Metabolic origin of BOLD signal fluctuations during extended rest and light sleep

M. Fukunaga[1], S. G. Horovitz[1], J. A. de Zwart[1], P. van Gelderen[1], S. C. Fulton[1], T. J. Balkin[2], J. H. Duyn[1]

[1]Advanced MRI, LFMI, NINDS, National Institutes of Health, Bethesda, MD, United States, [2]Department of Behavioral Biology, Walter Reed Army Institute of Research, Silver Spring, MD, United States

Introduction

Mapping of brain function with blood oxygen level dependent (BOLD) fMRI relies on the detection of focal changes in cerebral blood flow (CBF) in response to conditioned stimuli. However, in the absence of stimuli, the brain continues to show temporal fluctuations in blood flow as measured with BOLD and perfusion-based MRI [1]. These fluctuations are substantially synchronized across regions that have an apparent functional relationship, and therefore might allow mapping and classification of the networks that underlie human brain function without the need for carefully conditioned stimuli. Despite their potential functional significance, the origin of the fMRI fluctuations in absence of stimuli has not been established. For example, the fluctuations might be caused by purely vascular events (e.g. vasomotor effect), without a substantial metabolic or neuronal component. To investigate this, we performed simultaneous BOLD and perfusion based fMRI studies during rest and conditions of varying metabolic demand.

Materials and Methods

To obtain an estimate of brain metabolism, we aimed at determining the ratio between BOLD and perfusion fluctuation level [2]. Simultaneous BOLD and perfusion MRI at 3.0T scanner (GE) with a 16 channel detector on 11 normal volunteers (EPI, TR: 4 s, TI1: 1320 ms, TI2: 450 ms, TE_{perf}: 20 ms, TE_{bold}: 35 ms, spatial resolution: 3.4x3.4x5.0 mm^3, 5 slices, 600 volumes) [3]. The experimental paradigm was composed of a visual task (VT, 320s checkerboard/grey), followed by breath-holding task (BH, 600s) and an extended rest period (REST, 24minutes 40 s). BH consisted of 5 stages of one-time deep breathing, followed by 40 s breath-hold and 80 s normal breathing. Physiological monitoring (respiratory and cardiac cycles) was also performed. The subjects were deprived from external stimuli during REST and allowed to fall asleep, while their alertness was monitored by concurrent EEG (Synamps2 & Maglink, Compumedics). These EEG datasets were then visually inspected by a certified sleep expert (TJB) and each 30 s interval got scored as Wake or Sleep (Stage 1, 2 , SW or REM). MRI data was high pass filtered at 0.005 Hz and corrected for global intensity variations.

Results and Discussion

Eight of the 11 subjects showed a substantial amount of stage 1 and 2 sleep during the rest period, During both awake rest and stage 1 and 2 sleep, we found significant perfusion and BOLD signal fluctuations in most of the neocortex, with strong correlations between functionally related regions. No significant correlations were found with cardiac and respiratory cycles. Frequency analysis of the fluctuations suggested that most energy was concentrated in the 0.01-0.1Hz band, consistent with earlier reports. BOLD and perfusion signals were highly correlated over most of cortex (fig. 1; example correlation map from single subject). The BOLD-perfusion ratio (BPR) of their fluctuation amplitude in visual cortex averaged over subjects was 1.66±0.28, 3.88±1.22 and 1.57±0.60 for VT, BH, and REST respectively (fig. 2; example plot from single subject). During VT and REST, both BPRs were significantly ($p=2.7x10^{-6}$/$6.8x10^{-7}$) lower than during BH, suggesting an increased metabolic involvement during VT and REST, as compared BH. The BPR was not significantly different between VT and REST (p=0.71), suggesting similar metabolic involvement. The sleep subjects BPR during REST was 1.21±0.24, which was significantly lower than during BH (2.40±0.75, $p=2.4x10^{-3}$). These results suggest that resting state activity represents a metabolic process, and does not require a high level of alertness or consciousness.

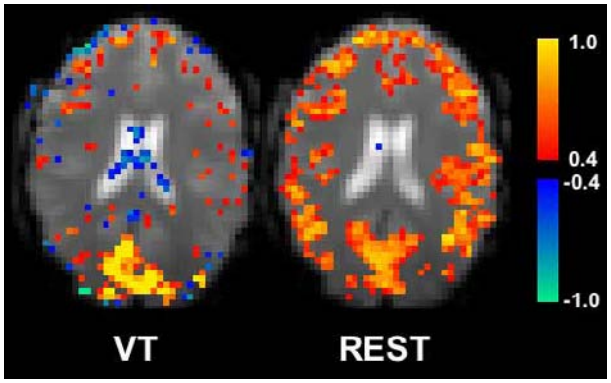

Figure 1: *Example of correlation map (single subject data) between BOLD and perfusion signals during visual task (VT) and rest (REST).*

Conclusion

BOLD fMRI resting state fluctuations are not a purely vascular phenomenon, but represent a metabolic process. They continue during sleep, suggesting they do not require ongoing conscious activity.

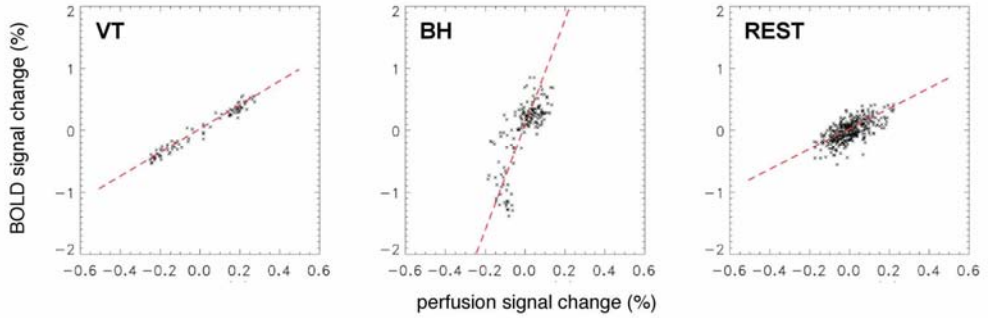

Figure 2: *Relationship between BOLD and perfusion signals in the visual cortex during each experimental stage.*

References

[1] Biswal BB, NMRBiomed 10:165, [2] Hoge, PNAS, 96:9403 [3] van Gelderen P, MRM 54:569