**Human Ethics Research Application - Faculty & Graduate Students & Undergraduate Students**

**Project Info.**

**File No:** Ref No : 8819

**Project Title:** The effects of increased sodium on endothelial function and arterial blood pressure

**Principal Investigator:** Dr. Mark Rakobowchuk (Faculty of Science\Biology)

**Start Date:** 09/07/2022

**End Date:** 04/30/2023

**Keywords:** Sodium; Arterial; Endothelial; Baroreflex; Exercise

**Project Team Info.**

**Principal Investigator**

**Prefix:** Dr.

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**Institution:** Thompson Rivers University

**Country:** Canada

**Comments:**

**Other Project Team Members**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Prefix** | **Last Name** | **First Name** | **Affiliation** | **Role In Project** | **Email** |
| Ms. | Gill | Jeeva | Faculty of Science | Undergraduate Student Researcher | jeeva\_gill@hotmail.com |

**Common Questions**

**1. Declaration**

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| **#** | **Question** | **Answer** |
| 1.1 | I verify that; a) this project has been reviewed and deemed to be methodologically sound and complies with the professional ethical standards and guidelines of the area of research. b) the information contained in this application is accurate; c) that the conduct of the proposed research will not commence until ethical approval/clearance has been granted. | I agree |
| 1.2 | Please indicate the type of research | Faculty Research|Undergraduate Student Research |
| 1.3 | If you checked the undergraduate student research box, please indicate if project is part of an Honours Thesis | Yes |
| 1.4 | If you are an graduate/undergraduate researcher you must include your supervisors name on the Project Team Member tab and confirm here that your supervisor has reviewed this application. | Yes - My supervisor is listed and has reviewed this application |
| 1.5 | What level of coursework does this project relate to? |  |

**2. Project Description, Methodology & Procedures**

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| **#** | **Question** | **Answer** |
| 2.1 | Describe the project including purpose and potential benefits. Please use the minimum of technical language | The objective of this study is to assess the effects caused by an increase in dietary sodium on the inner lining of the blood vessel (endothelium) and arterial blood pressure under conditions of disturbance to the sugar coat in the blood vessel (glycocalyx perturbation) that is induced by exercise. In assessing this question, the results may lay an important foundation for continuing future research in assessing how increases in sodium levels affect blood vessels and arterial blood pressure. Upon completion of this study, we expect that when there is an increase in sodium levels, the ability of arteries decreases and arterial blood pressure will increase. We will alter the glycocalyx in an isolated limb to test whether this salt sensitivity happens in young adults and is confined to the limb exercised. If these results are validated, future studies can assess differing sodium levels to determine when the ability of arteries to dilate and constrict and arterial blood pressure become affected. With this information, individuals will then be able to adjust their dietary sodium intake to a level that reduces the risk of cardiovascular disease and hypertension. |
| 2.2 | Provide a summary of the methodology and procedures. Please keep your summary short & concise. | Fifteen healthy individuals will be recruited to participate in this study. The participants will be asked questions about their diet to estimate their baseline sodium consumption. Participants will participate in this study for a three-week period, where their dietary sodium levels are increased and monitored throughout. For seven days, half of the participants (7 or 8) will be given gel capsules containing sodium chloride (dietary salt/table salt) to increase the amount of sodium in their diet. Participants will ingest an additional 18 grams of dietary salt (6 grams of sodium) each day, while maintaining their regular diet. Six, one gram salt capsules will be taken by the participants three times a day for the seven-day period. The other participants will be ingesting a placebo capsule, containing sugar, three times a day for the seven-day period. The decision on which participant will receive what capsule will be randomly decided. After the seven-day period has finished, all participants will be asked to continue their daily diet for another seven days, known as a “wash-out period”. Once the wash-out period has finished, the participants who received the capsules containing dietary salt will be given the placebo capsules. The participants who received the placebo capsules, will be given the capsules containing dietary salt. They will then follow the procedure they underwent in the first week.  The participants will be required to come into the laboratory four different times over the course of the three weeks. During each visit to the laboratory, measurements of arterial blood pressure, baroreflex function, arterial stiffness, and the ability of arteries to dilate will be measured. Arterial blood pressure will be assessed non-invasively using an arm cuff and finger continuous blood pressure monitor. Resting blood pressure will be measured for a 5-minute period at the beginning, with participants lying on their back. It will then continue to be collected throughout the entire testing session. Arterial stiffness will be measured at the carotid artery using ultrasound imaging, and blood pressure. We will also measure the speed of the pulse. The ability of an artery to dilate or construct (endothelial function) will be tested using a flow-mediated dilation protocol and measurements of the increase in blood flow after a 5 minute occlusion stimulus (reactive hyperemia) will also be taken. Flow-mediated dilation (FMD) involves a response of the inner lining of the artery to an increase in the speed of the blood flowing through the vessel. The inner lining (endothelium) releases a gas called nitric oxide (NO) which causes smooth muscle that is inside the blood vessel wall to relax and the vessel enlarges (vasodilation). The flow-mediated dilation protocol uses a 5-minute occlusion of the blood flow to the forearm and ultrasound imaging of the brachial artery. We will assess the dilation after releasing the cuff alongside the blood flow response. Following the first FMD protocol, the participant will perform a hand-grip exercise with their dominant arm for a 30-minute period (repeatedly squeezing a hand-grip device). Their non-dominant arm will be resting during this time. Once the exercise has been performed, another FMD protocol will be performed. They will then be asked to rest for a 30-minute period. A final FMD protocol will be performed on the participant after the rest period has finished.  We will also be assessing whether the salt diet will effect how well participants deal with a change in blood pressure before and after the salt and placebo administrations. This will only be done before the exercise described above. Briefly, we will assess using ultrasound imaging the expansion and recoil of the common carotid artery (located in the neck) at rest (10 minutes) and throughout a procedure called a Valsalva maneuver. The normal Valsalva maneuver involves participants attempting to breath out against a closed epiglottis, but for this study we will have participant blow into a pressure sensor to enable us to control the amount of pressure they exert. This is much like trying to blow up a difficult to inflate balloon. This procedure will last for 15 seconds. The process is repeated 5-8 times with 3 minutes of recovery between efforts (an average response is needed from multiple repeats). Throughout each effort, we monitor heart rate, arterial blood pressure and the size of the carotid artery using an ECG, non-invasive continuous blood pressure monitor and Ultrasound imaging, respectively. To get this information, participants are instrumented with the continuous blood pressure monitoring system that collects blood pressures from the finger (mentioned above). Much like an oximeter used in hospitals to monitor blood oxygen levels, this device wraps around the middle and ring fingers, inflates a small cuff, and maintains the amount of blood flowing to the finger constant by rapidly inflating and deflating the cuff. This change in pressure is measured and is proportional to the blood pressure in arteries but is completely non-invasive. A typical blood pressure cuff is also attached to the participant around their upper arm for calibration purposes. The Ultrasound imaging is done with a clinical ultrasound system by a Dr. Rakobowchuk who has been imaging for close to 20 years. The ECG is collected using 3 sticky electrodes and leads. These electrodes are placed on the skin after first cleaning a small spot just under each collarbone c and another small area on the left hip. All data is collected simultaneously and continuously throughout the testing sessions. |

**3. Risk Assessment**

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| **#** | **Question** | **Answer** |
| 3.1 | Estimate of Risk: What level of overall risk would you assign to this research project? | Minimal |
| 3.2 | Physical Risk? | Minimal |
| 3.3 | Psychological/Emotional Risk? | Minimal |
| 3.4 | Social Risks? | Minimal |
| 3.5 | Employment Risks? | Minimal |
| 3.6 | If you answered more than minimal risk to any of the above, please describe potential risks as well as the safeguards or procedures you have in place. Please provide justification for any potential risks involved and explain why alternative approaches (including revising the types of data collected or the method that data is collected) involving less risk cannot be used |  |

**4. Participant Information**

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| **#** | **Question** | **Answer** |
| 4.1 | How many participants will take part in total? | up to 15 |
| 4.2 | Who is being recruited and what is the criteria for the selection? | Healthy individuals who participate in physical activity at least once a week. They will also need to have what is considered a healthy diet in regard to sodium intake (~6 grams per day) |
| 4.3 | Will anyone be excluded from participation? Yes/No; If yes, who and why? | Those with diagnosed high blood pressure, cardiovascular disease (previous heart attack, stroke or peripheral artery disease) or respiratory illnesses (asthma, COPD, emphysema), Diabetes Mellitus (Type 1 or 2), bleeding disorders, and neurological conditions that may be triggered with exertion (i.e. seizures) will be excluded. |
| 4.4 | How are the participants being recruited? | Participant recruitment will be done through poster advertisement, social media, and email distribution. Posters will be displayed throughout the Thompson Rivers University Campus on designated bulletin boards and in the community when permission is granted. Social media platforms will include Facebook and Instagram. Email distribution lists will consist of students and faculty members of TRU. Participants are specifically volunteers and thus not necessarily compensated for their participation directly although remuneration for parking and time may be provided depending on funding ($20-25/participant). This helps ensure that participants are not enticed to participate. This may result is difficulty recruiting but that is preferable, compared to incentivizing participation. The researchers may be former, current, or future instructors of participants. Within the information sheet it is stipulated that participation will not benefit/harm the students’ academic standing and that withdrawing for any reason will also not affect their academic standing in any way. |

**5. Informed Consent**

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| **#** | **Question** | **Answer** |
| 5.1 | Who will consent (check all who apply) | Participant |
| 5.2 | Deception - Will participants be informed of everything that will be required of them prior to the research? Yes/No. If no, please explain. | Yes, participants will be informed of everything that will be required of them prior to agreeing to partake in the research. To ensure this, a participant information sheet will be provided with the consent form attached and informed consent must be obtained prior to the research commencing. |
| 5.3 | Are participants to be debriefed at the end of the research project? Yes/No.If yes, explain how it will be done. If not,explain why not. | Yes, participants will be debriefed at the end of the project in the form of a summary of both their own individual results and a report once all data has been analyzed. Participants will also be able to obtain a copy of all reports or publications that result from this research. These reports only contain summarized data like average responses of all participants and no personal data. To obtain these, participants will consent to communicate their results via email and to receive any publications created from this study. |
| 5.4 | Provide a description of the verbal explanation (if any) that will be given to the participants before they are asked to consent to participate (by attachment if required). If not applicable state why. | Participants will be given a verbal explanation based on the information sheet that they were provided before agreeing to participate in the study. This will be given prior to each testing session to ensure they are aware of all the procedures for that particular day. Before agreeing to participate at the outset, they will be provided with the information sheet (see attachment) and all participants will be asked to wait at least 24 hours after reading the information sheet before committing to the study. Encouragement will also be given to participants to ask questions or seek additional guidance when making their decision about participating. If they do not contact the researchers after having been asked to schedule their first testing session, they will not be contacted a second time and it will be assumed that they are not interested in participating. |
| 5.5 | To be sensitive to unique situations, including cultural differences, a written consent form may not be appropriate. If there is no consent form explain in detail your alternative procedures to ensure that consent is obtained and recorded as required. | Not applicable. To ensure the utmost safety of participants, all participants must be able to read and comprehend all procedures as well as provide written consent. This also ensures that researchers are not inappropriately held accountable should an adverse event not related to negligence occur during the study. |
| 5.6 | How and when are the participants informed of the right to withdraw? What procedures will be followed for participants who wish to withdraw at any point during the study. Please explain. | Prior to participation, the supervisor of the project will provide verbal and written information to all the participants, stating their right to withdraw from or not take part in the study at any point, without penalty, as stated in the attached information sheet. To withdraw or not participate in a part of the research, the participant need only verbally state they no longer wish to continue their participation. Following this, all data files, consent forms, and any entry containing their data in a database will be permanently deleted or disposed of through the confidential waste streams within the Faculty of Sciences. |
| 5.7 | Other Institutions: In the case of projects carried out at other institutions, the Committee requires written proof that agency consent has been received. Please indicate all that apply and provide copies of the consent letters through the attachments tab on this form. |  |

**6. Project Details**

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| **#** | **Question** | **Answer** |
| 6.1 | Where will the project be conducted? | All portions of this project in which the participant is interacting with researchers will be conducted at Thompson Rivers University. The Physiology laboratory where exercise testing will take place is in the Ken Lepin Science Building (S365). |
| 6.2 | Who will actually conduct the study? | All aspects of the study will be conducted by Dr. Mark Rakobowchuk and undergraduate research student Ms. Jeeva Gill. All testing sessions will have Dr. Rakobowchuk in attendance for both the trials involving physiological measures and the exercise trial. |
| 6.3 | Will the group of participants have any problems with giving informed consent on their own behalf? | No |
| 6.4 | If the participants are not competent to give fully informed consent, who will consent on their behalf. What measures will be used to inform and obtain consent on their behalf? | As previously described, any individuals not capable of giving fully informed consent will be excluded from the study due to safety concerns. As such, all participants will be 19 years of age or older and competent to provide informed consent. |
| 6.5 | Are participants considered members of a (potentially) vulnerable group? If yes provide details | No |
| 6.6 | Does your study have the potential for identifying distressed or disturbed individuals? If yes, provide details. | No |
| 6.7 | If your study has the potential to upset participants, or identify distressed or disturbed individuals, you must make arrangements to mitigate such effects. Describe the arrangements you have made. | N/A |
| 6.8 | What, if any, discomfort or perceived degree of coercion are the particpants likely to endure as a result of the research study? Please explain. | During the FMD protocol, blood flow is restricted to the forearm for 5 minutes. There can be discomfort as the participant might feel a tingling sensation in their arm and experience slight pain. This will easily subside once the FMD protocol is finished. |
| 6.9 | What monetary compensation, if any, is being offered to the participants. If none please state so. | None |
| 6.10 | How much time will a participant need to dedicate to the project? The control group participants? | Participants will be in the lab for ~1.5 hours on four different occasions (6 hours in total). |

**7. Data Details**

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| **#** | **Question** | **Answer** |
| 7.1 | Who will have access to the data? | Dr. Mark Rakobowchuk and Ms. Jeeva Gill |
| 7.2 | How will you handle the requirement of confidentiality and anonymity? | All participants are given an alphanumeric code (all identifiers removed) to be used for all data related to the study (digital and in any lab notebooks or forms). Consent forms are the only documents on which participant alphanumeric codes and their names are present. These forms are securely stored in a locked cabinet within the office of Dr. Mark Rakobowchuk. These forms will be stored in this manner for five years following the completion of the study data collection phase. All other documents, including participant data files, are alphanumerically identifiable only. Additionally, during the presentation of data no personal identifiers will be disclosed. Only summary statistics are presented at meetings and in presentations or publications. |
| 7.3 | Will you be using a transcriber? If yes, please provide a copy of a Transcriptionist Confidentiality Agreement with this application. | No |
| 7.4 | What are the specific details of storage and disposal of records/data? (Standard retention timeline is 5 years before disposal) | All data files, consent forms, and other documentation containing data will be stored in a locked cabinet within the office of Dr. Mark Rakobowchuk. Data disposal will be completed five years following completion of the data collection phase of the study, through confidential waste streams within the department. Electronic data files will be stored on the personal network space provided by TRU (Onedrive secure storage in Canada). Additionally, a copy of previously coded anonymous data will be kept on a password protected and encrypted removable storage drive in the office of Dr. Mark Rakobowchuk. This data will be deleted at that stage by writing over the data with zeros multiple times. |
| 7.5 | Will any data that identifies individuals be available to persons or agencies outside the Research Group? If yes, provide justification and assessment of risk. | No. The data will only be used by this group and should any data be shared with other researchers in the future, an amendment will be made to include them in the ethics application. In that case, the data that would be shared would be anonymous and participants information would not be shared. |
| 7.6 | Will your project use (please check all that apply) | Questionnaires (attach copy) |

**8. Additional Information**

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| **#** | **Question** | **Answer** |
| 8.1 | Provide any additional information you may wish to provide in this area. |  |

**9. Checklists & Good Practices**

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| **#** | **Question** | **Answer** |
| 9.1 | CONSENT: Title of Project - Have you included the title on your consent form? | Yes |
| 9.2 | CONSENT: On your consent form have you included the identification of investigators (including telephone numbers? | Yes |
| 9.3 | CONSENT: On your consent form have you included a brief but complete description (in non technical language) of the purpose of the project and all procedures to be carried out in which the participants are involved | Yes |
| 9.4 | CONSENT: On the consent form have you indicated in some way that the identity of the participant will be kept confidential and a description of how this will be accomplished? | Yes |
| 9.5 | CONSENT: On the consent form have you provided a statement of the total amount of time that will be required of the participant? | Yes |
| 9.6 | CONSENT; On the consent form have you provided details of monetary or other compensation, if any, to be offered to participants? | Yes |
| 9.7 | CONSENT: On the consent form did you offer to answer any inquiries concerning the procedures to ensure that they are fully understood by the participant and to provide a debriefing if appropriate? | Yes |
| 9.8 | CONSENT: On the consent form did you provide a statement of the participants right to withdrawal or refusal to participate will be jeopardize further treatment, medical care or influence class standing as applicable? | Yes |
| 9.9 | CONSENT: On the consent form did you provide a place for signatures of the participant consenting to participate in the research project, investigation or study? | Yes |
| 9.10 | CONSENT: On the consent form did you provide a statement acknowledging receipt of a copy of the consent form including any attachments? | Yes |
| 9.11 | CONSENT: On Parental Consent forms - Did you provide a statement of choice providing an option for refusal to participate (e.g. "I consent/do not consent to mu child's participation in this study") | N/A |
| 9.12 | CONSENT: On the consent form did you provide the contact information for the relevant Dean and Chair of the REB? (Chair contact information: TRU-REB@tru.ca or 250.828.5000) | Yes |
| 9.13 | CONSENT: On the consent form did you provide a statement as to what the information will be used for (presentation, publication, etc)? | Yes |
| 9.14 | CONSENT: On the consent form did you provide a statement as to how the participant can receive a copy of executive summary of completed projects and where appropriate, receive updated information during thecourse of the research? | Yes |
| 9.15 | CONSENT: On the consent form did you provide a statement of the likelihood of any discomforts and/or conveniences associated with the participation and known or suspected short or long term risks, and factors which might lead to refusal to participate? | Yes |
| 9.16 | CONSENT: Use this space to provide details on an item in which you indicated N/A regarding the CONSENT FORMS | 9.11 We do not have a parental consent form. |
| 9.17 | QUESTIONNAIRE: On the questionnaire did you include the title of your project? | N/A - Explain below |
| 9.18 | QUESTIONNAIRE: On the Questionnaire did you identify the investigator (including phone numbers) | N/A - Explain below |
| 9.19 | QUESTIONNAIRE: On the questionnaire did you include a brief summary that indicates the purpose of theproject, including potential presentation and publication if applicable? | N/A - Explain below |
| 9.20 | QUESTIONNAIRE: On the questionnaire did you provide a statement as to the benefits to be derived? | N/A - Explain Below |
| 9.21 | QUESTIONNAIRE: On the questionnaire did you provide a full description of the procedures to be carried out in which the participants are involved? | N/A - Explain below |
| 9.22 | QUESTIONNAIRE: On the questionnaire did you provide a statement of the participants right to refuse to participate or withdraw at any time without jeopardizing further treatment, medical care or class standing as application? | N/A - Explain below |
| 9.23 | QUESTIONNAIRE: On the questionnaire did you indicate the amount of time that will be required by the participant? | N/A - Explain Below |
| 9.24 | QUESTIONNAIRE: On the questionnaire did you provide a statement that indicates if the questionnaire is completed it will be assumed that consent has been given? | N/A - Explain Below |
| 9.25 | QUESTIONNAIRE: On the questionnaire did you provide assurance that the identity of the participant will be kept confidential and description of how this will be accomplished? | N/A - Explain below |
| 9.26 | QUESTIONNAIRE: On any questionnaire that will be circulated by mail did you include a copy of the explanatory letter as well as a copy of the questionnaire with this application? | N/A - Explain Below |
| 9.27 | QUESTIONNAIRE: Explain any reasons that you may have indicated N/A for any of the above questionnaire items. | No, questionnaires are used to gather data from our participants. A PAR-Q form is used for screening purposes. |