Model of vascular reactivity to investigate the basis of Grubb's relationship between cerebral blood flow and volume

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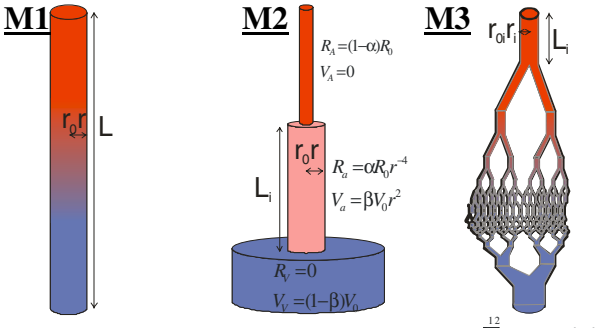
INTRODUCTION: Knowledge of cerebral blood flow and vascular volume are of major interest in mapping cerebral activity using modern functional imaging techniques[1-3]. We aim to better understand the governing relationship between cerebrovascular volume and flow (v(f); v=CBV/CBV$_0$ and f=CBF/CBF$_0$) with the help of three models of cerebrovascular reactivity.

METHODS:



$V = \pi L r_o^2 r^2 = V_0 r^2$

$R = \frac{\eta L}{8\pi r_o^4 r^4} = R_0 r^{-4}$

$F = P/R = F_0 r^4$

$V = (1-\beta+\beta r^2)V_0$

$R = (1-\alpha+\alpha r^{-4})R_0$

$F = F_0/(1-\alpha+\alpha r^{-4})$

$V = \sum_{i=2}^{12} N_i L_i \pi r_{oi}^2 r_i^2$

$R = \sum_{i=2}^{12} \frac{1}{N_i} \frac{\eta_i L_i}{8\pi r_{oi}^4 r_i^4}$

$F = P/R(r_2,\ldots,r_{12})$

Levels	Vessel	N	Length[mm]	D[µm]
2	ArteryL	2	150.	4000
3	ArteryM	25	45.	1300
4	ArteryS	300	13.5	450
5	ArterioleL	5500	4.	150
6	ArterioleS	140000	1.2	50
7	Capillary	135000000	0.65	8
8	Venules	500000	1.6	100
9	VenulesL	33000	4.8	280
10	VeinsS	2000	13.5	700
11	VeinsM	105	45.	1800
12	VeinsL	5.5	150.	4500

$$r_i(D_i, \Delta PaCO_2) = 1 + R(D_i)\cdot K(\Delta PaCO_2)\cdot \Delta PaCO_2$$

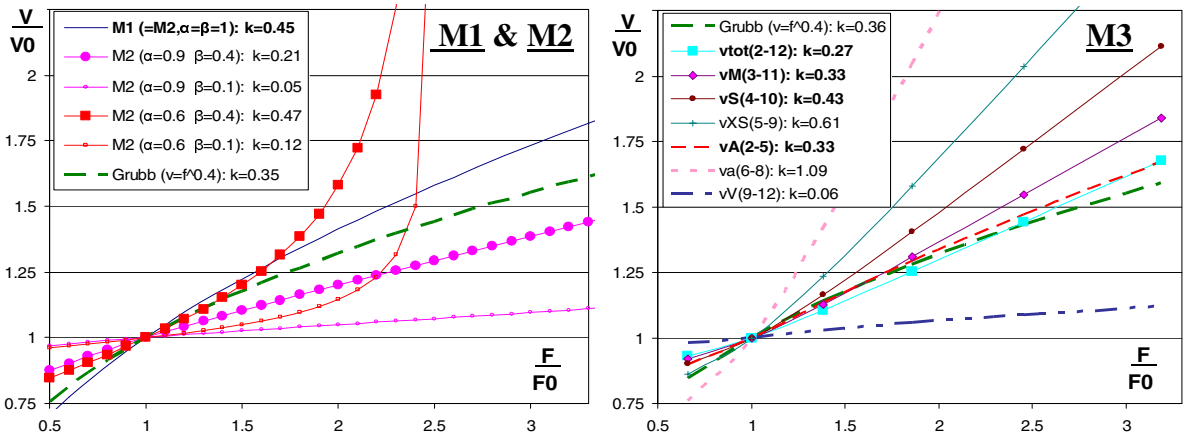
where : $R(D_i) = 0.01\cdot e^{3.57433-1.08934\cdot \ln(D_i)} + 0.00676765$

and : $K(\Delta PaCO_2) = 0.861515\, e^{0.385554\cdot \Delta PaCO_2/(\Delta PaCO_2+38)}$

$$\eta = \max(1,\ 3.76-10^{(0.500692)+(-0.00929)\cdot D+(3.14e-5)\cdot D^2+(-6.3e-8)\cdot D^3})\cdot \eta_{Macro}$$

The first two simple models (M1 and M2) are diagrammed above left, and show how volume (V), resistance (R), and flow (F) can be calculated, given a driving pressure (P), as a function of changes in radius r, such as due to effects of function or CO_2. A third model (M3, rightmost) is based on the distribution of diameters and lengths in a model of the vascular system in the dog[4]. Resting parameters of the scaled version (excluding levels 1,13 - aorta and vena cava) are given in the table. An expression for vascular reactivity $r_i(D_i,\Delta PaCO_2)$ in M3 was obtained by fitting data from 7 experimental studies[5-10]. M3 additionally accounts for the Fahraeus effect resulting in a lower viscosity η in the microcirculation. We simulate the distribution of the pressures, volumes and velocity as a function of reduced (f=0.5) to increased (f=3) flow. We assess the global v(f) relationship and its dependence on the model structure and inclusion of various vascular compartments in the model M3.

RESULTS:



DISCUSSION AND CONCLUSION: The results above show that the model choice changes the shape of the v(f) relationship from that of a simple power function used by Grubb (v=f$^{0.4}$), which itself was designed as a scaled version of M1 (v=f$^{0.5}$)[11, 12]. However, within the experimentally relevant range of changes (f=0.7 to 1.60) the relation closely approaches linear. The slope k depends strongly on the ratio of regulating to non-regulating vessels in the volume of interest indicated by combination of α, β (M2) or inclusion of specific vascular compartments (in brackets, M3). In M3, the microvascular compartments (va, vXS) have the steepest, and the less reactive venous compartments (vV) the flattest v(f) curve, in agreement with a recent PET study[15] showing highest coupling in white matter, which is predominantly devoid of large vessels. Such predicted systematic variability of v(f) coupling has a large potential impact on the interpretation of focal metabolic findings from high resolution MR imaging, where measurements of flow and volume may be weighted towards different cerebrovascular compartments[3, 13, 14].

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