A Multi-parametric Investigation of Vascular Alterations in Elderly with Hypertension

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Introduction:

Along with aging comes many cardiovascular and cerebral changes that impact a person's health. These changes manifest as variances in blood pressure, brain volume, cerebral blood flow, oxygen metabolism, and neurological functioning. The purpose of this study is to provide evidence to support new or previously known biomarkers for declining cerebrovascular health, such as cerebral arterial stiffness, reduced vessel capacity, and thickening of extracellular matrix. One of these markers currently being researched is the measurement of white matter hyperintensities (WMH) that are associated with hypertension. Unfortunately, this marker appears to be late-stage and only appears after cerebrovascular damage has already taken place and is no longer reversible. In this study, we compared blood pressure, age, gender, cerebral blood flow (CBF), venous cerebral volume (vCBV), venous oxygenation (Yv), cerebrovascular reactivity to CO_2 (CVR), and cerebral metabolic rate of oxygen ($CMRO_2$). Phase contrast (PC) and arterial spin labeling (ASL) imaging techniques were utilized to connect cardiovascular and cerebral changes.

Materials and Methods:

For this study, 45 participants volunteered and were chosen from the Dallas Heart Study. This gave us access to past medical information that might be relevant throughout the project. The participants had an age range from 61 to 79 years (mean = 67; SD = 5) with 23 being female and 22 being male. Blood pressure was acquired just prior to the imaging study. Cardiovascular reactivity (CVR) and venous cerebral blood volume (vCBV) were measured by using different combinations of CO_2, O_2, and N_2 concentrations for the participants to breathe in at distinct intervals. The three combinations that were used include hyperoxia gas (95%O_2 and 5% N_2), hypercapnia gas (5% CO_2, 21% O_2 and 74% N_2), and a mixed gas (95%O_2 and 5%CO_2). Blood-oxygen-level dependent contrast images and end-tidal CO_2 and O_2 measurements were acquired (Fig. 1). Two different MRI techniques were employed to acquire and analyze data, including phase contract (PC) and arterial spin labelling (ASL). A 3T system was used for all scans. PC MRI was used for acquiring images of moving fluid. In this case, images of four main arteries that supply blood to the brain (lica, rica, lva, rva) were visualized. Utilizing MATLAB, a computer program, the voxels containing blood flow were isolated so that whole-brain CBF could be calculated using previously established formulas (2).

Methods and Results:

Materials and Methods (Cont.):

The ASL imaging technique resulted in the acquisition of a perfusion image, which reflects localized arterial blood flow and allows for regional measurements to be obtained. Venous oxygenation (Yv) was assessed using T2-relaxation-under-spin-tagging (TRUST) MRI technique (3). Other data acquired during or immediately prior to the MRI scans include systolic blood pressure, diastolic blood pressure, brain volume, and the oxygen saturation level of venous and arterial blood. Linear regressions were performed to account for changes due to and dependence on age, sex, and blood pressure. Blood pressure values were also used to divide the participants into non-hypertensive (N=22) and hypertensive (N=23) with the threshold being a systolic BP of 140 mmHg. A p-value of 0.05 or less was used to determine statistical significance.

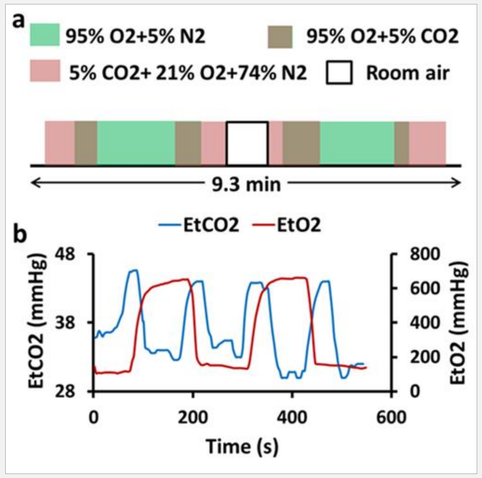


Fig. 1. Simultaneous CO2/O2 breathing challenge. (a) Paradigm design. (b) EtCO2 and EtO2 time courses.

Results:

Figure 2 shows the cardiovascular reactivity maps and that the CVR values derived from those scans after the participants were divided into two groups, non-hypertensive and hypertensive. The CVR for the hypertensive group appears lower than that of the non-hypertensive group in the scans (Fig. 2a), which is confirmed to be significant by quantitative analysis (Fig. 2b). Figure 3a plots CVR values against blood pressure and shows that CVR decreased as systolic blood pressure increases (p=0.02). CVR also decreased with age (p=0.02) and was higher in males than females (p<0.01). As seen in Figure 3b and 3c, CBF and Yv both increased with systolic blood pressure (p=0.03, p=0.02 respectively). CBF and Yv values were also strongly correlated with each other (p<0.001), and CBF was higher in females (p=0.03).

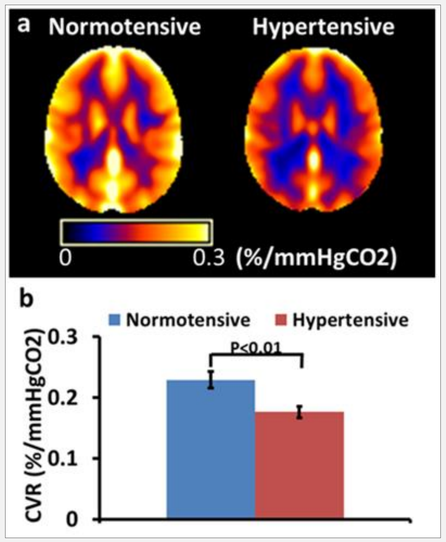
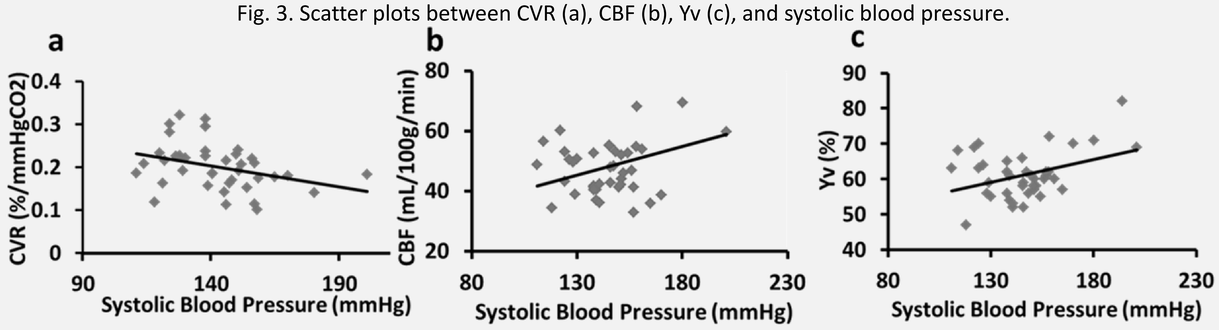


Fig. 2. CVR comparison between normotensive and hypertensive group.

Fig. 3. Scatter plots between CVR (a), CBF (b), Yv (c), and systolic blood pressure.



Discussion:

Our data showing decreased cardiovascular reactivity in hypertensive individuals is consistent with literature that supports increased arterial stiffness due to increased blood pressure over time. This stiffness diminishes the ability of the vessel to dilate in the CO_2 CVR study as seen in Figure 2. Unexpectedly, cerebral blood flow and venous oxygenation both increased in hypertensive individuals. This could be due to the hypertension providing a greater "driving force" for blood to the brain. Yv and CBF correlate with each other, as expected. When there is greater blood flow to the brain, the venous oxygen should also increase as long as the metabolic rate of oxygen is not increasing as well. Venous cerebral blood volume did not show a trend with blood pressure, most likely due to veins not having the same smooth muscle as arteries and the vessels not undergoing the same changes due to pressure.

Conclusion:

In summary, the results of this project support certain relationships between blood pressure and the brain's vascular markers. The vascular markers studied showed a decrease in CVR with blood pressure, and an increase in CBF and Yv with blood pressure. These markers may change before cognitive decline or clinical symptoms emerge, and when symptoms do finally appear, it is often too late to prevent or mediate the problem. This study is an early step on the path to discovering easily identifiable precursors to neurological changes that take place as normal aging processes occur. Future studies are necessary to discover new viable markers and their ability to predict future symptoms.

References:

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2) Liu et al. PLoS One, 9, e95721 (2014)
3) Lu et al. MRM, 60, 357 (2008)
4) Blockley et al, MRM, 65, 1278 (2011)

Disclaimer: I, Adam Sheffield, was only present for the analysis of the first 34 out of 45 participants in this study,.