Decrease in intracranial vascular compliance is associated with cerebral hypoperfusion

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Target audience: Neuroimaging scientists and clinicians interested in studying vascular function

Introduction:

Recently a vascular hypothesis of AD has emerged, which posits that cerebrovascular pathologies (e.g. blood-brain barrier breakdown, and hypoperfusion) precede, and may even cause AD pathologies[1]. Both arterial stiffening (or reduced compliance) and cerebral hypoperfusion have been found to be associated with AD[2,3]. It is hypothesized that arterial stiffening over time leads to decline in cerebral perfusion, which in turn may lead to AD pathologies. Cerebral perfusion in AD has been widely studied, using various techniques, from O15-H2O PET to ASL MRI[4]. Arterial stiffening, however, has been studied primarily in extracranial vessels[5] (e.g. aorta). Recently, a novel technique for measuring *intracranial* vascular compliance in small arteries and arterioles was introduced[6,7]. This technique uses dynamic arterial-spin labeling (ASL) MRI (with multi-phase True FISP readout) to directly measure the changes in cerebral blood volume (ΔCBV) between systolic and diastolic phases, and determine intracranial VC (=ΔCBV/pulse-pressure). In the current study, we compare intracranial VC with cerebral perfusion in a group with mixed vascular risks to demonstrate that intracranial arterial stiffening and cerebral hypoperfusion are correlated.

Methods:

All experiments were performed on a Siemens TIM Trio 3T scanner using 12-channel head coil. Twelve participants with mixed vascular risks (i.e. hypertension, smoking history, diabetes, or dyslipidemia), aged 21 to 64 years, were recruited in this study after providing written informed consents. To identify the time delays at peak systole and early diastole during the cardiac cycle, an ECG-triggered multi-phase phase contrast (PC) MRI was performed to measure the blood flow velocities in internal carotid arteries (ICA). Arterial CBV was measured at peak systole and early diastole using an ECG-gated dynamic ASL sequence using multi-phase segmented TrueFISP readout with pulsed spin labeling applied at the peak systolic and early diastolic phases (on average 150ms and 400ms for systole and diastole following the trigger), respectively. Imaging parameters were: FOV=220×220mm^2, matrix=96×96, FA=40°, TE/TR=1.87/3.74ms, 29 phases from 150 to 2250ms with an interval of 75ms. A single slice of 5-mm thickness at the level of M1 was imaged within a scan time of 3min. Arterial CBV maps were calculated based on Eq. [4] of Ref (7). The arterial ROI was defined with CBV>5%. A 5min resting perfusion scan using pCASL 3D GRASE was performed. Twenty-six 5mm axial slices were acquired to cover the whole brain with imaging parameters: FOV=220mm, matrix size=64×64, TE=22ms, TR=3.5s. The tagging plane was positioned 90mm inferior to the center of the imaging slab with a labeling duration of 1500ms and post-labeling delay of 1500ms. The brachial blood pressure (BP) was recorded before and after MRI scans using a MR compatible cuff sphygmomanometer. VC was calculated as the ratio between changes in CBV and BP between systolic and diastolic phases (VC=ΔCBV/pulse-pressure), which was correlated with global CBF of the whole brain measured by pCASL 3D GRASE.

Results:

The mean arterial CBV map at systolic and early diastolic phases was calculated from each subject. As expected, greater CBV was observed in the big arteries (baseline CBV>5%) compared to small arteries and arterioles (CBV 1-5%). In this analysis, we focused on ΔCBV and VC measures in the arterial ROI given the higher SNR and more reliable measurements. We divided the subjects into 2 groups depending on the vascular risk level. A declined VC was obtained from the subjects with higher vascular risks (p=0.058), which arose from the decrease of ΔCBV and elevated blood pressure, as shown in Figure a. A reduced global CBF was also obtained in the subjects with higher vascular risks (p=0.001). Figure b shows the scatter plot of VC as a function of age over the subjects with both low (green) and high (red) vascular risks. A reduction of VC with age and associated vascular risks was observed, which is consistent with previous finding[2]. Figure c shows the scatter plot between global CBF measured by pCASL 3D GRASE and age across subjects, which indicates a significant trend of decreasing global CBF with aging and associating vascular risks. Figure d shows the scatter plot between VC and CBF across subjects. A positive correlation between VC and CBF was observed, which indicates that subjects with reduced intracranial VC also have hypoperfusion.

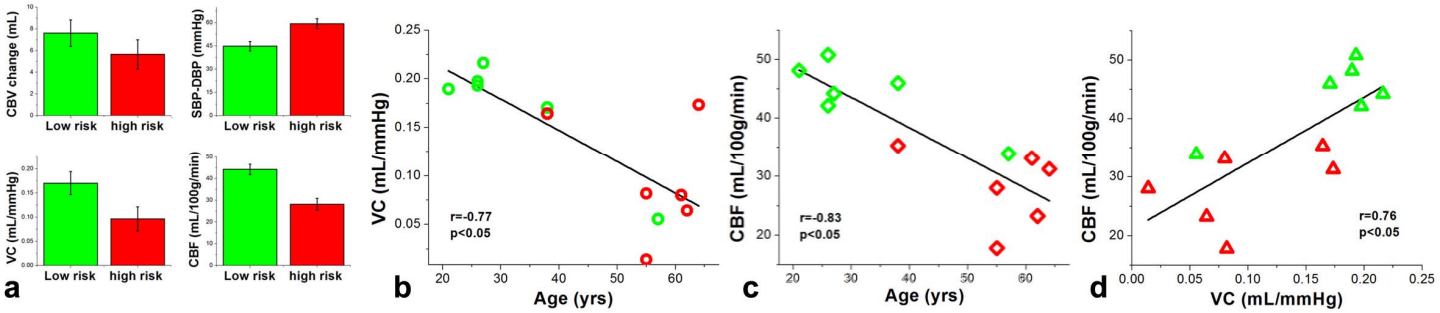

Fig a. Mean ΔCBV, ΔBP (SBP-DBP), VC, and CBF over the subjects with low (green) and high (red) vascular risks. Fig b, c and d: Scatter plots between VC and age (b) , CBF and age (c) , CBF and VC (d) across all the subjects. Green and red represent the subject with low or high vascular risks, respectively.

Discussion:

In the present study, we observed age-associated reductions in VC and CBF in a cohort of subjects with mixed vascular risks. It is well-known that arterial stiffening is associated with aging. This association is demonstrated using the novel intracranial VC measurement. In healthy aging (low vascular risks), cerebral hypoperfusion becomes apparent only after approximately age 60[4]. The observed age-associated decline in CBF likely reflects existing vascular pathologies from the known vascular risks. Furthermore, we demonstrated strong positive correlation between intracranial VC and CBF. This correlation is an extension of the association between extracranial (i.e. aorta) arterial stiffening and cerebral hypoperfusion in vascular risks and AD, to intracranial arteries. Our findings are not only consistent with literature, but also support the validity of the recently developed intracranial VC measurement as an early imaging marker of AD.

Reference:

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