Investigating the Relation between steady-state hBOLD and fBOLD signals in fMRI studies

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Introduction:

The neuron-activity related BOLD signals (fBOLD), which has been widely applied upon the investigation of human neural activity, could be interfered by the BOLD signals coming from the inhaled CO2 (hBOLD). Prior studies have focused on the relation between the fBOLD and hBOLD, however, leading to discrepant results. Some researchers report that the hBOLD and the fBOLD signal changes are independent and additive [1-3]. Other research groups argue that fBOLD signal change is dependent on the hBOLD [4, 5]. The discrepancy has been related to the inhaled CO2 fractions [6]. None ever proceeded conclusive study to explain this discrepancy. We hypothesize that the cerebrovascular reserve might be limited by original global vasodilatation at high inspired CO2 fractions, restrict further neuroactivity-related vasodilatation, and then attenuate the BOLD signal change. Therefore, in our study, we broaden the range of CO2 concentration from room air to 7% and extend the experiment duration to cover the transient and steady states BOLD responses. We aim to verify our hypothesis that the fBOLD signal will be attenuated by the hBOLD signals.

Materials and Methods:

The study consisted of six healthy volunteers (mean age: 29 years) with six experiments for each subject under different fractions of inhaled CO2 from room air to 7%. BOLD signals were measured using the EPI sequence on a 3 Tesla MR scanner. Each experiment consisted of 205 scans with a sampling time of 3 seconds. The first 10 dummy scans were discarded. Visual stimulation via a checkerboard flashing at the frequency of 8 Hz was given with the block design with 5 scans (15 seconds) "ON" and 5 scans (15 seconds) "OFF" in the following 195 scans and additional 10 scans "OFF" at the end. Each experiment included 3 phases: pre-hypercapnic phase (150 seconds), hypercapnic phase (300 seconds), and post-hypercapnic phase (165 seconds). The CO2 gas mixture was given at the hypercanpic phase. Room air was supplied at the pre-hypercapnic and post-hypercapnic phases. The hBOLD percent changes under the perturbation of inhaled CO2 levels were computed. The fBOLD signals related to the visual stimulation was analyzed using the cross correlation method. The hypercapnic fBOLD percent changes were normalized by dividing the pre-hypercapnic fBOLD percent changes for comparison. Statistical analysis: Student paired-t test.

Results:

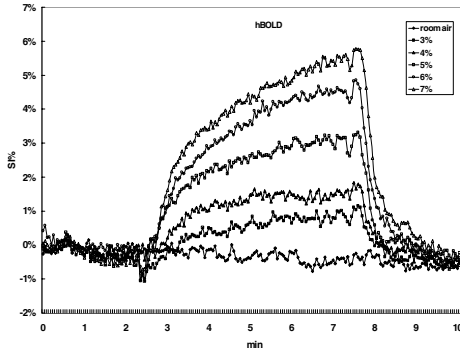
Our study showed that the hBOLD signals ascended as the CO2 was inhaled. The transient states ranged from 2 minutes to 4 minutes, longer in higher inhaled CO2 fraction (Fig. 1a). The steady-state hBOLD percent changes increased significantly in all level of inhaled CO2 fractions (Fig. 1b). The steady-state absolute fBOLD signal changes and the normalized fBOLD ratios descended significantly in all but 3% of CO2 fractions (Fig. 1c).

Discussion:

There are two distinguishing features of our study. First, we broaden the range of inhaled CO2 from room air stepping to 7%, which is the upper limit tolerated by all healthy subjects. The full range investigation allows us to observe the fBOLD response to the inhaled CO2 directly. Second, we measure the BOLD signals from transient to steady state and compute the hBOLD and fBOLD signal changes quantitatively under the steady state. This concept is of paramount importance since the transient state BOLD signals, which were used by prior researchers, are variable and do not fully reflect the effect of the inhaled CO2. Our results show that the fBOLD signal change remains unchanged in low CO2 fractions (3%) and gradual attenuates as the CO2 fraction increases. This finding is consistent with the concept of cerebrovascular reserve, which might remain unchanged in lower CO2 fractions but be damped in higher CO2 fractions.

Conclusion:

In this study, we provide simple but important concepts in approaching the influence of inhaled CO2 on the fMRI experiments.



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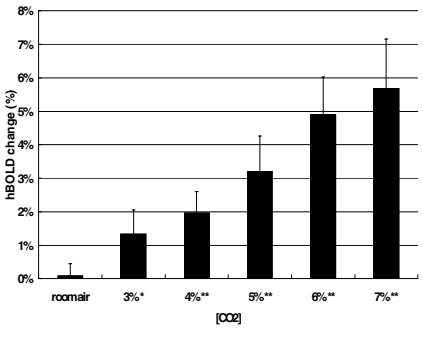

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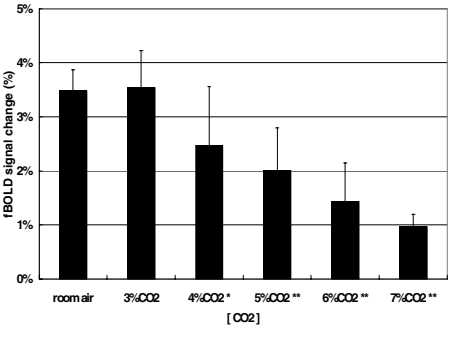

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Figure 1. (a) hBOLD signals-time course. (b) hBOLD percent-change versus CO2 concentration. There is a tendency that the hBOLD signal change is positively correlated with the concentration of inhaled CO2. (c) fBOLD percent-change versus CO2 concentration. The fBOLD percent-change steps down as the CO2 concentration becomes higher from 3% to 7%. There is no significant difference of the fBOLD percent0change between the room air and 3% of inhaled CO2. (Note: * represents $P < 0.05$; ** represents $P < 0.01$)

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