Validating a power relationship between cerebral blood volume and cerebral blood flow

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Introduction: Cerebral blood volume (CBV) is related with cerebral blood flow (CBF); an increase in CBF accompanies an increase in CBV and vise versa. If CBV is quantitatively related to CBF, knowing this relationship may have significant implications for investigating the quantitative relationship between neuronal activity and blood oxygenation level-dependent (BOLD) fMRI response measurements. A recent MRI study reports a varied CBV-CBF relationship both spatially and with sex [1]. In a region of interest (ROI) with stimulus-induced activation in CBV and CBF at a significance level of the $P < 0.05$, a power function fit resulted in $CBV = 0.8\ CBF^{0.51}$ for female subjects and $CBV = 4.4\ CBF^{0.15}$ for male subjects, suggesting a sex-dependent CBV-CBF relationship. This study tests these power functions using the mean values of CBV and CBF at both rest and activation states.

Methods and Materials: Absolute CBV and CBF were quantified noninvasively at both rest and activation states for 5 female and 5 male subjects [1]. Nine region of interest (ROI) masks in the primary visual cortex covering a range of sizes were identified, and then mean CBV and CBF values were calculated within each ROI mask. This resulted in one data point for each subject at rest and activation states in each ROI. For each sex, group-mean CBV and CBF values at rest and during activation are shown in Table 1 (columns from 2nd to 5th). For each ROI, the CBV-CBF relationship was estimated by fitting to a power function ($CBV=a\cdot CBF^b$), and the corresponding mean a and b values for each sex are shown in Table 1 (columns from 6th to 7th) [1]. Using this power function with the mean a and b values, we computed CBV for each CBF at both rest and activation states for each ROI, and then compared these computed CBV values with their corresponding measured CBV values for each sex using paired t-test.

Table 1. Measured, estimated, and computed values for CBV, CBF, a, and b across all ROIs for Female and Male subjects. The numbers in the columns from 2nd to 5th are the measured mean values of CBV and CBF at rest and during activation from table 2 in Ref. [1]; the numbers in the columns from 6th to 7th are the mean values of a and b from table 4 in Ref. [1]; and finally the numbers in the last two columns are the computed CBV values at rest and during activation using the power function with the mean values of a and b. CBV values are in mL/100 mL and CBF values are in mL/min/100 mL, same as in Ref. [1]. act: activation.

	CBV		CBF		$CBV=a\cdot CBF^b$		$CBV(=a\cdot CBF^b)$	
ROI	rest	act	rest	act	a	b	rest	act
Female subjects								
1	8.1	11.6	90.1	143.9	0.6	0.57	7.8	10.2
2	7.5	10.6	90.3	134.2	**0.8**	**0.51**	8.0	9.7
3	7.1	9.8	88.8	126.5	1.0	0.47	8.2	9.7
4	6.8	9.1	88.3	118.6	1.3	0.40	7.8	8.8
5	6.8	9.3	87.9	120.0	1.3	0.40	7.8	8.8
6	6.6	8.8	90.6	118.4	1.5	0.35	7.3	8.0
7	6.3	8.3	89.8	114.7	2.0	0.29	7.4	7.9
8	6.0	7.7	88.0	109.6	2.2	0.25	6.7	7.1
9	5.6	7.0	86.9	103.9	2.9	0.17	6.2	6.4
Male subjects								
1	7.7	10.4	55.6	97.6	3.4	0.23	8.6	9.8
2	7.0	9.4	55.3	90.0	**4.4**	**0.15**	8.0	8.6
3	6.7	8.9	53.6	83.5	4.6	0.13	7.7	8.2
4	6.5	8.4	54.1	79.1	4.9	0.10	7.3	7.6
5	6.6	8.6	55.0	80.9	3.8	0.17	7.5	8.0
6	6.3	8.1	57.2	80.5	4.8	0.10	7.2	7.4
7	6.0	7.6	57.5	78.6	3.7	0.15	6.8	7.1
8	5.6	7.0	57.3	76.1	5.0	0.06	6.4	6.5
9	5.2	6.4	58.6	73.9	5.9	0.00	5.9	5.9

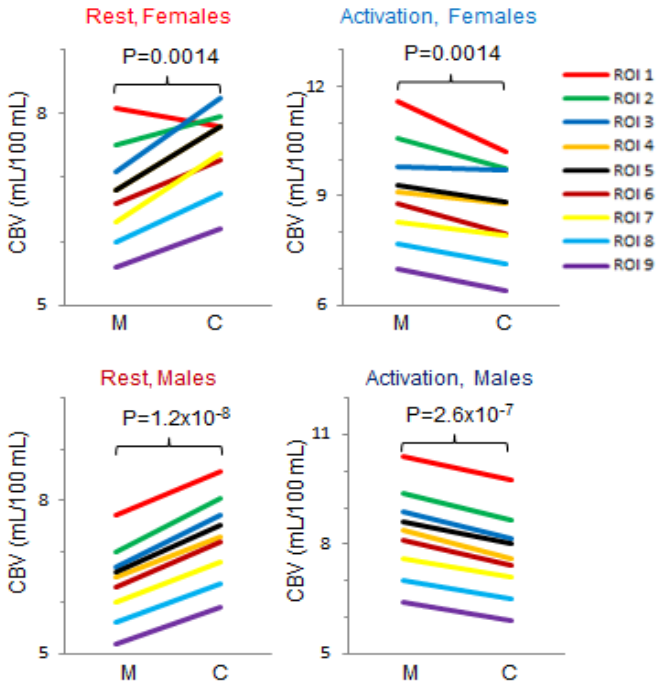

Figure 1. Comparisons of measured CBV versus computed CBV at both rest and activation states for Female and Male subjects. The P values represent the corresponding paired t-test results. M: measured CBV; C: computed CBV.

Results: The computed CBV values are provided in the last two columns in Table 1. The paired t-test of the computed CBV with the measured CBV revealed a significant difference for each state and sex (max P=0.0014, Fig. 1). The estimated power function ($CBV=a\cdot CBF^b$) produced CBV values systematically larger than that of the measured values for the rest state (the left two plots, Fig. 1), regardless of sex. This power function, however, yielded CBV values systematically smaller than that of the measured values for the activation state (the right two plots, Fig. 1), again regardless of sex.

Discussion: The CBV-CBF relationship was estimated by fitting to a power function in the study[1]. If the CBV-CBF relationship is best characterized by such a power function, then the best fitted power function should be expected to characterize the mean trend of the CBV-CBF relationship, and consequently the computed CBV values with the power function should be expected to be similar to their corresponding measured CBV values. But this expectation is not supported by the observed significant difference between the computed and measured CBV values for each state and sex. One possibility is that the group average of CBV and CBF values for each ROI somehow produced a systematic error which resulted in the observed significant difference. If this is the case, then we may expect this systematic error would produce a similar effect on both rest and activation states. This expectation, however, is not consistent with the observation that the power function systematically over-estimated the CBV values for the rest state but under-estimated them for the activation state, regardless of sex (Fig. 1). Another possibility is that the CBV-CBF relationship is not best characterized by a power function, as reflected in these significant differences. Further studies are needed to better understand these significant differences and the underlying causes.

References: 1. Ciris PA, Qiu M, and Constable RT. Noninvasive MRI measurement of the absolute cerebral blood volume – cerebral blood flow relationship during visual stimulation in healthy humans. Magn Reson Med 72: 864-75, 2014.