Is T2* always the optimum Echo Time in BOLD fMRI? Challenging a common concept with a new Contrast to Noise Ratio BOLD model

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Introduction

It is generally accepted that BOLD response in Gradient Echo fMRI peaks at its maximum when the echo time (TE) matches T_2*, with optimum activation at TE=T_2^* [1,2]. Accordingly, matching TE with T_2* in GE BOLD fMRI time series should improve activation detection. This is particularly important in areas where T_2* values become shorter either because of susceptibility induced local B_0 gradients, or within structures with high deposition of ferromagnetic particles such as the globus pallidus. Traditional BOLD models, however, have been challenged by some studies where similar fMRI activation detection were obtained at different echo times [3-5]. Furthermore, it has been demonstrated that a large fraction of noise in fMRI series has physiological origins and varies with TE and signal intensity [6]. In this paper, we propose a new model for BOLD functional Contrast to Noise Ratio (*CNR*) which explicitly accounts for the heterogeneous sources of noise. This model predicts that BOLD CNR varies very slowly as a function of TE. It also predicts that in some cases the optimal TE can actually be longer than T2*. Those findings may significantly impact existing strategies aiming at optimizing BOLD fMRI acquisition parameters.

Theory

In initial BOLD models [1,2] only a constant thermal noise σ independent to MR signal magnitude S was considered, thus functional CNR was assumed to be proportional to activation induced signal changes ΔS with $CNR = \Delta S \div \sigma = \mathrm{TE} \cdot \Delta R_2^* \cdot S$ and $S=S_0 \cdot \exp(-\mathrm{TE} \cdot R_2^*)$ where S_0 is S a TE=0 and ΔR_2* is the activation induced change in R_2*. In this approximation (with $\mathrm{TE} \cdot \Delta R_2^* << 1$), CNR is max for TE=$T_2^*$, as shown in Fig. 1. Krueger et al. [6] have shown that the total noise σ_{tot} in fMRI BOLD series actually consists of multiple components: background noise σ_0 (thermal and system noise) independent to S and TE, and physiological noise σ_P^2 which varies with TE and S and can be split into σ_B^2 (BOLD) and σ_{NB}^2 (non BOLD) sub-components: $\sigma_{tot} = \sqrt{\sigma_0^2 + \sigma_B^2 + \sigma_{NB}^2}$ with $\sigma_P^2 = \sigma_B^2 + \sigma_{NB}^2$. Those terms can be written as: $\sigma_B = \sigma_{R_2^*} \cdot TE \cdot S$ (where σ_{R2*} represents R_2* baseline fluctuation) and $\sigma_{NB} = c_2 \cdot S$ (where C_2 is a scalar) [6]. Thus, $CNR = \Delta S \div \sqrt{\sigma_0^2 + \sigma_{R_2^*}^2 TE^2 S^2 + c_2^2 S^2}$.

Here we introduce κ as the ratio, normalized with regards to TE, between the BOLD and non BOLD components of the physiological noise $\kappa = \left(\sigma_B \div \sigma_{NB}\right) \div TE = \sigma_{R_2^*} \div C_2$. After normalizing by S_0, *CNR* can be written as: $CNR = \mathrm{TE} \cdot \Delta R_2^* \cdot e^{-\mathrm{TE} \cdot R_2^*} \div \sqrt{\sigma_0^2 \div S_0^2 + c_2^2 e^{-2\mathrm{TE} \cdot R_2^*} (\kappa^2 \mathrm{TE}^2 + 1)}$.

Each noise component, shown in Fig. 2, has a different impact on activation detection. The BOLD component considerably smoothes the curve of *CNR* against TE. The non BOLD component tends to shift the same curve to the right, so that for low values of κ the optimal TE becomes longer than T_2*.

Comparison with Experimental Reports

Our modified BOLD *CNR* model provides a rationale for apparently contradicting results from previous reports that we summarize hereby. Hyde et al. found cortical activation undistinguishable between 20ms and 40ms TE's in a motor taping task at 3T [3]. They proposed a modified BOLD model but the latter did not include analytical noise formalism. However, such noise formalism has been introduced by Krueger et al. [6]. Gorno-Tempini et al. acquired fMRI series with two TE's (27ms and 40ms) to recover BOLD activation in the temporal lobes[4]. Surprisingly, the reduced loss of signal at TE=27ms did not improve activation detection in susceptibility affected areas, whereas activations in non affected areas were still robustly detected at TE=27ms compared with TE=40ms. Recently, Lehericy et al. in an attempt to optimize fMRI in basal ganglia structures with short T2*, performed fMRI series with TE=28ms and 42ms, matching locally measured T_2* of the Globus Pallidus and the Putamen respectively[5]. Although $\Delta S/S$ was strictly proportional to TE, there was no difference in activation detection between the two TE's. Moreover, the overall activated volume tended to always be larger at TE=42ms. In Fig. 3 we have estimated an average value of κ from Table 1 in [6], and we utilized noise measurements obtained in the study by Lehericy et al.[5] The resulting *CNR* simulated curves show: a) very slow *CNR* variations as a function of TE and b) a shift to the right with maximum detection for TE=31ms and 47ms assuming a local T_2* of, respectively, 28ms and 42ms. Thus, our BOLD *CNR* model effectively predicts higher activation detection for TE's longer than T_2*'s and is consistent with the aforementioned reports.

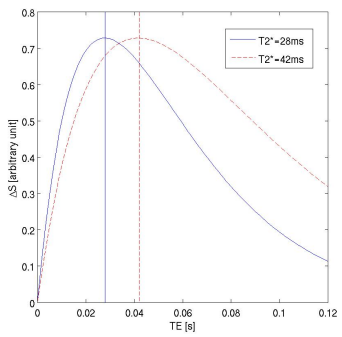

Fig 1. BOLD signal change ΔS as a function of TE for T2*=28ms (solid blue line) and 42ms (dashed red line). In intial BOLD models CNR was assumed directly proportional to ΔS.

In both **Figs. 1, 2 and 3**, S_0=100 and ΔR_2* is determined in order to obtain $\Delta S/S$=2% at TE=T2*. In **Figs. 1 and 3** the two vertical bars indicate TE=28ms and TE=42ms

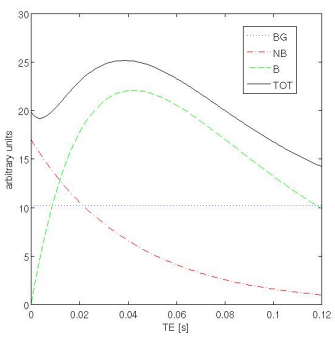

Fig 2. BOLD noise components plotted against TE: σ_0 (horizontal dotted line), σ_{NB} (dash-dot red line), σ_B (dashed green line) and resulting total noise σ_{TOT}(black solid line) based on σ_P measured in the Putamen (local T2*=42ms) and σ_0 measured in the background in ref [5], merged with κ parameter derived from Krueger's study [6].

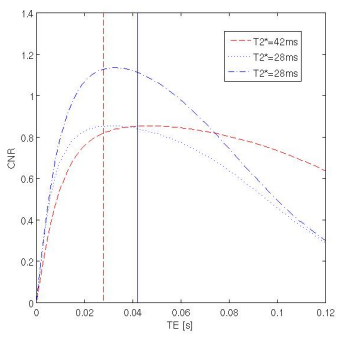

Fig 2. Dashed red line: CNR simulation with our BOLD model based on σ_P measured in the Putamen (T_2^*=42ms) from ref[5] and κ derived from[6]. Note the smoothness of the curve and its max at TE=47ms. Two additional curves are shown for T2*=28ms (Globus Pallidus) with C_2 derived either from the putamen (dotted line) or from σR_2*≈TE, (dotted/dashed) because σ_P measures were not available in Globus Pallidus.

Discussion

We propose a modified BOLD *CNR* model accounting for heterogeneous sources of noise. This model predicts that activation detection varies only slowly with TE, mostly due to BOLD physiological noise, and that optimal TE can be longer than T_2*, due to non BOLD physiological noise. Those findings may have critical impact on BOLD acquisition parameters by relaxing some limiting constraints, especially when T_2* becomes shorter (e.g. higher magnetic field) or when TE increases (e.g. higher spatial resolution).

References: [1] R.S. Menon et al., MRM,30,380-6(1992) [2] S. Posse et al. MRM,42,87-9 (1999) [3] J. Hyde et al., MRM,46,114-25(2001) [4] K.L. Gorno-Tempini et al., Neuroimage,15,136-42(2002) [5] S. Lehericy et al. , ISMRM,2825 (2006) [6] G. Krueger et al.,46,631-7(2001) **Acknowledgment**: R01 MH070800, P41 RR008079, MIND Institute, P30 NS057091