Modeling the Effect of Baseline Arteriolar Compliance on BOLD Dynamics

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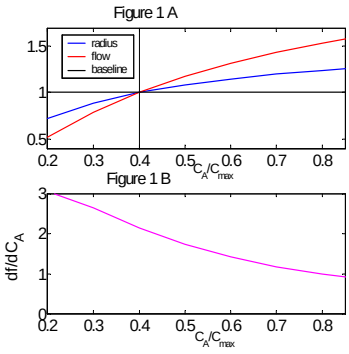
Introduction

The blood oxygenation dependent level (BOLD) signal is a complex function of cerebral blood flow (CBF), cerebral blood volume, and the cerebral rate of oxygen metabolism. Previous studies have highlighted the variable nature of the BOLD hemodynamic response function (HRF) between different subjects [1]. In our studies of the HRF, we observed pronounced variability within the same subject between scanning sessions. Anecdotal evidence suggested that caffeine ingestion was correlated with the observed variability, most notably an increase in the BOLD peak amplitude and distinct oscillatory behavior in the post-stimulus response [2]. The oscillatory behavior is consistent with a recently proposed autoregulatory model for CBF [3]. Coupling the CBF model with the Balloon model [4] provides reasonable fits to the observed BOLD responses. However, significant changes in the estimated autoregulatory time constants are required to account for the increase in oscillatory behavior. Because caffeine acts as a vasoconstrictor, we hypothesized that the observed behavior might be better explained by a decrease in the initial arteriolar compliance. Here we propose a modified CBF-Balloon model in which the dynamics of the arteriolar compliance are explicitly modeled. Using this model we show that a decrease in the baseline compliance can account for the observed BOLD dynamics without a significant change in the autoregulatory time constants.

Theory\Background

Previous investigators have proposed a coupling of synaptic activity and CBF through a simple linear relationship between the change in CBF (f) and a flow inducing signal s; that is assumed to be composed of many neurogenic and diffusive signal subcomponents and is generated by neuronal activity u(t) [3]. This model is represented by the following equations: $ds/dt = \varepsilon u(t) - s/\tau_s - (f-1)/\tau_f$; $df/dt = s$; where ε, τ_s, and τ_f represent the neuronal efficacy, time-constant for signal elimination and/or decay, and the time-constant for autoregulation based on flow, respectively.



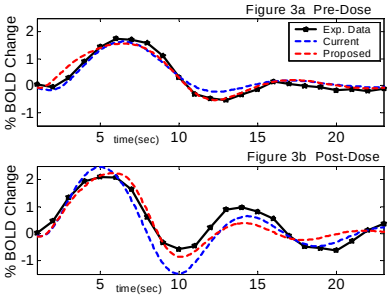
Biomechanical studies have revealed nonlinear length-tension relationships in the arterioles[6]. Assuming the overall hoop tension (T) is the sum of the tension in the connective tissues (P) and the tension in the smooth muscle (S), an equation relating S to normalized diameter is presented in [6]. A simplified model, for purposes of parametric estimation, can be constructed by assuming the overall vessel compliance is dependent on the elastic properties of the passive connective tissue (C_p) and the active smooth muscle (C_A) elements acting in parallel. This model captures the general dynamic nature of the full model reasonably well. The normalized radius as a function of normalized smooth muscle compliance is depicted in Figure 1A for the simplified model. At low values of C_A, corresponding to vasoconstriction, the rate of change of flow with respect to a change in the smooth muscle compliance (df/dC_A) is increased, as depicted in Figure 1B. It is assumed that the signal s affects the smooth muscle compliance by the relationship $dC_A/dt = \beta s$, where β represents the signal efficacy. Under the assumption of bulk flow, represented in normalized fashion as $f = r^2$, the flow can be represented in terms of C_A, C_P, and the baseline value of the smooth muscle compliance normalized by the maximum smooth muscle compliance (C_A^0) by $f = (C_A (C_A^0 + C_P))^2 / (C_A^0 (C_A + C_P))^2$.

Methods

Imaging data were acquired on a Varian 4T whole-body system utilizing a single-surface coil placed proximal to the occipital lobe. A stimulus event was defined as a one second presentation of a 8Hz, full-field, maximal contrast, flickering checkerboard. Two experimental designs were utilized per subject and they consisted of a block design (4 periods of 20/40 on/off) and a periodic design (8 events at 31 second intervals). Six 4mm oblique slices about the calcarine sulcus were imaged. Scanning sessions consisted of 3 repetitions of block and periodic designs, performed pre and post ingestion of caffeine (approximately 200mg). Imaging parameters were FOV 24cm, 64x64 matrix, TE=27ms, flip $\theta=70^0$, and a TR=1 s. An additional block design (PICORE TR=2s, TI = 1100ms) was run and used to select activated voxels based on correlation of the perfusion time series (control-tag) with a reference function and correlation coefficient threshold 0.4. Average BOLD time series were formed by motion registering, detrending and averaging individual time-series over selected voxels and across runs. Model fitting consisted of maximizing the correlation between the model response and the average subject response. Balloon model parameters (k1,k2,k3) at 4T were calculated to be 8.08, 0.135, and -0.69, respectively [7]. In addition, transit time τ_0, Grubb's law constant α, and oxygen extraction fraction E_0 were estimated in the model fitting process.

Results\Discussion

Figure 3a and 3b show the model fits of the current and proposed model to averaged periodic design data pre/post dose, respectively. There is a 20% increase in the maximum BOLD response along with pronounced oscillations in the post-stimulus response. Table 1 compares the model parameters of the fit of the proposed model to that of the current model. Changes in E_0 are attributed to the rise in deoxyhemoglobin concentration with vaso-constriction due to caffeine[8]. Although, the current CBF-Balloon model fits reasonably well it requires significant changes of +32% and -27% in τ_S and τ_f, respectively. Currently, there is no compelling argument to explain this level of change in time constants following caffeine ingestion. The modified CBF-Balloon model can explain the HRF variability primarily in terms of decreased C_A, assuming constant Cp. The post-dose decrease in flow (~20%) computed from fitted C_A values is consistent with the CBF decrease reported in [5]. Fitting of block designs also resulted in similar findings. These findings indicate that arteriolar compliance has a significant impact on BOLD dynamics and needs to be considered when modeling or interpreting the BOLD response.



	Current Model	Current Model Caffeine	Modified Model	Modified Model Caffeine
τ_S	2.5	3.3	2.5	2.5
τ_f	2.6	1.9	2.6	2.6
ε	0.7	0.75	0.72	0.72
E_0	0.4	0.45	0.42	0.47
τ_0	2.75	2.5	2.35	2.35
α	0.33	0.30	0.33	0.33
C_A	-	-	0.48	0.37
C_P	-	-	0.18	0.18
β	-	-	1	1
Cor	.98	.84	.94	.92

References:

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