Vasomotor Independence of BOLD-based fMRI Resting Rhythms

T-C. Yeh[1,2], C-M. Cheng[1,2], W-J. Kuo[2], J-C. Hsieh[1,2], L-T. Ho[1,2]

[1]Department of Medical Research and Education, Taipei Veternas General Hospital, Taipei, Taiwan, Taiwan, [2]National Yang-Ming University, Taipei, Taiwan, Taiwan

Background

Nondeterministic fMRI signals with very low frequency (VLF) of 0.01~0.2 s^{-1} presented at visual, auditory and somatomotor regions with significant overlapping of the physiological signals (Biswal et al, 1995; Kiviniemi et al, 2003). One of resting signal components (Tripod component) involved bilateral occipital, precuneus, posterior cingulate, inferior parietal lobule and prefrontal cortices as identified in the characteristic tripod pattern (Yeh et al, 2005). Physiological cardio-respiratory aliasing signals and spontaneous vasomotor reactivity have been proposed for the origins of resting rhythms. Vasomotor activities, e.g. cerebral blood flow (CBF), can be independently modulated by inhaling carbongens or breath holding (Kastrup et al, 1999; Kastrup et al, 2001; Duong et al, 2001). In this blood-oxygen-level-dependence (BOLD)-based fMRI study of normal subjects, verification of cerebral resting tripod signal was obtained when cerebral blood flow (CBF) was independently modulated by the inhaling graded carbogens (1~5% CO_2, 20% O_2 and 79~75% N_2) and air. Resting tripod component was concluded to represent the true neural network during awake resting state.

Materials and Methods

Modulation of human hemodynamic auto-regulation or vasomotor activities was observed using the BOLD-based fMRI for twelve normal right-handed subjects (male : female = 6 : 6, age: 24 +/- 2 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 SPM2 (Wellcome Department of Cognitive Neurology, London, UK) for spatial extension of resting tripod component. 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. Resting tripod and CO_2-relevant signal components were identified by (1) specific distribution of tripod component (bilateral BA 6, 7, 8, 19, 23, 29, 30, 31, 39, 40 and right BA 21) and (2) correlation analysis of the temporal profiles by using the ideal function of gas-delivery paradigm, respectively.

Results

Carbogen-relevant signal components and resting tripod components were consistently identified by ICA and cross correlation with carbogen paradigms. Carbogen-relevant ICA components showed various delays upto about 20 seconds as compared to ideal carbogen paradigm. By inhalation of 1~5%CO_2/20%O2/79~75%N_2 gas, the 2~5 fold augmentation of normalized BOLD signals was observed in normal subjects (an example of 1-2-5-4-3 CO_2 paradigm was demonstrated as **Figure 2**). Index of carbogen modulation, using the maximal correlation coefficients (Max. C.C.) with ideal carbogen paradigms by temporal shifting (**Table 1**), showed less carbogen effect on tripod component (p = 0.0004, by two-tail Student t-test).

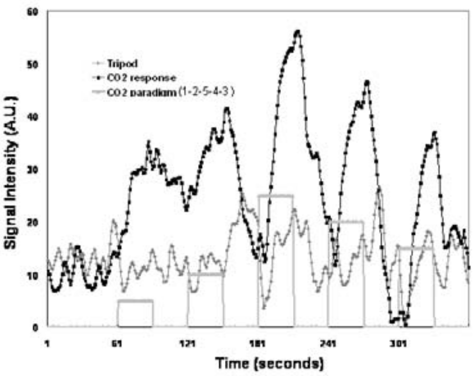

Figure 2 : Co-existence of resting tripod and carbogen-relevant BOLD signal components was detected by ICA. (⬆)

Table 1 : Index of carbogen modulation (➡)

Subject	Carbogen Paradigm	Max. C.C. of Tripod component	Max. C.C. of carbogen-relevant component
1	5-1-3-2-4	0.50	0.54
2	1-3-5-2-4	0.12	0.65
3	4-1-5-3-2	0.26	0.69
4	1-2-5-4-3	0.28	0.33
5	4-5-1-2-3	0.57	0.65
6	1-2-3-5-4	0.56	0.81
7	3-1-5-2-4	0.34	0.78
8	1-2-5-4-3	0.12	0.73
9	2-1-4-3-5	0.41	0.50
10	5-4-1-3-2	0.45	0.48
11	1-5-2-3-4	0.30	0.60
12	5-1-3-2-4	0.57	0.75
Average +/- 1 SD		0.37 +/- 0.16	0.63 +/- 0.14

Discussion

Co-existence of resting tripod and carbogen-relevant signal components was verified during inhalation of graded carbogens which changed cerebral vasomotor activity. ICA detected the unknown delayed response of $PaCO_2$ during carbogen inhalation. By applying the maximal correlation coefficients as the index of carbogen modulation, the VLF signal fluctuation of resting tripod component was independent to carbogen modulation as compared to carbogen-relevant signal. Resting tripod component was concluded to represent the true neural network during awake resting state.

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References

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