Potential of dynamic models to investigate neurovascular coupling using ASL fMRI

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Clément Huneau[1,2*], Hugues Chabriat[2,3], Habib Benali[2]

[1] Laboratoire d'Imagerie Biomédicale, Sorbonne Universités, UPMC Paris 06, CNRS U7371, Inserm U1146, F-75013, Paris, France.
[2] Inserm U1161, F-75010, Paris, France.
[3] Service de Neurologie, Hôpital Lariboisière and DHU NeuroVasc, Assistance Publique des Hôpitaux de Paris, F-75010, Paris, France.
*Corresponding author, clement.huneau@inserm.fr

Abstract – Arterial spin labeling (ASL) is an fMRI technique that allows specific measurement of the cerebral blood flow (CBF), without any tracer injection. Combined with dynamic models, ASL could permit to investigate neurovascular coupling (NVC), possibly implied in several brain diseases. We have used ASL data to test three models of NVC. All models were able to fit the CBF change. However only one model could be identified regarding the data.

Index terms - Magnetic Resonance Imaging, Modeling.

I. INTRODUCTION

The mechanism that links a transient neural activity to the corresponding increase of cerebral blood flow (CBF), termed neurovascular coupling (NVC), is possibly impaired at early stage in small vessel diseases or neurodegenerative diseases [1]. Arterial spin labeling (ASL) is an fMRI technique that can specifically measure the cerebral blood flow, in real time (2-5s resolution) and without any tracer injection. In this study, we acquired CBF data acquired using ASL sequence to test three dynamic models of NVC, initially developed for other functional neuroimaging techniques [2–4].

II. THEORY

II.1. Friston flow (FF) model

Friston and coworkers were the first to propose an explicit model of NVC applied to fMRI [2]. This dynamic model calculates the flow variation f corresponding to the transient neural activity N, using three parameters (ε, k_s, g_f) in a second order differential equation.

$$\frac{d^2 f}{dt^2} = -\varepsilon N(t) - k_s \frac{df}{dt} - \mathrm{g_f}(f-1)$$

II.2. Arteriolar compliance (AC) model

This model is an extension of the FF model, but includes a nonlinear component specifically modeling the muscle compliance of arterioles as a state variable [3].

$$\frac{d^2 c_M}{dt^2} = -\varepsilon N(t) - k_s \frac{dc_M}{dt} - \mathrm{g_f}(r(\mathrm{c_M})^\gamma - 1)$$
$$r(c_M) = r_{max}(1 - a_1 e^{-a_2 c_M})$$
$$f(t) = r(c_M)^\gamma$$

The parameters in the first equation are the same than those in the FF model. This AC model also consider the maximum dilation r_{max}, the laminar flow exponent γ and two fix parameter a_1 and a_2.

II.3. Dilation-constriction (D-C) model

This model has been proposed to consider the emerging concept of concurrent dilation (y_d) and constriction (y_c) signaling from astrocytes to contractile cells [4].

$$\frac{d^3 y_d(t)}{dt^3} + a_1 \frac{d^2 y_d(t)}{dt^2} + b_1 \frac{dy_d(t)}{dt} + c_1 = K_1 c_1 N(t)$$
$$\frac{d^3 y_c(t)}{dt^3} + a_2 \frac{d^2 y_c(t)}{dt^2} + b_2 \frac{dy_c(t)}{dt} + c_2 = K_2 c_2 N(t)$$
$$f(t+\tau) = y_d(t) - y_c(t)$$

This D-C model includes eight dimensionless parameters $(K_1, a_1, b_1, c_1, K_2, a_2, b_2, c_2)$ and a time delay τ.

III. MATERIALS AND METHODS

Experimental data were acquired from three young (25-30 years old) healthy subjects at 3 Tesla using a VERIO (Siemens, Erlangen) whole body MRI system, equipped with a 12-channels head volume coil. To assess cerebral blood flow change, pseudo-Continuous Arterial Spin Labeling was used (TE=10ms, TR=2760ms, 4x4x7mm voxels).

We performed twenty blocks of 30s of visual stimulation (flickering checkerboard, 6 Hz) interlaced with 30s resting periods of fixation cross. Actually, the CBF signal has a bad signal to noise ratio and a different temporal dynamic compared to the BOLD signal. Hence, activated regions were assessed visually because the classical general linear model method was not efficient. Model fitting was performed using the Levenberg-Marquardt method implemented in Matlab (function lsqcurvefit).

IV. RESULTS

As expected activated region was found in the primary visual area (V1). All voxels in the activated region of all subjects were pooled and averaged to obtain the nominal CBF response for the considered region (Figure 1).

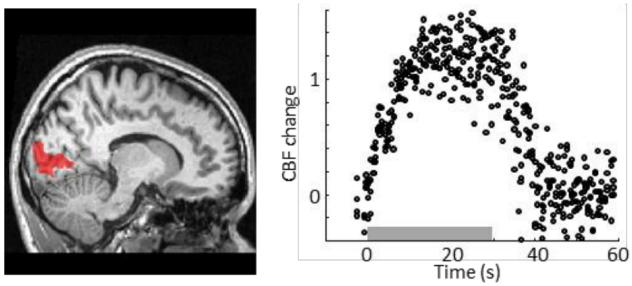

Figure 1: Activated region and cerebral blood flow (CBF) change. Scatter plot represents the mean flow in the whole activated region. Grey bar indicates the stimulation period.

As shown in Figure 2, all the three models were able to fit experimental data with approximatively the same quality (SSE, sum of squared error). Both the FF and AC models, based on a second order differential equation resulted in a very similar fitted curve. Conversely, we observed that the higher order D-C model over-fit the data.

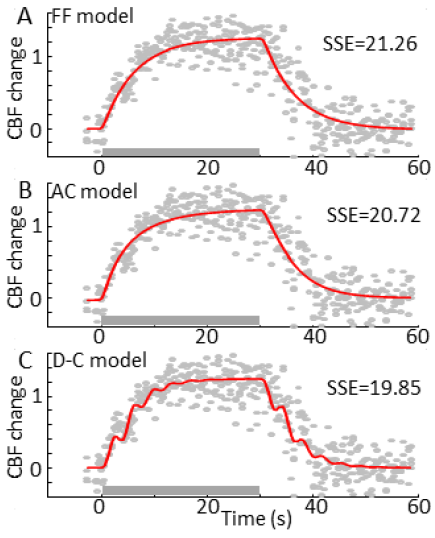

Figure 2: CBF change in the visual cortex fitted with three models of NVC. A, Friston flow (FF) model. B, Arteriolar compliance (AC) model. C, Dilation-constriction (D-C) model.

Estimated values and confidence interval are presented in Table 1. In particular, we observed that the AC and D-C models present a very large confidence interval. In this context these models are not identifiable in this context.

Parameter		Estimated value	Confidence interval
FF	ε	0,629	[0,595 ; 0,662]
	k_s	3,18	[3,17 ; 3,19]
	g_f	0,498	[0,463 ; 0,533]
AC	ε	0,576	[-0,00286 ; 1,16]
	k_s	3,83	[-0,525 ; 8,18]
	g_f	0,461	[-0,00456 ; 0,927]
	r_{max}	1,33	[1,3 ; 1,35]
D-C	K_1	2,66	[-0,24 ; 5,56]
	a_1	0,682	[0,17 ; 1,19]
	b_1	3,17	[2,7 ; 3,64]
	c_1	0,783	[0,496 ; 1,07]
	K_2	1,42	[-1,48 ; 4,32]
	a_2	1,5	[0,00312 ; 3]
	b_2	3,13	[1,32 ; 4,93]
	c_2	1,3	[0,0713 ; 2,54]

Table 1: Parameter values estimated to fit the visual cortex CBF response.

V. DISCUSSION – CONCLUSION

Here, we showed that the three models of NVC are able to reproduce the CBF response to block stimulation of the visual cortex. However, considering these kind data, only the FF model is identifiable. More complex stimulation with different paradigm and duration should be considered to identify the AC and D-C models.

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