AGE AND GENDER RELATED ALTERATIONS IN BRAIN PERFUSION DYNAMICS

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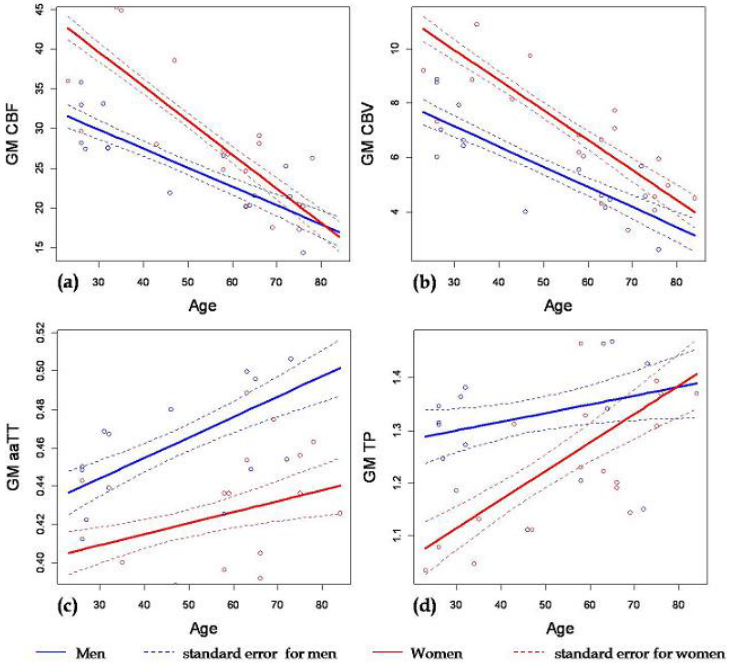
INTRODUCTION: For many years, multiple imaging studies have reported a decrease in cerebral blood flow (CBF) with advancing age primarily in regions including the frontal and parietal cortices[1]. In general, these CBF reductions have been interpreted as a consequence of reduced brain activity, such as reduced cerebral metabolic rates of glucose and oxygen, with advancing age. However, there is also compelling evidence for compromised cerebrovascular integrity with advancing age that could be a cause for the CBF reduction. Specifically, it has been recognized that small vessels, i.e. arterioles, undergo morphological alterations with advancing age, such as thickening and damage of vessel walls that result in diminished arterial compliance. From this perspective, a reduction in CBF (and metabolism) could be a secondary effect of reduced brain activity rather than a dependent factor. In this study, we investigate how perfusion dynamics varies with advancing age, and to determine the extent to which cerebrovascular components, especially the time it takes blood to propagate through small vessels before reaching the capillary bed, are altered as a function of aging. In addition, we explored the gender effects on perfusion dynamics.

Variables/ Regions	Intercept	Age	Sex	t_{age}	t_{sex}
Units	mL/100mL/min	mL/100mL/min/decade	mL/100mL/min men versus women		
CBF GM	47.67±2.95	-3.6±0.5	-5.62±1.86	7.18 ***	3.02 **
PCC	62.41±5.31	-4.9±0.9	-9.29±3.35	5.64 ***	2.78 **
PRE	41.69±4.44	-3.7±0.7	-5.78±2.80	5.11 ***	2.07 *
Units	mL/100mL	mL/100mL/decade	mL/100mL men versus women		
CBV GM	12.33±0.84	-0.9±0.1	-2.02±0.53	6.86 ***	3.81 ***
PCC	20.41±2.41	-1.9±0.4	-3.15±1.52	4.98 ***	2.08 *
PRE	12.90±1.58	-1.3±0.3	-2.25±1.00	5.01 ***	2.26 *
Units	seconds	seconds/decade	Seconds men versus women		
TP GM	1.05±0.66	0.04±0.01	0.10±0.04	3.49 **	2.52 *
PCC	1.03±0.12	0.06±0.02	0.16±0.08	3.30 **	2.10 *
PRE	0.98±0.11	0.02±0.02	0.16±0.07	1.06	2.34 *
aaTT GM	0.38±0.02	0.008±0.003	0.046±0.01	2.25 *	3.31 **
PCC	0.25±0.05	0.02±0.009	0.056±0.03	2.60 *	1.63
PRE	0.27±0.03	0.008±0.005	0.057±0.02	1.50	2.67 *
BAT GM	0.26±0.04	0.03±0.007	0.093±0.03	4.60 ***	3.7 **
PCC	0.24±0.09	0.05±0.02	0.079±0.06	3.6 **	1.3
PRE	0.22±0.05	0.03±0.07	0.11±0.03	4.20 ***	3.4 **

Significant code: < 0.001 '***'; 0.001 '**'; 0.01 '*'; 0.05 '●'; 0.1 ' '



METHODS: The study included 20 female and 15 male cognitive normal (CN) subjects, who were equally distributed across the age range from 23 to 84 years (mean age ± SD: 52.7 ± 18.7 years). At least 3 subjects were represented in each decade of age, with the exception of the eighth decade, which included 1 subject only. Imaging was performed on a 4 Tesla MRI system (Bruker Biospec, Germany). Pulsed ASL-MRI, using gradient- and spin echo (GRASE) images, with variable post-labeling delay times[2] were acquired. The ASL signal was fitted to a four phase model [3], which segments the propagation of the labels through the vasculature from large arteries to smaller vessels and finally capillaries, thereby providing estimates of CBF, cerebral blood volume (CBV), the bolus arrival time (BAT), the arterial-arteriole transit time (aaTT), as well as descriptive measures such as time-to-peak (TP). The mean values of each perfusion dynamics was calculated within global grey matter (GM), posterior cingulated cortex (PCC) and precuneus (PRE). Linear regression was used to model relationships between the perfusion dynamic parameters and age and gender.

RESULTS: Linear regression results of age and gender effects on each perfusion dynamics, as well as by regions of interests are summarized in **Table 1**. With respect to aging, CBF and CBV declined significantly in all ROIs by up to 9.9% per decade. On the other hand, aaTT increased with advancing age, but with variable rate (2.1% per decade of age in GM, 8.0 % increase per decade for PCC, 2.9% for PRE). TP also increased by 3.8% per decade of age in GM, compared to 5.8% for PCC and 2.0% for PRE. BAT increased in all three regions significantly between 12% and 21% per decade of age from baseline.

With respect to gender, we found significant differences across the perfusion dynamic parameters and regions but no significant interactions between advancing age and gender, implying that gender effects were independent of age. Specifically, for the GM region, women had 11.7% higher CBF, 16.4% higher CBV, 12.1% shorter aaTT, 9.5% shorter BAT values than men (**Figure 1**).

CONCLUSION: Besides our finding of significant CBF and CBV reductions with advancing age, which are largely confirmational,we also found prolonged arterial-arterioles transit times with advancing age globally in gray matter as well as regionally in the PCC and PRE. The finding implies that the role of vascular factors for reduced perfusion with aging cannot be neglected. The finds also suggest the age effect together with differences between genders should be taken into account when studying brain perfusion.

REFERENCE: [1] Farkes E, et al., Progress in Neurobiology 64:575–611(2001). [2]Gunther, et al., Magnetic Resonance in Medicine 54:491-498 (2005). [3] Li, et al., Magnetic Resonance in Medicine 53:511–518 (2005).