Relationship between cardiovascular health, cerebral physiology and cognition in healthy aging

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Introduction: The aging brain exhibits both vascular and cognitive changes. While arteries throughout the body are known to stiffen with age, this vessel hardening is believed to start at the level of the aorta and progress to other organs, including the brain[1,2]. Progression of this vascular impairment may contribute to cognitive changes observed with aging. Furthermore, it may be that regular exercise acts as a modulator to partially attenuate the effects of age on vascular and metabolic physiology[3]. The present study seeks to address these questions by identifying vascular, metabolic and cognitive properties that change within a cohort of 54 older adults.

Methods: Acquisitions were conducted in 54 older healthy participants on a 3T MRI system (17 male, mean age of 63 ± 5 years). Sessions included an anatomical, 1mm^3 MPRAGE acquisition (TR/TE/flip angle = 2300ms/3ms/90°, 256x240 matrix) and two pseudo-continuous arterial spin labeling (pCASL) runs, providing simultaneous BOLD contrast using dual-echo readouts (TR/TE1/TE2/flip angle = 2000ms/10ms/30ms/90° with 4x4x7mm voxels, 64x64 matrix and 11 slices, post-label delay=900ms, tag duration=1.5s, with a 100mm gap) during a modified Stroop and a hypercapnia challenge (5mmHg end-tidal CO_2 change, iso-oxic during two, 2min blocks). The Stroop task is described in Figure 1A. ROIs were determined from the intersection of significant group BOLD and CBF change to the Stroop task. Two functional ROIs were drawn over frontal and parietal areas (Figure 1B). A weighted average of BOLD percent effect, taking into account grey matter volume fraction, was calculated over each ROI. Simultaneous brachial pressure recording was done during the aortic exam. All acquisitions were ECG gated and acquired during cued breath holds. A series of black blood turbo spin echo images were acquired to visualize the aortic arch (TR/TE/alpha: 700ms/6.5ms/180°, with 1.4x1.4mmx7mm). In a plane plane perpendicular to the ascending and descending aorta, at the level of the pulmonary artery, a phase-contrast velocity encoded series was acquired (TR/TE/alpha: 28.6ms/1.99ms/30°, with 1.5x1.5x5.5mm, during 60 phases of the cardiac cycle, velocity encoding =180cm/s through plane. Carotid applanation tonometry was performed on both carotids. Augmentation index (AI; in %) was determined for both carotids as the ratio of augmented pressure to the pulse pressure.

All participants underwent a cardiorespiratory fitness exercise test. Initial workload was set at the individual body weight and increased by 15 W every minute until voluntary exhaustion. Oxygen uptake (in ml/min/kg) was determined continuously on a 30-second basis using an automated cardiopulmonary exercise system. Blood tests were done on the day of the MRI exam to measure HDL and cholesterol levels and participants' BMI was measured. The Framingham's general cardiovascular risk factor was calculated for each participant. Partial correlations were done between relevant parameters, taking into account the effects of age, gender and cardiovascular risk factor.

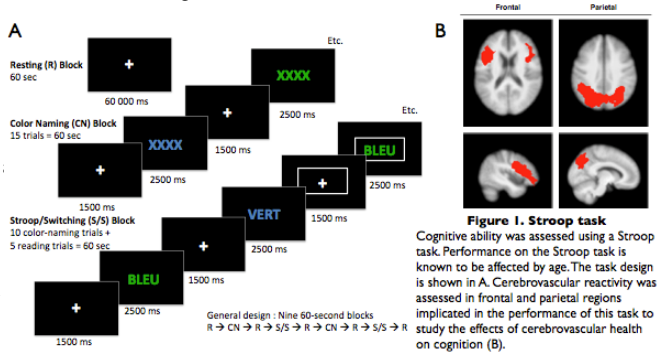

Figure 1. Stroop task
Cognitive ability was assessed using a Stroop task. Performance on the Stroop task is known to be affected by age. The task design is shown in A. Cerebrovascular reactivity was assessed in frontal and parietal regions implicated in the performance of this task to study the effects of cerebrovascular health on cognition (B).

Results: In order to investigate the link between vascular health, fitness and cognition, cognitive performance was assessed using a Stroop task (Figure 1A) and cerebrovascular reactivity (CVR) to CO_2 was assessed in the regions implicated in the performance of this task (Figure 1B). Older adults with poorer aortic health, as assessed using pulse wave velocity (PWV) were found to have lower CVR in both frontal and parietal regions (Figure 2B and Table 1). Furthermore, older adults with poorer carotid health - measured in terms of augmentation index (AI) - were found to have a lower cardiovascular fitness level and poorer performance on the Stroop task (Figure 2A and Table 1). Partial correlations of AI, VO2max, Stroop performance and CVR identified putative links between poorer cardiovascular fitness and cerebrovascular reactivity, and between Stroop performance (Table 1).

Discussion: The results presented here support the hypothesis that while the aorta may be the first vessel affected in the body, the brain may also suffer from early damage since it is unprotected from heart pulsations[1]. Aortic elasticity is known to be linked to cardiovascular fitness[4] and lifestyle and these may affect the elasticity of other vulnerable vessels such as the carotids and cortical arteries. Here we see showed links between VO2max and AI, as well as with CVR in both frontal and parietal areas. It has also been hypothesized that vascular changes associated with aging and lifestyle may underly some of the cognitive decline observed with age. In agreement with this hypothesis, we have here found that older adults with higher AI (less healthy carotids) perform more poorly on a Stroop task.

Conclusion: In conclusion, the results presented here support the hypothesis that declining vascular health and cognition during healthy aging at the level of the brain is associated with poorer vascular health at the level of the aorta and the carotids. Furthermore, cardiovascular fitness may modulate cerebrovascular health and better fitness be associated with preserved cerebrovascular and central vascular health.

References: [1] O'Rourke et al. (2007) J Am Coll Cardiol 50: 1-13; [2] Laurent et al. (2007) Hypertension 49: 1202-1206; [3] Colcombe et al. (2003) Psychol Sci 14: 125-130; [4] Arena et al. (2009) J Cardiopulm Rehabil Prev 29: 248-254

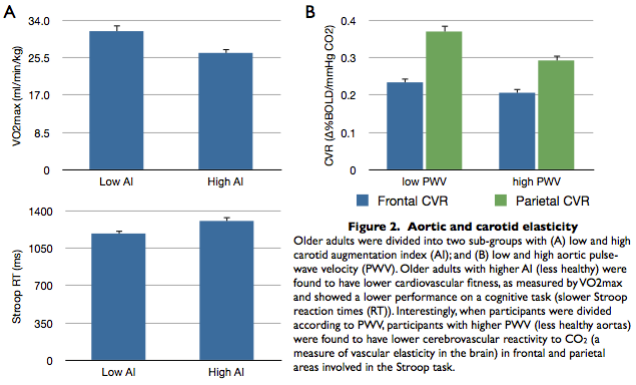

Figure 2. Aortic and carotid elasticity
Older adults were divided into two sub-groups with (A) low and high carotid augmentation index (AI); and (B) low and high aortic pulse-wave velocity (PWV). Older adults with higher AI (less healthy) were found to have lower cardiovascular fitness, as measured by VO2max and showed a lower performance on a cognitive task (slower Stroop reaction times (RT)). Interestingly, when participants were divided according to PWV, participants with higher PWV (less healthy aortas) were found to have lower cerebrovascular reactivity to CO_2 (a measure of vascular elasticity in the brain) in frontal and parietal areas involved in the Stroop task.

	VO2max	AI	Stroop RT	Frontal CVR	Parietal CVR	
VO2max	•	-0.123	-0.138	-0.297	-0.285	Cor
		0.205	0.177	**0.021**	**0.026**	Sig
AI		•	0.308	-0.022	0.073	Cor
			0.018	0.442	0.313	Sig
Stroop RT			•	0.064	-0.016	Cor
				0.335	0.458	Sig
Frontal CVR				•	0.599	Cor
					< 0.0001	Sig
Parietal CVR					•	Cor
						Sig

Table 1. Partial correlations
Partial correlation between VO2max, augmentation index (AI), Stroop reaction time (RT) and cerebrovascular reactivity (CVR) in frontal and parietal regions. Uncorrected significant comparisons are shown in bold type. Cor = correlation; Sig shows the p value.