Calibrated BOLD in the Medial Temporal Lobe During a Memory Encoding Task

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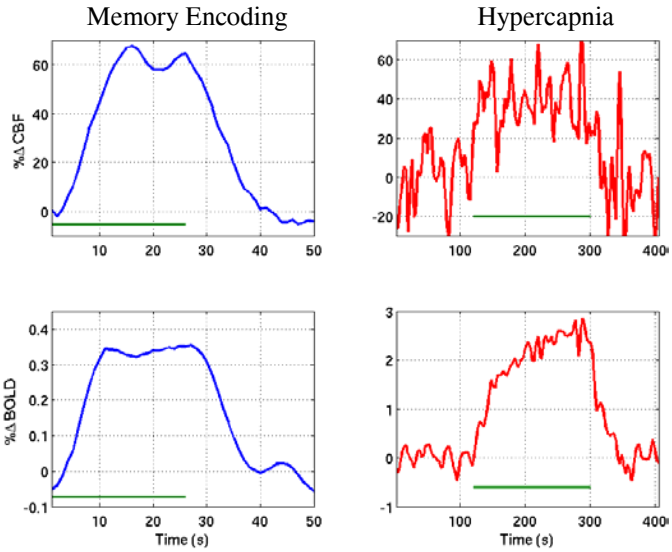
Introduction

Although most fMRI studies use the BOLD signal as an indirect measure of neural activity, there is increasing evidence to suggest that the BOLD signal can be significantly altered by other factors such as medication, age, and disease [1]. Calibrated BOLD measures of functional changes in the cerebral metabolic rate of oxygen consumption ($CMRO_2$) offer a potentially more robust measure, since $CMRO_2$ has been shown to be tightly linked with neural activity [2,3]. However, the application of the calibrated BOLD approach has been primarily limited to sensory areas in which the task was either a visual or motor stimulus. Previous studies have measured the neurovascular coupling ratio, $n = \Delta\%CBF/\Delta\%CMRO_2$, in cortical brain regions, particularly the visual cortex [4] and motor cortex [5,6], with a wide degree of variability observed from 2 to 5 [4,5,6]. In addition, a previous study reported preliminary measurements of n~2 in the sub-cortical basal ganglia in response to a motor task [7]. These data suggest that the coupling ratio may vary across the brain. To our knowledge, measures of the coupling ratio using a cognitive task have not been reported. In this study, $\Delta\%CMRO_2$ and n is measured in the hippocampal region during a memory encoding task. We show that there appears to be a tighter coupling between CBF and $CMRO_2$ in this brain region as compared to sensory areas.

Methods

Four young (ages 25-40, 2 males, 2 females) subjects participated in the study. Subjects viewed a series of novel and familiar landscape scenes, presented in a block design and repeated over three 4-min runs [8]. Data were also acquired at rest for quantification of baseline CBF. To calibrate the BOLD and CBF measurements, a 5% CO_2 challenge was administered for two runs consisting of 2 min of room air followed by 3 min of CO_2 and 2 min of room air. Imaging parameters were: dual echo PICORE QUIPSS 2 sequence with spiral readout [9], TR=3s, TI1/TI2=700/1400ms, TE1=2.8ms, TE2=24 ms, flip angle 90, FOV 240mm, 64x64 matrix. Five 6mm slices aligned with the hippocampus were acquired. Perfusion and BOLD time series were acquired from the running difference and average of tag and control images, respectively. Physiological noise was removed from the data using an extension of RETROICOR for perfusion-based fMRI [10,11]. For each subject, a hippocampal region of interest (ROI) that included both the hippocampus and parahippocampal gyrus was defined using a high resolution anatomic T1-weighted image. BOLD and ASL data were averaged over runs and correlated with a smoothed boxcar reference function. Active BOLD and CBF voxels were selected based on a threshold of $p < 0.05$ (corrected for multiple comparisons) with a nearest neighbor clustering criteria. CBF was quantified for each of the resting scans, using CSF as a signal intensity reference [12]. Average CBF values of activated voxels from the perfusion functional runs were used to calculate baseline CBF values. Hypercapnia calibration constant (M), neurovascular coupling ratio (n), and $\Delta\%CMRO_2$ were calculated based on the Davis model [2].



	Mean	STD
Measured Variables		
Δ%CBF	58.80	*±39.26*
Δ%BOLD	0.40	*±0.16*
$\Delta\%CBF_{Hypercapnia}$	42.42	*±28.93*
$\Delta\%BOLD_{Hypercapnia}$	2.67	*±0.94*
Baseline CBF (ml/100 ml/min)	54.96	*±12.97*
Calculated Variables		
M	0.09	*±0.02*
$\Delta\%CMRO_2$	36.35	*±26.16*
n	1.69	*±0.25*

Results

Reliable and robust activation was observed in all subjects. The figure shows responses of percent change CBF and BOLD during memory encoding and hypercapnia for one representative subject. The table shows means and standard deviations of the measured responses and calculated responses. Although values of $\Delta\%CBF$ and $\Delta\%CMRO_2$ showed considerable variation across subjects, the coupling constant n shows less variability. Our mean calculated n of 1.69 is lower then the previously reported values of ~2.6 (range 2.1 to 3) in the motor cortex [5,6] and ~3 (range 2.25 to 5) in the visual cortex [4]. In contrast, previously reported values of M for the visual and motor cortex, which ranged between 0.06 and .09 [2,5,6] are similar to those measured in the hippocampal region.

Discussion

Robust measures of hippocampal BOLD and perfusion changes during memory encoding and hypercapnia were obtained in all subjects. As compared to previously reported values of $\Delta\%CMRO_2$ (64% ± 219%) in the hippocampus of healthy elderly adults [13], our values are lower and less variable. However, a direct comparison is complicated by the fact that no hypercapnia data were collected in the previous study. Our preliminary data suggest that there is a tighter coupling between CBF changes and $CMRO_2$ changes in the medial temporal lobe as compared to sensory areas. Further study is required to validate this finding. The results of this study support the feasibility of obtaining quantitative measures of functional changes in $CMRO_2$ in the hippocampal regions and lay the groundwork for further studies aimed at examining the effects of aging and disease, such as Alzheimer's disease, on functional changes in $CMRO_2$.

References

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