A General Contrast-to-Noise Ratio Model of BOLD Signal

G. Wu[1], S-J. Li[1]

[1]Department of Biophysics, Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Introduction: Contrast-to-noise ratio (CNR) is a very important measurement of an fMRI time course to map the activation areas evoked by a specific task. CNR models of BOLD signal have been investigated, and controversial conclusions have been observed regarding CNR dependence of echo time (TE) in previous studies (1, 2). Given the BOLD contrast by a specific stimulation, Menon *et al's* CNR model (1) predicts that CNR dependence of TE is the same as the BOLD contrast, which is maximized when TE = T_2^* and tends to be zero when TE = 0 and TE $\rightarrow \infty$, because the noise is considered only from the thermal noise of the scanner and is independent of TE. Hyde *et al*. (14) included low-frequency fluctuations as one of the noise sources in BOLD signal, and found that CNR is independent of TE when the BOLD-originated physiological noise dominates other noise. In this study we present a new BOLD CNR model to unify and extend the existing models.

Theory: The noise of BOLD signal is composed of three components: thermal white noise, fluctuations of apparent spin density and fluctuations of transverse relaxation rate (3). Taking into account the three noise components and the correlation between fluctuations of S_0 and R_2^*, we have proposed a noise model of BOLD signal as Eq. [1] (3), where σ_n is the overall noise level of resting BOLD time course, σ_{S_0}/S_0 is the normalized standard deviation of S_0 fluctuation, $\sigma_{R_2^*}$ is the standard deviation of R_2^* fluctuation, σ_0 is the standard deviation of white noise, $\rho_{S_0R_2^*}$ is the cross correlation coefficient between the fluctuations of S_0 and R_2^*, $S = S_0 \cdot \exp\{-TE \cdot R_2^*\}$ is the mean intensity of resting BOLD time course, and S_0 and R_2^* are mean values of apparent spin density and transverse relaxation rate, respectively. The BOLD contrast induced by stimulation can be given by $C_{BOLD} = S \cdot TE \cdot (-\Delta R_2^*)$, where ΔR_2^* is the change of R_2^*. The CNR model we introduced is shown in Eq. [2]. The CNR dependence of TE is complicated according to Eq. [2], and we can separate each noise component to study the dependence as shown in Eqs. [3]. The TE dependence of CNR on the overall noise and on each noise component was simulated in this study. The TE dependence of signal-to-noise ratio (SNR), which is the ratio of the mean intensity S of resting time course to noise, was simulated also.

$$\sigma_n^2 = (\sigma_{S_0}/S_0)^2 \cdot S^2 - 2TE \cdot \rho_{S_0R_2^*} \cdot (\sigma_{S_0}/S_0) \cdot \sigma_{R_2^*} \cdot S^2 + TE^2 \cdot \sigma_{R2*}^2 \cdot S^2 + \sigma_0^2 \quad [1]$$

$$CNR = \frac{TE \cdot (-\Delta R_2^*)}{\sqrt{(\sigma_{S_0}/S_0)^2 - 2TE \cdot \rho_{S_0R_2^*} \cdot (\sigma_{S_0}/S_0) \cdot \sigma_{R_2^*} + TE^2 \cdot \sigma_{R_2^*}^2 + (\sigma_0/S)^2}} \quad [2]$$

$$CNR|_{S_0} = \frac{TE \cdot (-\Delta R_2^*)}{(\sigma_{S_0}/S_0)}\ ;\quad CNR|_{R_2^*} = \frac{(-\Delta R_2^*)}{\sigma_{R_2^*}}\ ;\quad CNR|_{white} = \frac{\exp(-TE \cdot R_2^*) \cdot TE \cdot (-\Delta R_2^*)}{\sigma_0/S_0} \quad [3]$$

Materials and Methods: Six subjects were recruited and informed consent was obtained. Experiments were conducted on a Bruker 3T Biospec 30/60 scanner using a local gradient coil and an end-capped birdcage RF coil. A single-shot, gradient echo EPI sequence with interleaved variable TEs was used with TR = 500 ms, FOV = 20 cm, slice thickness = 3 mm and a matrix of 64 × 64. A bilateral self-paced finger-tapping paradigm was used and two axial slices of the motor cortex with four inter-leaved TEs of 30, 50, 70 and 90 ms were acquired. The experimental paradigm was 180 s resting followed by two epochs of 20 s ON/30 s OFF and a total of 560 images were acquired in 4 min 40 second period. The interleaved fMRI dataset was separated according to their TEs, resulting in four new datasets. For each TE, the new dataset had 140 images with effective TR = 2000 ms. The first five images of each new dataset were discarded to account for spin saturation effects, and the remaining 135 images were divided two segments: 1) resting data from image 1 to 70, and 2) functional data from image 71 to 135. For each TE, the activation map was determined with a threshold of 0.32 ($p < 0.01$) in the voxel-wise cross correlation coefficient between the functional time course and the reference waveform. All the four activation maps were combined into one map with union operation and the union of set was referred to as the finger-tapping activated areas. The BOLD contrast was calculated from the signal difference between ON (from 6 s to 20 s after onset of stimulation) and OFF period, and the overall noise level was calculated from the temporal fluctuation of the resting time course. In order to simulate the CNR and SNR dependence of TE, besides the empirical results of $\sigma_{S_0}/S_0 =$ 1.86 %, $\sigma_{R_2^*}$ = 0.63 s^{-1} and $\rho_{S_0R_2^*}$ = 0.10 from ref. 3, we estimated the values of σ_0/S_0 and R_2^* from the resting data and ΔR_2^* from the functional data in the activation areas from the six subjects. They (± SD) are 0.91 ± 0.07 %, 20.18 ± 1.24 s^{-1} and -0.92 ± 0.08 s^{-1}, respectively. Note that the estimated $T_2^* = 1/R_2^*$ = 49.6 ms in brain motor cortex at 3T is consistent with the previous studies (4, 5).

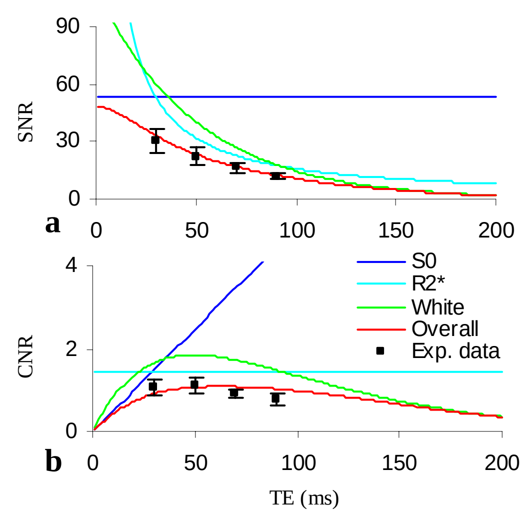

Fig. 1. Simulation of TE dependence of SNR (a) and CNR (b), and their experimental data

Results and Discussion: Fig. 1 shows the simulation results of TE dependence of SNR (a) and CNR (b), and their experimental data from the finger-tapping activation areas. The experimental data of both SNR and CNR is very close to the simulated overall values. Each component of noise behaves differently with TEs for SNR and CNR. With TE increase, S_0 fluctuation-related SNR keeps constant; R_2^* fluctuation-related SNR decreases as a hyperbolic decay, and white noise-related SNR decreases as an exponential decay. Therefore, the overall SNR decreases with TE increase. As predicted by Eqs. [3], with TE increase, S_0 fluctuation-related CNR linearly increases with a slope rate $-\Delta R_2^* / (\sigma_{S_0}/S_0)$ = 49.46 s^{-1}, the ratio of simulation-induced R_2^* change to S_0 fluctuation level; R_2^* fluctuation-related CNR keeps constant as $-\Delta R_2^* / \sigma_{R_2^*}$ = 1.46, the ratio of simulation-induced R_2^* change to R_2^* fluctuation level; and white noise-related CNR varies in the same pattern of BOLD contrast, which tends to be zero when TE = 0 and TE $\rightarrow \infty$, and reaches a maximum when TE = 1/ R_2^* = 49.6 ms. The TE independence of R_2^* fluctuation-related CNR is the same as that of Hyde *et al*'s model (2) although the intrinsic mechanisms between them are different, and the TE dependence of white noise-related CNR matches Menon *et al*'s model (1). With TE increase, the overall CNR increases before TE ≈ 50 ms, reaches a plateau between TE ≈ 50 ms and 70ms, decreases slowly after TE ≈ 70 ms, and tends to zero when TE $\rightarrow \infty$. Note that the point at which the overall CNR reaches its maximum is around TE = 60 ms, larger than R_2^* = 49.6 ms, which is the maximum TE point that is predicted by Menon *et al*'s model (1). In conclusion, a unified and extended CNR model of BOLD signal was proposed, which shows different behavior for the noise components of thermal white noise, S_0 fluctuations and R_2^* fluctuations, and the proposed unified model is much closer in agreement with experimental data than that of other models.

References: 1. Menon RS, *et al*., *MRM*, 30:380-386, 1993; 2. Hyde JS, *et al*., *MRM*, 46:114-125, 2001; 3. Wu G, and Li SJ, *Proc. ISMRM*, p1788, 2002; 4. Wansapura JP, *et al*., *JMRI*, 9:531-538, 1999; 5. Kruger G, *et al*., *MRM*, 45:595-604, 2001.

Acknowledgements: This work was supported by National Institutes of Health grants AG20279, EB01820, and EB02014.