

Hemodynamic Response Function (HRF) Modulation by Inhaled CO₂ Concentration using Event-Related fMRI

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Introduction:

Blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) can measure vascular oxygenation change associated with neuron activity [1]. Carbon dioxide (CO₂) is a potent vasodilator that could increase the cerebral blood flow prominently [2]. Our prior study has demonstrated that the inhaled CO₂ (hBOLD) [4] can change the cerebral hemodynamics [3] and the BOLD fMR signal [4]. Instead of long-time box-car stimulus, event-related fMRI (ER-fMRI) with short-time visual stimulus is applied to investigate the transient hemodynamic response function (HRF). The time curve of HRF is recorded with controlled stimulus condition (strength, duration and interval time) and physiological factor (cerebral blood flow, oxygen consumption). In this study, we aim to investigate the influence of different controlled stimulus condition on HRF change after inhalation of different CO₂ concentrations.

Materials and Methods:

Three healthy volunteers were enrolled in this study (mean age: 32 years). Each subject received visual box-car stimulation with inhalation of different CO₂ concentrations (3%, 5%, and 7%). BOLD signals were measured using the EPI sequence on a 3 Tesla MR scanner (GE, Signa). 14 slices (FOV: 192 mm, 64x64, 3 mm thickness) were acquired to cover the visual cortex. The box-car visual stimulus duration per cycle (30 seconds) was set with different protocol (1, 2, and 4 sec in one cycle) when the subject inhaled a fixed CO₂ concentration. The event-related fMRI are set with 720 scans (1 sampling/ sec), and comprise of three phases: pre-hypercapnic phase (the first 180 seconds), hypercapnic phase (the subsequent 360 seconds), and post-hypercapnic phase (the final 180 seconds). During a whole event-related fMRI scan, the box-car visual stimulus is turned on with a set-up duration (1, 2, 4 sec) in the cycle of every 30 seconds (Fig. 1). A circular checkerboard flashing at 8 Hz was triggered by the synchronous RF signal of EPI. The image data in the first 2.5 min was analyzed using the statistical parametric mapping software (SPM5) to find the active pixels in visual cortex. The activated areas were defined as pixels with significant signal change (<0.01 statistical threshold of P value) within the visual cortex. The averaged signal intensity of these pixels in one event-related fMRI (720 scans with 12 min 5sec) was used for HRF computation. The HRF in pre-hypercapnic phase (room air) was averaged by the first 5 cycles. After CO₂ inhalation, the cerebral perfusion was increased and it took about 150 seconds to reach the steady-state hypercapnia [4]. The HRF in hypercapnic phase (3, 5, 7% CO₂) was averaged by the last 5 cycles of hypercapnia.

Results:

The results were presented in the Figure 2 and 3. Figure 2 shows the active pixels of one subject with 1, 2, 4 second box-car visual stimulus. Figure 3 shows the HRF of 1, 2, and 4 sec visual stimulus with inhalation of room air, 3%, 5% and 7% CO₂.

Discussion:

The number of active pixels increases with longer visual stimulus duration (Fig2). It is similar with previous study [5]. The peak of HRF curve is decreased and delayed when the subject inhaled higher CO₂ concentration. In addition, the width of HRF curve is wider with higher inhaled CO₂ concentration. This finding is consistent with the concept of cerebrovascular reserve, which might remain unchanged in lower CO₂ fractions but be inhibited in higher CO₂ fractions. In conclusion, the HRF can be influence by different inhaled CO₂ concentrations and different stimulus control conditions.

Reference:

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4. Liu YJ, et al, *AJNR*. 2007; 28:1009-14.
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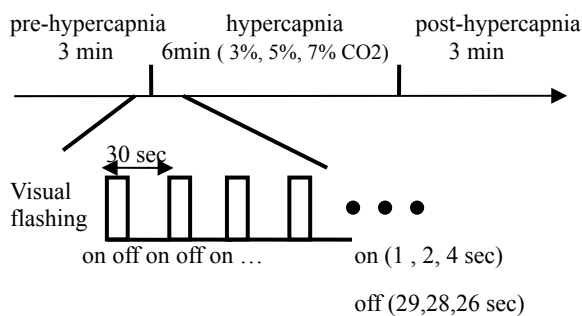


Fig 1. Illustration of the experiment paradigm

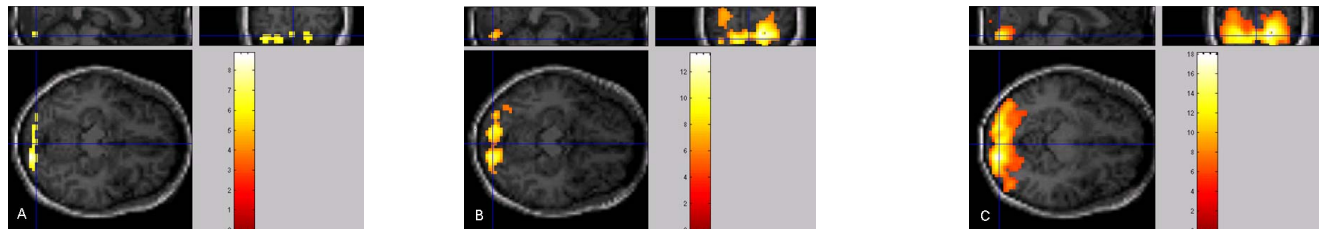


Fig. 2. The active pixels of one subject in visual stimulus of (A) 1, (B) 2, (C) 4 sec.

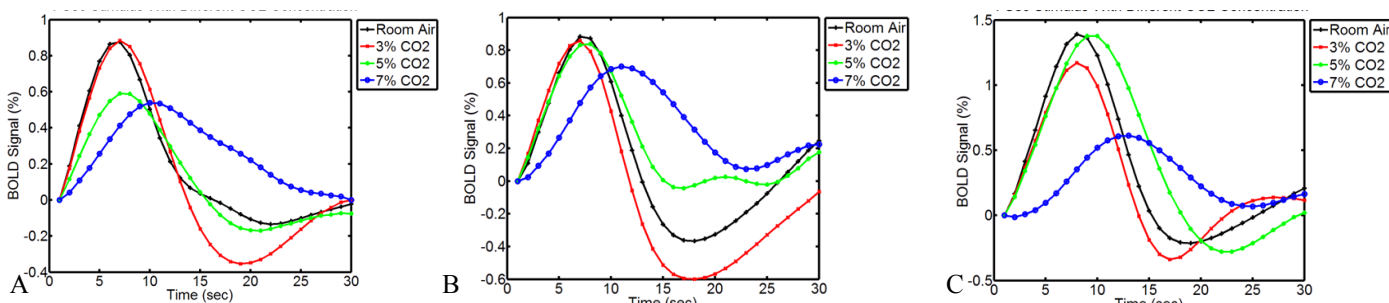


Fig 3. The mean HRF curve of room air, 3, 5 and 7%CO₂ in (A) 1 sec visual stimulus (B) 2 sec (C) 4 sec for the six subjects included in this study.