Physiological Origin of Low Frequency Drift in BOLD FMRI

L. Yan[1], Y. Zhuo[1], Y. Ye[1], S. Xie[2], J. An[3], G. Aguirre[4], and J. Wang[5]

[1]State Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, CAS, Beijing, China, People's Republic of, [2]Department of Biostatistics & Epidemiology, University of Pennsylvania, Philadelphia, PA, United States, [3]Siemens Mindit Magnetic Resonance Ltd., Shenzhen, China, People's Republic of, [4]Neurology, University of Pennsylvania, Philadelphia, PA, United States, [5]Radiology, University of Pennsylvania, Philadelphia, PA, United States

Introduction

Low frequency fluctuation or drift is commonly observed in functional MRI data acquired using BOLD contrast, which is an important factor affecting the reliability of BOLD fMRI and suitable experimental design. Earlier studies showed drifts may be attributed to scanner instabilities which can be observed with inert phantoms as well as human subjects [1]. Other evidence suggests low frequency fluctuations or baseline drift effects may reflect spontaneous neuron events arising from fluctuations in metabolic-linked brain physiology [2]. Such metabolic-linked noise can be modeled by its unique dependence on echo-time, image intensity [3]. More recently, there has been other evidence suggesting that respiratory and cardiac pulsation effects contribute to the enhanced low frequency noise in BOLD fMRI through aliasing due to the low sample rate or variations in cardiac and respiratory rate [4,5]. Due to the inconsistencies in the existing understanding of drift effects, the purpose of the present study was to investigate which of the above 3 sources was the main origin of slow drifts in BOLD fMRI (<0.01Hz) by systematically comparing drift effects on human brain and that of an agarose phantom.

Methods

All experiments were performed on a Siemens 3T Trio system. 15 healthy subjects (age 26.5±7.0 yrs, 10 males) participated in this study after they provided written informed consent. The fMRI study consisted of three main experiments: (1) resting state with varying TE: To investigate the TE dependency, a single-shot dual-echo gradient-echo EPI with interleaved TE was developed to acquired 4 different TE data sets for every 2 consecutive TRs (TE_1=20ms and TE_2=50ms for one TR, TE_3=35ms and TE_4=65ms for the following TR). Seven subjects (age 23.4±1.7 yrs, 4 males) were scanned in this experiment using the product 12 channel head coil. Ten oblique slices with 5mm thickness and 1mm gap were scanned parallel to the anterior-posterior commissure (AC-PC). Other parameters included: FOV=220mm; matrix=64×64; bandwidth=2442Hz/pixel; TR=1s; flip angle=65°; the scan time was 8min. (2) Task activation experiment with varying TE: The above 7 subjects also underwent an 8 min 30s off/on flashing checkerboard visual stimulation following the resting scans above during the same MRI session, to investigate the relationship between task induced signal change and the drift effect at baseline. The identical dual-echo EPI sequence was used. (3) Resting state with varying flip angle: To investigate the relationship between drift and image intensity, we modulated MR image intensity by systematically varying the flip angle. Eight subjects (age 29.2±8.7 yrs, 6 males) were scanned using a standard single-shot EPI with four different flip angles (30/45/60/75°). Each scan with a fixed flip angle took 4 min, and a single TE of 35ms was applied for all 4 scans. Imaging parameters were the same as above except TR=2s. The experiment 1&3 were repeated on a 2% agarose gel phantom (T1 = 1159±30ms, T2 = 80.3±0.5ms).

EPI data were corrected for motion using SPM2. The respiratory and cardiac pulsations were recorded in real time during the human experiments, which were removed by retrospective correction (RETROICOR)[6]. In each brain pixel, the magnitude of low frequency drift was determined by

$$M_{abs} = \frac{2}{\sqrt{2}N}\sqrt{\sum_{k=1}^{K}|X(k)|^2}$$

where X(k) is the DFT of the fMRI time series with N acquisitions, K is the number of the frequency components in the low frequency band 0~0.01Hz (excluding the term at zero frequency). Here M_{abs} is equivalent to the standard deviation (SD) of the low frequency drifts, which has been verified empirically. To account for the effect of variations in raw image intensity, relative drift magnitude, M_{rel}, was calculated by scaling M_{abs} as reference to the mean intensity of the corresponding raw EPI time series (expressed as percentage). Statistical analyses were performed using SPSS software.

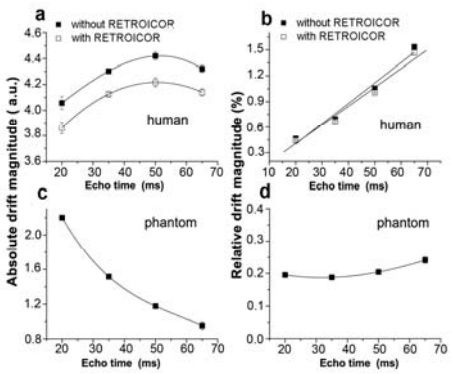

Fig. 1 Mean absolute (a&c) and relative (b&d) of low frequency drift as a function of TE in human brain and agarose phantom. Data before and after RETROICOR of cardiac and respiratory effects are shown in human.

Results and discussion

Fig. 1 shows mean M_{abs} and M_{rel} as a function of TE in the whole brain of 7 healthy subjects and the agarose gel phantom. Both human and phantom data demonstrated significant variations of both M_{abs} and M_{rel} with TE ($p<0.001$). In humans (Fig. 1a&b), with or without correction of respiration and cardiac effects, M_{abs} reached the maximum when TE approximated the T2* of the brain (T2* = 51.8 ± 3.1ms), and M_{rel} showed linear increase with TE; In the agarose phantom (T2* = 56.8±1.2ms) M_{abs} decreased with TE, and the change in M_{rel} across TE was much smaller than that of the human brain (Fig. 1c&d). The observed TE dependence of drift in human brain is consistent with the characteristic TE dependence of the BOLD contrast and physiological noise in BOLD fMRI [3]. Brain segmentation analyses suggested such TE dependence was mainly observed in gray matter in our study. From Fig. 1a&b, the contribution of respiration and cardiac fluctuations to low frequency drift accounted for approximately 4.4% of M_{abs} in whole brain, which was not significant affected by TE ($p=0.57$). We further found that, there was a strong positive correlation between drift magnitudes at baseline and BOLD signal changes during task activation across subjects as well as across pixels within the visual cortex. Fig. 2 shows scatter plot of mean M_{rel} at baseline vs. the mean fractional BOLD signal change during activation in visual cortex ROI at 4 different TEs in the 7 subjects ($r=0.79$, $p<0.01$). Fig. 3 displays the scatter plot of baseline drift (M_{rel}) vs. signal change across activated pixels from a representative subject ($r=0.80$, $p<0.01$). Both correlations were highly significant. In addition, M_{abs} in human subjects was found to increase with flip angle ($p<0.01$), which can be translated into a positive dependence on the image intensity. Correspondingly, M_{rel} was largely insensitive to variations in flip angle ($p=.09$) after the contribution of raw image intensity was removed. Such relationship was not observed in the agarose phantom.

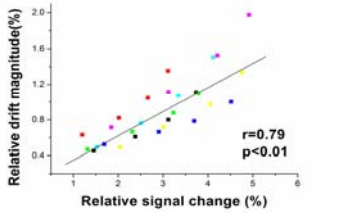

Fig.2 Scatter plot of mean relative signal change during activation and drift at baseline in visual ROI, each color represents one subject.

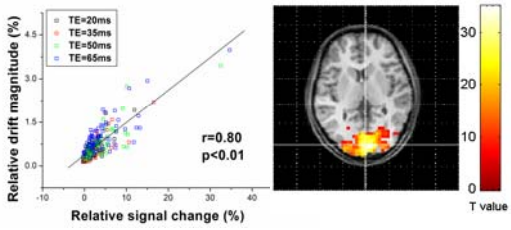

Fig.3 Scatter plot of relative BOLD signal change during activation vs. relative drift at baseline from a subject across activated pixels in visual ROI

Conclusions

The differences in the dependence of low frequency drifts on TE and image intensity between human and phantom, the correlation between task induced BOLD signal changes and slow drifts at baseline in human brain provide converging evidence supporting the primarily physiological origin of low frequency drifts in BOLD fMRI. We further demonstrate that respiratory and cardiac pulsations are not a main source of low frequency drifts. Therefore, spontaneous fluctuation in metabolic linked brain physiology should be the main source of drift effects in BOLD fMRI.

References

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