by correlating EPI time series with ideal task functions with various temporal delays of hemodynamic response (2, 6, 10 and 14 sec). By utilizing the optimal hemodynamic response as a template of correlation analyses, averaged time course of selected thirty voxels with the maximal correlation coefficients was smoothed to get the peak value for each **on**-period. For each session, top 60% of time points within the six **on**-periods were included for calculating the averaged BOLD change of activation using raw data, when the first 120 sec baseline condition was used to estimate baseline signals. Thus BOLD change was calculated as following: **[(activation-baseline)/baseline] ×100%**

Results

Time courses of fMRI visual study with and without CO_2 modulation were demonstrated for one subject as **Figure 2**. BOLD change of visual activation with CO_2 modulation was larger than that without CO_2 modulation. Signal fluctuation of **off**-period after visual stimulation may be affected by activation period because of slow hemodynamic change. Therefore, the first 120-second **off**-period was applied as baseline condition. BOLD changes of two sessions of 9 subjects were summarized in **Table 1**. BOLD change of visual sessions with CO_2 modulation was larger than those without CO_2 modulation with statistical significance (p = 0.03, two-tail paired t-test). Most of the optimal hemodynamic delay was about 6 seconds in these fMRI visual studies.

Subject	Task	HD(sec)	BOLD(%)
A	VCO2	10	6.29
	V	6	2.92
B	VCO2	6	6.14
	V	4	4.05
C	VCO2	6	5.58
	V	6	5.02
D	VCO2	6	8.10
	V	2	6.98
E	VCO2	6	2.74
	V	6	2.84
F	VCO2	6	3.20
	V	6	3.39
G	VCO2	14	5.32
	V	2	2.54
H	VCO2	4	4.79
	V	6	3.27
I	VCO2	6	5.25
	V	6	5.68
Mean±SD	VCO2		5.27±1.62
	V		4.08±1.51

Table 1 BOLD signal change (%) of visual task for 9 subjects (A-I). *V: Visual task without CO_2 ; VCO2: Visual task with CO_2 ; SD: Standard Deviation ; HD : the optimal hemodynamic delayed time*

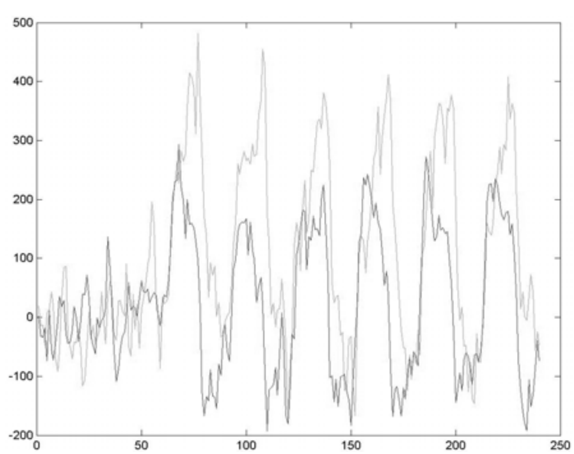

Figure 2 The normalized time course for visual task with (gray line) and without CO_2 modulation (black line)

Discussions

Significant difference of BOLD change between visual fMRI studies with and without CO_2 modulation was demonstrated as CO_2 modulates the cerebral blood flow (CBF) to increase positive BOLD signal. Because BOLD change was increased by CO_2 modulation, BOLD response of brain wasn't driven to limit by general fMRI visual study. However, individual variation of CO_2 modulation was observed, and effect on negative BOLD signal needed further evaluation.

Acknowledgement

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References

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