To Investigate the Hemodynamic Response Function Alterations in Hypercapnia Using Visual Stimulus fMRI

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Introduction:

Functional magnetic resonance imaging (fMRI) using blood oxygenation level-dependent (BOLD) contrast has appeared to measure vascular oxygenation change due to neuron activity [1]. Recently, it is found that BOLD signals could be altered solely by hypercapnia and it might cause misinterpretation of fMRI studies with concurrent hypercapnia [2]. Carbon dioxide (CO2) is a potent vasodilator that could increase the cerebral blood flow prominently [3]. Our prior study has demonstrated the neuron-activity related BOLD signals (fBOLD) interfered by the BOLD signals coming from the inhaled CO2 (hBOLD) [4]. Most fMRI studies used long-time box-car stimulus design for evaluating BOLD effect in hypercapnia. To the best of our knowledge, no study has evaluated the changes in the hemodynamic response function (HRF) in terms of hypercapnia degree. In this study, instead of long-time box-car stimulus; event-related fMRI (ER-fMRI) with short-time visual stimulus was applied to investigate the transient HRF. We explored the HRF change from short to long time stimulus in different hypercapnia conditions.

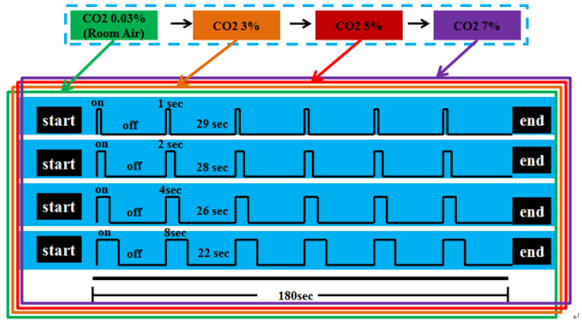

Fig1. Illustration of the experiment paradigm.

Materials and Methods:

Experiment design: 8 healthy volunteers (21~40 years, mean 25 years, 2 females and 6 males) were enrolled in this study. BOLD signals were measured using the EPI sequence on a 3 Tesla MR scanner (GE Signa HDx, GE Healthcare, Milwaukee,Wis). 14 slices (TR/TE=1000/35 ms, FOV: 192 mm, 64x64, 3 mm thickness) were acquired to cover the visual cortex. Each volunteer was given visual stimulus of 8 Hz circular checkerboard pattern flashing within inhalation of four different fractions of CO2 (room air, 3%, 5% and 7%). As shown on Fig 1, four experiments were randomly arranged and continually applied, each experiment consisted of four sub-experiments of different visual stimulus durations (1, 2, 4, and 8 sec) with 6 repeated cycles of 30 sec period. The synchronous RF signal of EPI was counted to accurately control the on-off of a circular checkerboard flashing. For each sub-experiment, the EPI sequence was performed at 1 sec interval with total of 180 scans following 5 dummy scans. In 3, 5 and 7% CO2 experiment, there is a 3 minutes prepared time for steady-state hypercapnia after CO2 gas inhalation. **Data analysis:** The image data was analyzed using the Statistical Parametric Mapping software (SPM8) to find the active pixels and Anatomical Automatic Labeling (AAL) software to label the mask of visual cortex. The activated areas were identified as the pixels within the mask of visual cortex fulfilling the statistical threshold of P value less than 0.05. The mean signal intensity of these active pixels in whole 180 scans (6 cycles) was obtained and the HRF of 30 sec period was averaged from the mean signal of 6 cycles. The HRF was a presentation of signal percentage change by normalized to an initial value. The peak amplitude and time-to-peak (TTP) were calculated for characterization of HRF. The Wilcoxon test was applied for statistical analyses of the differences between the room air and graded inhaled CO2 perturbations.

Results:

Fig. 2 depicts the average HRF of 8 subjects of 1, 2, 4 and 8 sec visual stimulus with inhalation of room air, 3%, 5% and 7% CO2. Fig. 3 shows peak amplitude and TTP of HRF with respect to room air, 3, 5 and 7% CO2 (mean and standard deviation) under different visual stimulus duration.

Discussion:

The amplitude and duration of HRF are ascended as the visual stimulus duration (Fig. 2). It is similar with previous study [5]. The width of HRF curve is wider as higher inhaled CO2 concentration. The peak of HRF curve is decreased and TTP is ascended with inhaled CO2 fractions (Fig.3). In statistical analysis, both peak and TTP are no statistic different between room air and 3% CO2 group, but statistic different between room air and high CO2 concentration group (5% and 7%) in all four stimulus durations. This finding is consistent with the concept of the cerebrovascular reserve may be limited by global vasodilation at high inspired CO2 fractions, restricting further vasodilation due to visual stimulation. Our results show the restriction of HRF is related to CO2 concentration and independent with visual stimulus duration under the steady-state hypercapnia.

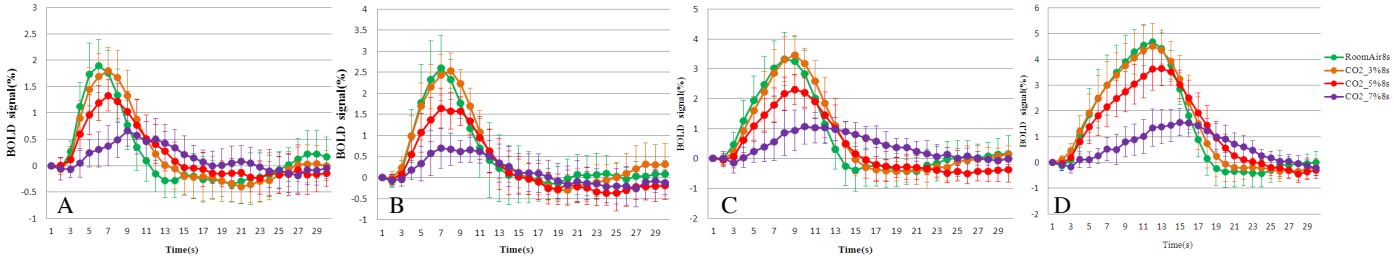

Fig. 2 The mean HRF of 8 subjects with inhalation of room air, 3%, 5% and 7% CO2 in (A) 1, (B) 2, (C) 4 and (D) 8 sec visual stimulus.

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Reference:

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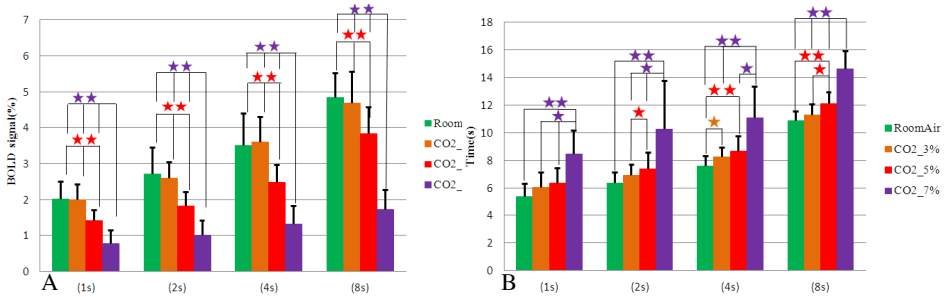

Fig 3. The mean and standard deviation (A) peak amplitude, (B) TTP of room air, 3, 5 and 7% CO2 under different visual stimulus duration. (* p<0.05, ** p<0.01)