DECREASED CEREBRAL BLOOD FLOW AND CO2 REACTIVITY IN HEALTHY AGING: A PULSED ASL STUDY
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PURPOSE: The understanding of cerebral perfusion variations in healthy aging is essential to comprehend neurovascular signs of age-related neurological diseases. Besides baseline cerebral blood flow (CBF), cerebrovascular reactivity (CVR) can give additional information about the dilatatory capacity of cerebral arterioles in normal and pathological conditions. Therefore, in the present study, pulsed arterial spin labeling (PASL) technique and CO2 inhalation were used to investigate regional CBF and CVR in elderly volunteers, and evaluate changes related with normal aging.

METHODS: Seventeen young volunteers (13 men, age: 26 ± 6 years) and eight elderly volunteers (5 men, 62 ± 8 years) participated in this study, which was approved by the Ethics Review Board of the institution. Written consents were obtained in accordance with the guidelines. All volunteers of both groups had no history of hypertension, diabetes and neurological disorders. High resolution T1-weighted images and PASL images were acquired at a 3T scanner (Achieva, Philips). For PASL, a single-shot EPI sequence was used (TR/TE = 3000/15 ms, FOV = 240 x 240 mm\(^2\), matrix = 64 x 64, 12 slices, slice thickness = 5 mm). Post-labeling delay was 1500 and 2000 ms for the young and elderly groups, respectively. For hypercapnic challenge, a home-built device consisted of micro-controlled valves was used to deliver 5L/min of CO2 mixed with air. ASL protocol consisted of 40 dynamics under normocapnia and 40 dynamics under hypercapnia. Image processing was performed using Matlab2011 (The MathWorks, Inc., MA, USA) and SPM8. CBF and CVR were obtained for gray matter (GM), white matter (WM), and territories supplied by the anterior (ACA), middle (MCA) and posterior (PCA) cerebral arteries. CVR was computed as the percent increase in CBF per mmHg in end-tidal PCO\(_2\). All values are given as mean ± standard deviation. Statistical analysis was done using ANOVA and t-Test, and significance was supplied by the anterior (ACA), middle (MCA) and posterior (PCA) cerebral arteries. CVR was computed as the percent increase in CBF per mmHg in end-tidal PCO\(_2\). All values are given as mean ± standard deviation. Statistical analysis was done using ANOVA and t-Test, and significance was set to p<0.05.

RESULTS: Physiological parameters were within normal limits for all subjects and did not change during the experiment, except for PetCO\(_2\), which increased during hypercapnia (ΔPetCO\(_2\) = 5 ± 2 mmHg). CBF maps showed high SNR and good gray versus white matter contrast. For all subjects, CBF values were lower in white matter compared to gray matter (p<0.0001), for both conditions. For normocapnia (PetCO\(_2\) = 36 ± 3 mmHg), mean CBF across the entire gray matter was negatively correlated with age (figure 1), with a slope of -0.31 mL/100g/min per year (p<0.05). Average CBF value in gray matter was significantly reduced for the elderly group (48 ± 13 mL/100g/min) compared to the young group (60 ± 11 mL/100g/min, p<0.05) (figure 2a). No regional difference was observed in CBF for the young group; however, baseline CBF was higher in PCA territory elderly subjects (figure 2a). During hypercapnia, global increase in cerebral perfusion was observed for both groups. Average gray matter CVR was significantly reduced for elderly subjects (1.7 ± 1.3 %/mmHg) compared to young subjects (3.4 ± 1.6 %/mmHg, p < 0.05) (figure 2b).

DISCUSSION: The protocol used in this study allowed the quantification of CBF as well as assessment of CVR to a hypercapnic stimulus. For the young group, baseline CBF and its increase in response to hypercapnia was consistent with other studies published recently1, showing the ability of the technique to detect global increases in CBF associated with a vasoactive stimulus. Elderly volunteers showed reduced baseline CBF and CVR in large parts of the cerebral cortex compared to young volunteers2; but no regional differences were observed within the groups. The decreased CBF and vascular response to dilatory demand in healthy aging is likely to be associated with arteriosclerosis and small vessel disease.

CONCLUSION: CBF and CVR were successfully investigated using a protocol that causes minimal or no discomfort for the subjects. In large parts of the cerebral cortex, CBF and CVR decreased with age, showing altered vascular reserve in healthy aging. Further analysis will be performed to identify altered CBF and CVR in different cortical and subcortical regions, and investigate if the impaired vascular reserve is related to vulnerability to neurological disorders.