LIVERPOOL JOHN MOORES UNIVERSITY
PARTICIPANT INFORMATION SHEET

Title of Project

Skin function and morphology: effects of age and physical activity

Name of Researcher and School/Faculty

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Research Supervisors: Dr David Low, Prof Helen Jones, Prof Dick Thijssen

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You are being invited to participate in a research study. Before deciding whether to take part, it is important that you understand why this research is being done and what it involves. Please take some time to read the following information sheet and familiarise yourself with the project; if anything is unclear to you, or you would like more information, then please ask. Take time to decide if you wish to take part or not.

1. What is the purpose of the study?

The skin is the largest and most accessible organ in humans, and acts as a barrier between our internal and external environments. It also helps regulate blood flow and body temperature through a vast array of structures, such as small blood vessels called capillaries. Cardiovascular disease is the leading cause of death globally, and the risk of disease is higher with ageing and inactivity. The small vessels of the body, such as those in your skin, are affected before the larger vessels, such as those supplying your brain and heart. We know that the function of skin blood vessels are affected by age and physical activity, but we are not sure what happens to the key structures in the skin during such processes. Skin biopsies allow researchers to look at these small skin structures to better understand how ageing and physical activity affect such structures. This study hopes to recruit 60 participants from various ages and physical activity levels in order to assess and compare skin blood vessel function and structure.

2. Do I have to take part?

No, it is entirely your choice whether you want to take part in this study. If you do, you will be asked to sign an informed consent form. This confirms your willingness to take part.
You are free to withdraw from the study at any point, and you don't have to give a reason. This will not affect your future status should you wish to participate in any further studies or interventions.

3. What will happen to me if I take part?

Before participation, you will be required to complete a health questionnaire and a physical activity questionnaire (IPAQ). These ensure you are suitable to take part, and that there isn't any reason you can't take part. No information from this screening will be shared and the data will be securely stored and destroyed after the study has finished if you participate, or destroyed immediately if you cannot participate.

The inclusion criteria for taking part are:

- Aged 18-30 years old **OR** aged 60-75 years old, **AND**
- Recreationally active (less than 3 hours per week moderate-intense exercise)
  OR
- Aged 18-45 years old **AND**

- Endurance/distance-runner **OR** racquet-sportsman (tennis, squash, badminton) **OR** rock climber/boulderer participating in training equal to or more than 3 sessions per week, 30 minutes or more per session, for a period of 2 years or over.

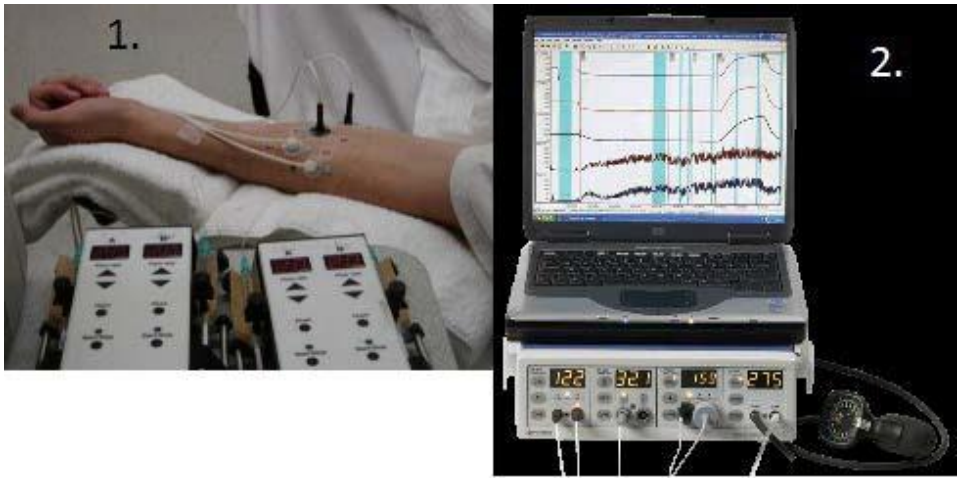
We will exclude people with the following;

- Pre-existing heart conditions
- High blood pressure
- Diabetes
- High cholesterol
- Previous heart attack or stroke
- On heart medications
- Current smokers
- History of any bleeding disorders, medications (anticoagulants) that might affect bleeding or a history of bleeding problems after a surgery or local procedure

These questionnaires will be followed by a full verbal explanation of all of the different tests and procedures. If you would like to participate in the study you will also be asked to sign a consent form. Subsequently, we will plan the testing days.

The study involves a single visit to the physiology laboratories in the Tom Reilly Building, Byrom Street, Liverpool John Moores University. This will last approximately 3 hours. Before each visit, you must fast from food for at least 6 hours, and should not exercise or consume alcohol or caffeine for 24 hours prior to testing. Water can be consumed up to arriving at the laboratory. You will undergo two procedures as follows;

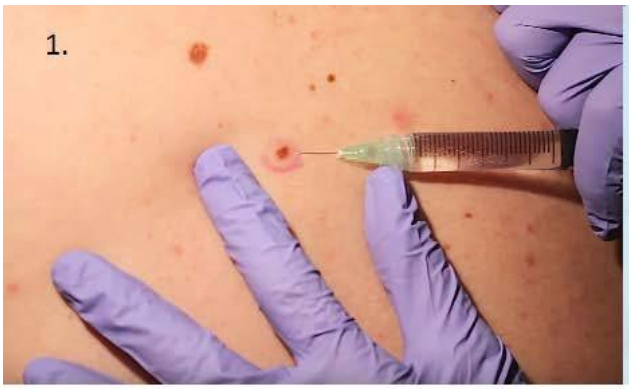
Skin blood flow measurement – This technique measures the movement or flow of blood within the skin, and provides information on how well the skin is functioning. A small probe and separate heating-disc (1.) will be attached to the skin of one of your forearms, at first, and then to one of your calves. The temperature under the disc slowly increases from 33°C to 44°C, which changes the skin blood flow in that area. The probe then measures these changes in flow (2.). This process should take around 1.5 hours.



Blood pressure / heart rate – a cuff will be placed on the upper portion of your arm not being assessed for blood flow to monitor blood pressure. The cuff will inflate at the start, end, and periodically during the procedure. Inflation of the blood pressure cuff during the protocol may cause a mild sensation of “pins and needles” in your arm, but this will disappear when the cuff is deflated.

Skin punch biopsy (see image below) – This is collected from the same sites tested above for skin blood flow. This will allow the researcher to look at the microscopic structures in the skin, known as the ‘morphology’ of the sample. The skin will be made sterile via cleaning with alcohol/antimicrobial wipes. A small amount of local anaesthetic (‘Marcain’) will then be injected under the skin at the marked site of investigation (1). This will be left

for 10 minutes to give the injection time to work. When fully anaesthetised (numb), a 'punch' instrument (like a hollow pencil, 2) will collect a 3mm diameter biopsy. This biopsy is then placed in a specimen container (3), and stored at -80°C in a freezer within the Life Sciences Building, Liverpool John Moores University, and is accessible only by authorized personnel. The biopsies will have chemical stains added to them which highlight the blood vessels within them under a microscope, and we will compare the amount of blood vessels between each participant. The biopsy samples the top 2 layers of skin, and will not require any stitches. The biopsy site will be bandaged with gauze and tape after collection, and should heal completely within 7-10 days. Topical creams, gels, or ointments may be applied to the site during this period by the participant if they feel it necessary. We want to obtain samples from 'normal' skin, and so we will avoid taking samples from any parts of your skin which has lesions or pigmentation. If no such site can be found to take the biopsy from, we will remove you from the study.



4. Are there any risks / benefits involved?

The increasing heat under the heater-discs may cause a slight warm sensation at the site of heating on your arm, however it will not leave any permanent marks or cause damage to your skin after the experiment. Although it is unlikely, some participants may experience some discomfort or pain during this heating process, therefore a familiarisation session is offered to potential participants who wish to confirm whether or not they want to continue with the study. You will also be constantly monitored during the assessments and can provide feedback immediately if you feel it is too uncomfortable.

The inflation of the blood pressure cuff can cause a slight feeling of "pins and needles" in the arm, but this will disappear once the cuff is deflated.

The local anaesthetic can cause some discomfort or pain whilst the injection is in place before the anaesthetic starts to work. The needle used is small and the solution will be injected slowly to prevent discomfort. The local anaesthetic can take some time to take effect, so plenty of time will be allowed to make sure the area is fully numbed, and this will be thoroughly checked before the procedure begins.
Allergic reactions to Marcain are rare, and can cause tingling, itching, faintness, nausea, reddening of the skin, swelling of the skin, and anaphylaxis. For this reason, if you are known to have, or suspect you are, allergic to local anaesthetic/Marcain/amide-group anaesthetics you will not be able to participate in this study.

The biopsy instrument measures 2-3mm in diameter, and a small wound will be left after sampling. No stitches will be required, minor complications (bleeding, bruising, infection etc.) are rare, and full healing will take place within 7- 10 days. This procedure is a standard tool which has been used in research and clinical practice over the last 25 years. Trained staff will perform the biopsies and have extensive experience of this procedure. You will not feel any pain during the biopsy due to the effects of the local anaesthetic. The biopsy procedure may cause mild discomfort or a feeling of pressure, but this shouldn't last long. The procedure will take place under sterile conditions to minimize the risk of infection, and a bandage/gauze will be applied after sampling to cover the wound. This should be removed after ~24 hrs and a new bandage/gauze applied at your discretion. A small scar may form where the biopsy was collected. We will give you all the instructions you need to reduce any risks to an absolute minimum on the day. In the unlikely event you experience any of the above symptoms after your visit,

please feel free to contact us for advice, or visit your local GP.

At any time during the experiment, you are free to voluntarily terminate the procedure and stop the experiment. You are also free to leave the study at any point, without reason, and all data collected will be destroyed accordingly. There are no personal benefits associated with participating in this study, but the data will be useful for researchers investigating cardiovascular disease, diabetes, ageing, and ways of diagnosing these conditions.

Infection can be serious; therefore, if you experience a lot of bleeding from the biopsy site, swelling or infection around the biopsy site, light headedness, heart pain, chest pain or increasing pain which is not relieved by Paracetamol, you must contact the study team who will put you in touch with the study medic. However, if for some reason, you are not able to the study team then you should contact your GP.

THIS STUDY HAS RECEIVED APPROVAL FROM LJMU's RESEARCH ETHICS COMMITTEE: 17/SPS/005

5. Will my taking part in the study be kept confidential?

All the information gathered will be kept strictly confidential. All data will be anonymised. All information and data will be stored in accordance with current Data Protection Act legislation. A secure site for data storage will be used within the School of Sports & Exercise Sciences, Liverpool John Moores University, and will be kept for a period of 5 years. All computer files will be password protected and subject identities coded so that only the investigators can gain access to participant information, and data cannot be traced back to any participants. Biopsy samples are stored in accordance with the Human Tissue Act (HTA, 2004) in the Life Sciences Building, Liverpool John Moores University, and are kept anonymised with Subject ID codes. Samples are destroyed after analyses have been performed on them, and are not shared with any external parties. Personal/contact details will be store separately from the health screening information. We will not disclose individual results to anyone unless you specifically request such information that is relevant to you. We will combine all the results from the many participants taking part in the study, and publish any important results in medical journals and in the departmental reports confidentially. This will not affect the security of the information given for the study.
There is a possibility that the biopsy samples obtained will be further used for future research studies by the University and/or commercial partners. If this is the case, your confidentiality will be maintained throughout the sharing process. The samples will not leave the premises of the University in any circumstance.

If you wish to make a complaint, please contact researchethics@ljmu.ac.uk and your communication will be re-directed to an independent person as appropriate.

6. What to do if you wish to take part?

If you do wish to take part in this study, please contact the principal investigator (by email or telephone). Please note that you are free to withdraw from this project at any time. Signing the consent form does not release or waiver any rights that you have. Participation in this investigation is voluntary and you have the right to withdraw from this investigation at any point with no explanation.

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