MRI Mapping of Carbogen Cerebro-Vascular Reactivity Using Independent Component Analysis

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Background

Cerebral blood flow (CBF) can be independently modulated by inhaling carbon dioxide (CO_2) or breath holding (Kastrup et al, 1999; Kastrup et al, 2001; Duong et al, 2001). Because of no significant effect of CO_2 on cerebral metabolism, increased CBF by inhaling CO_2 may booster the blood flow component of blood-oxygen-level-dependence (BOLD) response during task performance of fMRI. Cerebrovascular reactivity (CVR) depends on the intact mechanisms of vascular auto-regulation, which can be challenged by inhalation of carbogen, breathing holding and intravenous vasodilators (e.g. acetazolamide). In this study, human carbogen CVR was explored by dose-dependence of carbogen inhalation (0.03 ~ 5% CO_2, 20% O_2 and 80~75% N_2) with mapping CVR using independent component analysis (ICA) and linear regression.

Materials and Methods

Modulation of human hemodynamic auto-regulation was observed using the BOLD-based fMRI for ten normal right-handed subjects (male : female = 5 : 5, age: 20~25 years old) recruited for the studies with written consent form. All subjects were healthy without medical history, especially heart and chronic pulmonary disease.

Brain MRI studies were conducted by using a 3T Medspec S300 system (Bruker GmbH, Ettlingen, Germany) equipped with an actively shielded gradient coil and a quadrature transceiver. Single-shot echo planar images (64x64 matrix, 5 mm slice thickness, gap = 1 mm, 20 slices) covering whole brain were acquired with TE = 50 milliseconds, TR = 2000 milliseconds, and number of repetition = 360 (dummy scans = 5). With head fixation by a vacuum pad, medical grade carbogens (volume/volume, 1-5% CO_2, 20% O_2 and 79~75% N_2) and air was delivered from individual tanks and central supply 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 (**Figure 1**). Vital signs (heart rate and end-tidal CO_2) were monitored during scans using the MagLife C system (Bruker, Ettlingen, Germany). Subjects were instructed to close their eyes during study.

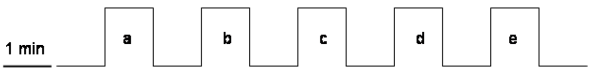

Figure 1 : Blocked-paradigm of carbogen inhalation (a~e: arbitrary sequence of 1, 2, 3, 4 and 5% carbogens)**.**

The data analysis was performed using spatial informax ICA (Computational Neurobiology Laboratory, The Salk Institute for Biological Studies, La Jolla, USA) for unknown delay of CO_2 effect on arterial CO_2 ($PaCO_2$) and AFNI (Analysis of Functional NeuroImages, NIMH, Bethesda, USA) for linear regression of signal amplitude and spatial extension. Inclusion criteria of MR quality control by utilizing a home-made on-line real-time analysis was head translation < 1 mm and rotation < 0.5 degree. Without pre-processing of motion correction, 100 response functions of carbogen challenge were derived from infomax ICA with data reduction by principle component analysis. CO2-related signal components were identified by (1) correlation analysis of the temporal profiles by using the ideal function of gas-delivery paradigm, and (2) distribution of response regions supporting the vascular involvement by visual inspection. Voxel-based parametric mapping of CVR by linear regression was performed by segmenting original data using the CO_2-related signal components obtained from ICA.

Results

Carbogen-modulated signal components were identified by ICA and cross correlation with carbogen paradigms. Selected ICA components showed various delays upto about 20 seconds as compared to carbogen paradigm. By inhalation of 5%CO_2/20% O2/75%N_2 gas, the 2~5 fold augmentation of normalized BOLD signals was observed in normal subjects (an example was demonstrated as **Figure 2**). Linear regression of segmented BOLD signals and CO_2 percentage showed the averaged slope of 570±180 (mean ± one standard deviation, individual data as **Table 1**). CVR mapping by linear regression showed global response of brain and higher carbogen CVR of gray matter.

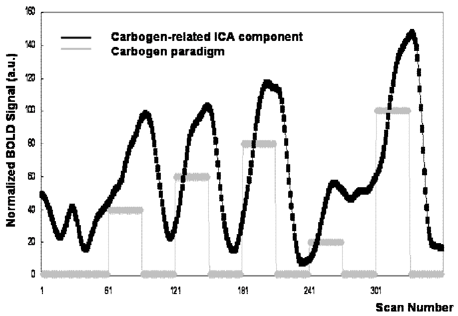

Figure 2 : Carbogen modulation of BOLD signal was detected by ICA.

Subject	Carbogen Paraqdigm	Slope	R^2 Value
1	1-3-4-2-5	814	0.82
2	3-4-1-5-2	519	0.65
3	2-3-4-1-5	755	0.79
4	3-4-1-5-2	506	0.73
5	2-5-1-4-3	321	0.64
6	2-4-1-3-5	644	0.61
7	4-2-1-3-5	754	0.83
8	5-2-4-1-3	298	0.62
9	2-1-4-3-5	533	0.67
10	3-1-4-2-5	563	0.67

Table 1 : Carbogen CVR by linear regression of modulated BOLD signals

Discussion

Linear or near-linear modulation of BOLD signal was achieved by carbogen inhalation in the range of 1~5%. ICA detected the unknown delayed response of $PaCO_2$ during carbogen inhalation. MRI mapping by carbogen CVR may provide quantitative analysis of cerebro-vascular auto-regulation which plays the important roles in the patho-physiological mechanisms of cerebrovascular diseases and BOLD-based fMRI studies.

Acknowledgement

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References

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