Undergraduate Research Experience Award Program Report

Are long arteries a problem with ageing and can this be prevented with lifestyle modifications?

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Introduction

In developed societies and most developing nations, cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in both men and women[11,12]. This is because the prevalence of CVD, including coronary heart disease, heart failure, stroke, and hypertension, in adults over 20 years of age is 49.2% overall, and increases with age in both males and females[11]. As we age, our arteries become longer and more tortuous, altering blood flow patterns and predispositioning us to maladaptive CVD processes, with the main contributing event being the stiffening of the central elastic arteries[1,6]. This age-related stiffening is caused by changes to the composition of the walls typified by a loss of elastic fibres which cushion blood pressure. This lack of cushioning alters the blood flow which becomes more pulsatile in these arteries. Arteries also respond to this flow profile which controls their shape, structure, and function[4-7]. In small blood vessels that supply blood to the brain, heart, and other vital organs the blood flow becomes intermittent, with elevated or decreased pulsatile flow depending on vessel location. This even leads to discontinuous flow within the smallest microvascular vessels, forcing the heart to maintain a higher blood pressure overall[13]. This may be a cause of long-term high blood pressure.

A characteristic of arteries that often goes overlooked is their length and how they are under tension within the body. Specifically, arteries are stretched lengthwise as we develop and the elastic fibres in the walls are under what we call “arterial pre-stretch”[5]. This “pre-stretch” or lengthwise tension seems to be important since arteries stiffen when this force is removed[5]. In fact, as we age, we see a loss of this “pre-stretch”, suggesting the elastic portion of the vessel has degraded; researchers believe that the tortuosity we see using complex techniques like MRI is related to the degradation of elastic fibres[2,3,8].

Treatment to limit the age-related arterial stiffness of large elastic arteries is difficult once we reach old age, however, primary prevention for many CVD-related illnesses can happen by adopting a healthy lifestyle involving healthy diets, and regular exercise. Specifically, regular aerobic/endurance exercise is the most convincing evidence-based strategy used to prevent CVD in both men and women, as it limits arterial stiffening[8]. Currently, we are not sure whether the protective effects of exercise are caused by limiting the inherent stiffness of the artery, or preventing the loss longitudinal tension, otherwise known as artery "pre-stretch". It is possible that aerobic exercise directly affects the maintenance of arterial length over time, but this has not been assessed before.

Project Aims

The objective of the proposed research was to gain novel insight into how central elastic artery length and stiffness can be measured accurately and repeatedly, how both characteristics change with ageing, and if these characteristics are modifiable by lifestyle interventions like exercise training and diet.

Central elastic artery length and stiffness was to be measured in young (n=10 age: 19-35), older active (n=10, age: 55-75), and older inactive (n=10 age: 55-75) adults using ultrasound imaging. Prior to completing the ultrasound portion participants were to complete a physical activity recall survey to assess their level of regular exercise and this would have been used to categorize older participants. Participants would have visited the lab on two occasions to enable us to assess the reproducibility of the measurements. This is important since ultrasound is not routinely used to measure the length of artery segments. On these two occasions, the exact same procedures were to be performed. Specifically, ultrasound imaging was to be used to obtain a video clip of the entire carotid artery (located in the neck) from its division near the heart to where it divides before it continues up to the brain. To measure stiffness, we would have also captured video clips of the expansion and retraction of the common carotid artery in the neck, because it is a central artery prone to stiffening with ageing and disease. Finally, we would have had our participants complete a sub-maximal exercise stress test that would have been used to determine their physical fitness. The results would have been analyzed by quantifying the differences between the three groups of participants using statistical tests (1-way ANOVA and correlations).

Unfortunately, challenges arose when recruiting participants to come into the lab for exercise stress tests, and ultrasound imaging to measure the length and stiffness of a central elastic artery. Thus, instead of beginning this study and quantifying the differences between the groups of participants, the remainder of the project timeline consisted of method training and development, as well as analysis practice in preparation for a future study.

Project Progress

Specifically, the remainder of the project timeline consisted of blood pressure, electrocardiogram, $\dot{V}O_{2max}$, resistance exercise, and aerobic exercise method training, as well as ultrasound and baroreflex sampling method training and development, and analysis.

Training in common physiology sampling techniques

Over the course of the summer, I learned how to non-invasively measure continuous beat-to-beat arterial blood pressure using continuous non-invasive arterial pressure (CNAP) methodology, to recognize normal arterial blood pressures at rest and with increasing exercise intensity, and to handle adverse blood pressure responses during participant testing. With prior knowledge from BIOL3540, I also refined my electrocardiogram administration skills and expanded my understanding of adverse heart rate responses and common arrhythmias. Additionally, throughout the summer I aided in the administration of resistance and aerobic exercises tests, as well as $\dot{V}O_{2max}$ tests, gaining knowledge of standard testing protocols, important factors to monitor during exercise testing, rates of perceived exertion, ventilatory thresholds, and equipment set-up and calibration.

Development and assessment of novel baroreflex sampling and analysis techniques

Furthermore, and in addition to the above five methods, I learned how to create my own protocols on the Philips EPIQ 5 Doppler Ultrasound, how to use the Ultrasound to record a video of the diameter changes in the carotid artery, and how to back-up the ultrasound videos and open them in CAROLAB.

Using Doppler Ultrasound images in conjunction with blood pressure data, complete baroreflex can be assessed. Baroreflex function measures how well the cardiovascular system adjusts to a change in blood pressure. In our lab, we used a manipulation called the Valsalva maneuver to abruptly increase and decrease participants' blood pressure[9]. The Valsalva maneuver involves participants blowing into a pressure sensor at constant pressure for 15 seconds, while their heart rate, arterial blood pressure, and carotid artery size are continuously measured by ECG, CNAP, and ultrasound, respectively. As baroreflex can be divided into its mechanical and neural components, it can be assessed in two ways to understand the complete baroreflex function, and to compare each component[10]. The mechanical, or cardiac, aspect of the baroreflex can be analyzed using the traditional analysis method of graphing the slope of the relation between the participant's R-R interval and their first systolic blood pressure peak as a measure of their arterial blood pressure during their recovery period post-Valsalva[10]. The neural, or sympathetic, aspects of the baroreflex can be analyzed by comparing the distention of the participant's carotid artery to their heart rate response[10].

Upon beginning baroreflex analysis on previous participant data, it was noted that the physiological response to a Valsalva, which includes a drop in blood pressure during Phase II, due to the pressure in participants' chest cavities reducing the amount of blood returning to the heart through the veins, would also include peripheral vasoconstriction[9]. This posed a problem with our methodology, as CNAP is measured indirectly using plethysmographic signals from fingers, which are vascularized with peripheral arteries. Therefore, a small-scale supplementary experiment was mounted to determine if the peripheral vasoconstriction effect could be mitigated by the addition of a heating pad at the fingers.

Participants were invited to the lab for a singular session where their bodies' responses to a series of Valsalvas with three-minute breaks in between each Valsalva were measured. This was done using ECG, and CNAP, allowing us to determine the neural component of each participant's baroreflex. For the first half of the Valsalva series, a heating pad was not used on the fingers of the participant, whereas for the second half of the Valsalva series, a heating pad was used for 10 minutes prior to and during testing. The mechanical aspect of the baroreflex was analyzed using both the traditional analysis method of graphing the slope of the relation between the participant's R-R interval and their first systolic blood pressure peak as a measure of their arterial blood pressure during their recovery period post-Valsalva. At this time, a new analysis method of graphing the slope of the relation between the participant's R-R interval and their second systolic blood pressure peak as a measure of their arterial blood pressure during their recovery period post-Valsalva was also implemented in the protocol.

Novel Baroreflex Sampling Techniques Results

A Repeated Measures ANOVA test was performed to examine the differences between the mean slope (ms/mmHg) and R^2 values of participants' neural baroreflex components when comparing the traditional and new methods of analysis and when using, versus not using, a heating pad on their fingers.

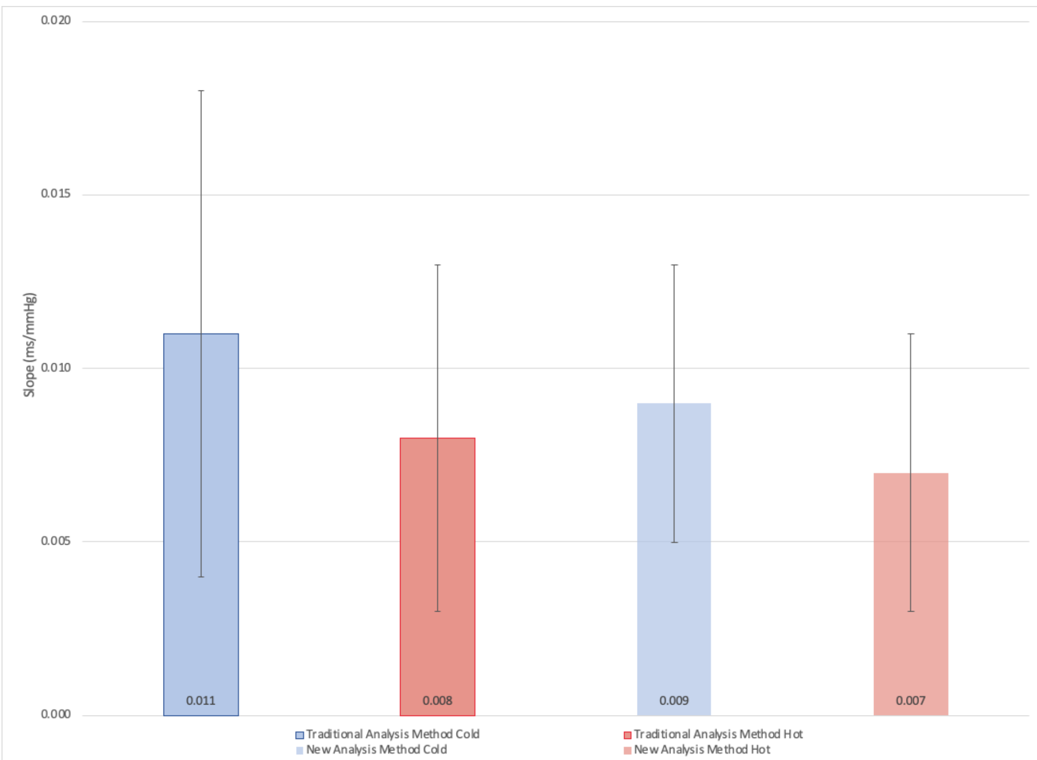

Figure 1. A comparison of the mean slope (ms/mmHg) values of the traditional neural component of the baroreflex method without a heating pad, the traditional neural component of the baroreflex method with a heating pad, the new neural component of the baroreflex method without a heating pad, and the new neural component of the baroreflex method with a heating pad (n = 9).

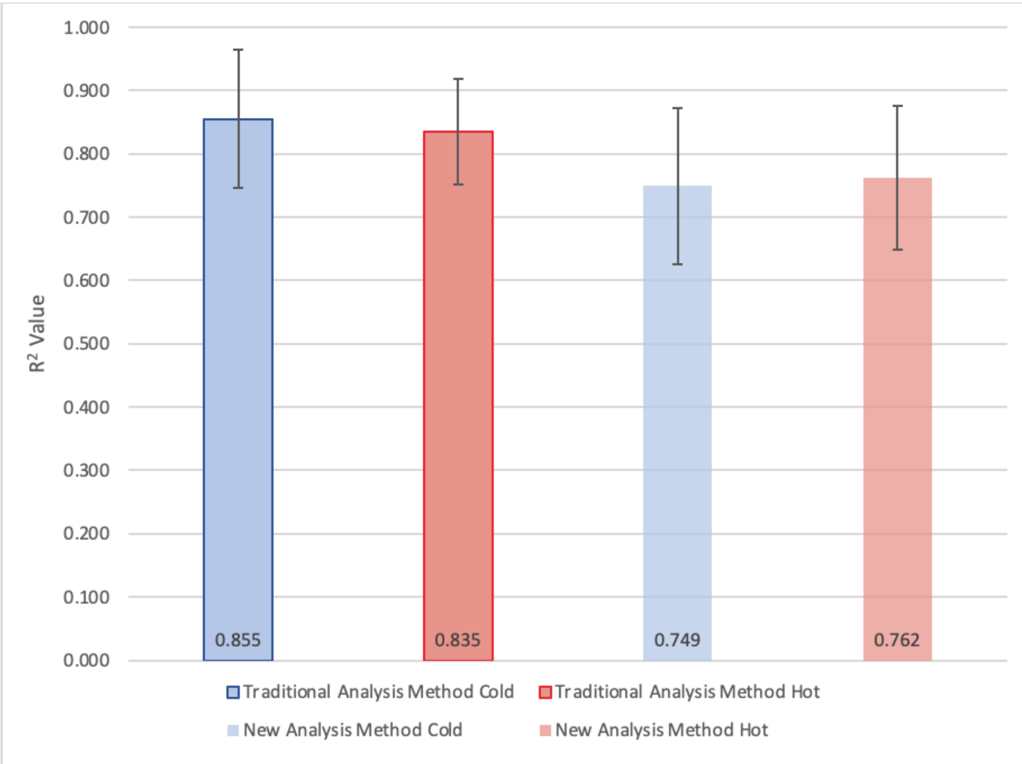

Figure 2. A comparison of the mean R^2 values of the traditional neural component of the baroreflex method without a heating pad, the traditional neural component of the baroreflex method with a heating pad, the new neural component of the baroreflex method without a heating pad, and the new neural component of the baroreflex method with a heating pad (n = 9).

The Repeated Measures ANOVA test indicated that there were no significant differences between the mean slope and R^2 values of a participants' neural baroreflex components when comparing the traditional and new methods of analysis and when using, versus not using, a heating pad on their fingers (Methods: F-value = 3.740, p-value = 0.089; Temperature: F-value = 0.014, p-value = 0.909; Methods×Temperature: F-value = 0.118, p-value = 0.740).

Discussion

Although it was presumed that peripheral vasoconstriction during the Valsalva manoeuvre would pose a problem with the CNAP methodology, the preliminary results of the small-scale supplementary experiment, which included an effort to mitigate peripheral vasoconstriction with the use of a heating pad at the participants fingers, indicate otherwise. It also appears as though the traditional and new method of analysis are analogous. No significant differences between the mean slope and R^2 values of a participant's neural baroreflex component when comparing the traditional and new methods of analysis and when using, versus not using, a heating pad on their fingers were found after performing a Repeated Measures ANOVA test. These findings indicate that using a heating pad at the participants fingers as a measure to mitigate peripheral vasoconstriction during baroreflex sampling is not necessary, and that the use of either the traditional or the new method of analysis are acceptable. Future research may look to expand upon this preliminary study by increasing the number of participants, because even though no significant differences between the variables compared were noted, the values F-value and p-value for Methods was approaching significance. Contrastingly, a variation of this experiment could also be performed by using an alternate mitigating factor to peripheral vasoconstriction.

Overall, the training in common physiology sampling techniques in tandem with the development and assessment of novel baroreflex sampling and analysis techniques will allow this project and future projects to continue in a proper and timely manner, and the plan to disseminate the research findings as described in the original UREAP application will be carried out upon project completion.

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