Quantification of cerebral blood flow, oxygen extraction fraction, and oxygen metabolic index in human with inhalation of air and carbogen

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Introduction

Noninvasive MR methods, such as arterial spin labeling method and an asymmetric spin echo methods, have been explored to provide quantitative measurements of cerebral blood flow (CBF), oxygen extraction fraction (OEF), and oxygen metabolic index (OMI=CBF*OEF) [1, 2]. However, whether these MR methods can provide reliable and repeatable measurements has not been demonstrated in human under normal and physiologically altered conditions. To this end, CBF, OEF and OMI were estimated in a group of normal subjects who underwent repeated episodes of gas challenge using room air and carbogen inhalation. We sought to evaluate whether the CBF, OEF and OMI measurement can reflect the expected physiological changes in human brain under alternative normal and hyperoxic hypercapnic conditions.

Methods

Nine normal healthy human subjects were scanned using a Siemens 3T MR system (Siemens Allegra, Erlangen, Germany). During the experiment, the subjects were breathing via a mask with alternating inhaled gas of either room air (baseline control) or carbogen (3% CO_2 and 97% O_2, hyperoxia hypercapnia) in a sequential order as air, carbogen, air, carbogen and air. Before data acquisition, ten minutes were allowed after each adjustment of gas to achieve a stabilized physiological status. During each gas challenge states, CBF and OEF images were obtained from images acquired using a CASL and an asymmetric spin echo EPI sequence, respectively [1, 2]. In the computation of CBF based on a CASL method, an assumed arterial blood T1 was usually utilized. However, it has been reported that carbogen inhalation increased blood pO_2 substantially[3] and blood T1 depends on several physiological parameters including pO_2 [4]. To account for the effects of carbogen inhalation on blood T1 and then CBF, T1 was approximated by adapting a linear relationship between R1(1/T1) and pO_2 [4]. After obtaining CBF and OEF, OMI maps were then computed as the product of CBF and OEF. In addition, high resolution T1-weighted anatomical images were also collected. A rigid image registration was performed to align all images across all series of scans for each subject. Manually defined ROIs covering both hemispheres were utilized to obtain CBF, OEF and OMI from the whole brain at each gas challenge state for each subject. Mean values of CBF, OEF and OMI were compared between baseline air and carbogen inhalation with Bonferroni correction for multiple comparison.

Results

Representative OEF, CBF and OMI maps were demonstrated during each gas challenge state in the Figure and summarized results were shown in the Table. As illustrated by the Figure and the Table, a global increase of CBF and a decrease of OEF were detected across the whole brain when subjects inhaled carbogen. When the gas mixture was switched back to room air again, both CBF and OEF returned to baseline. Similar to the first hyperoxia hypercapnia manipulation, the 2nd carbogen inhalation induced similar degree of increase in CBF and decrease in OEF. Finally, the last episode of air inhalation brought both CBF and OEF back to normal. During both hyperoxia hypercanic conditions, a significant increase of CBF (+9.8%, $p<0.05$) and a significant decrease of OEF (-10.5%, $p<0.05$) were observed when compared to the initial baseline air inhalation. The concurrent reciprocal changes of CBF and OEF led to a minimum change in OMI throughout the entire experimental procedure. These trends of CBF and OEF changes at each gas manipulation were consistently observed in all subjects, suggesting that reliable measurements of CBF and OEF might be obtained in repeated gas manipulations.

Table

Whole brain	Air	Carbogen	Air	Carbogen	Air
CBF	41.0±10.5	45.0±11.6*	40.2±9.6	44.9±10.8*	38.6±10.0
OEF	33.3±2.5	29.8±2.4*	33.8±1.9	29.4±3.2*	35.0±3.6
OMI	13.8±3.7	13.6±3.9	13.9±4.0	13.4±3.9	13.9±4.7

*** p<0.05**

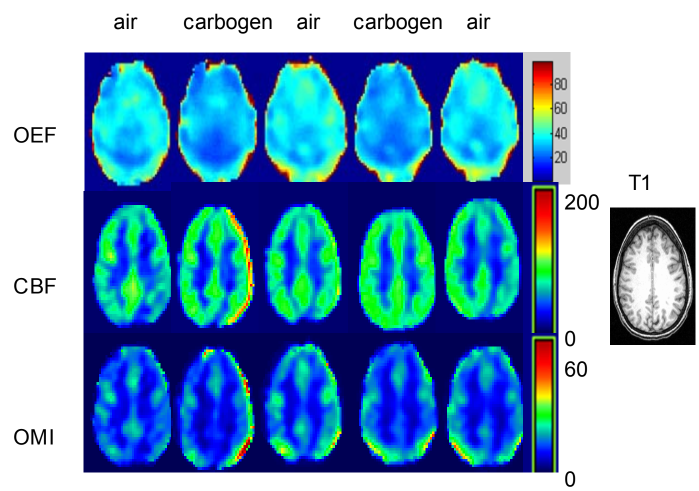

Figure. Representative OEF, CBF and OMI maps in a sequential inhalation of air, carbogen, air, carbogen and air.

Discussion and Conclusions

It has been suggested that carbogen, a mixture of a small percent of CO_2 with oxygen, can relax vessel tone that may lead to vasodilation and increased blood flow. In response to the elevation of CBF, the autoregulation mechanism of the brain will lead to a decreased OEF in a reciprocal manner to maintain a stable oxygenation metabolic rate [5]. A recent PET study has demonstrated that a carbogen gas with 5% CO_2 mixed with oxygen induced a global CBF increase of 15% and a concomitant global OEF reduction of similar level, resulting in an almost unchanged $CMRO_2$[6]. In agreement with these previous reports, our study has consistently demonstrated a 10% increase of CBF, a similar level decrease of OEF and a stable OMI during a 3% CO_2 carbogen inhalation. These results demonstrate the utility and reproducibility of the MR measured OEF and OMI.

Reference

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