Exercise as a countermeasure against the effects of ageing on muscle mitochondria, diffusive oxygen transport and muscle volume

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON56510

Source
ToetsingOnline

Brief title
Skeletal muscle mitochondria in ageing/AGAMEMNON

Condition

- Other condition

Synonym
Healthy ageing

Health condition

Healthy ageing

Research involving

Human

Sponsors and support

Primary sponsor: Vrije Universiteit
Source(s) of monetary or material Support: Amsterdam Movement Sciences Ageing & Vitality Grant

Intervention

Keyword: Ageing, Exercise, Mitochondria, Muscle

Outcome measures

Primary outcome

The primary outcomes are: maximal oxygen uptake (V*O2max), muscle volume, muscle strength, muscle power, muscle diffusing capacity for oxygen (DmO2), and indicators of mitochondrial morphology.

Secondary outcome

The secondary parameters can be categorised into the following groups of variables: exercise capacity, mitochondrial content and morphology, ex-vivo mitochondrial respiratory function, in vivo mitochondrial energetics, histology and immunohistochemistry, muscle morphological variables, mitochondrial dynamics proteins, and physical activity status. Further details are given in the protocol section 8.1.2.

Study description

Background summary

Healthy ageing is associated with a loss of muscle mass and physical function. This loss of physical function is underpinned by reductions ins characteristics such as muscle strength, power, and maximal oxygen uptake (V*O2max; reflecting exercise capacity). However, the causal contributors to these age-associated

impairments, and the role of exercise training status in mitigating them, remain poorly defined. Skeletal muscle mitochondrial function has been proposed to be a key contributor to age-associated effects on physical function, however many conflicting results are present in the extant human literature. Moreover, diffusion of oxygen from capillaries to mitochondria is a key determinant of V*O2max, however, whether the skeletal muscle diffusive capacity for oxygen (DmO2) declines with age is unknown. A new technique utilizing near-infrared spectroscopy (NIRS) will enable the non-invasive assessment of skeletal muscle diffusive capacity in young and elderly subjects for the first time to resolve this issue.

Study objective

The primary aims of this study are therefore to 1) compare DmO2 derived via NIRS between young sedentary, young endurance-trained, older sedentary, and older endurance-trained subjects; 2) to compare non-invasive (i.e. with NIRS and 31phosphorous magnetic resonance spectroscopy [31P-MRS]) and invasive (i.e. measures of mitochondrial morphology and respiration obtained by skeletal muscle biopsy) markers of mitochondrial function between the same groups, and 3) to assess the relationships between DmO2, mitochondrial measures and assessments of capillarization with functional measurements of muscle strength, power, and V*O2max.

Study design

This study will be a cross-sectional study comparing young sedentary, young endurance-trained, middle-aged sedentary, and middle-aged endurance-trained subjects. Assessments of muscle strength and power will be performed via isometric and isoinertial dynamometry; muscle volume will be determined via 3D-ultrasound; exercise capacity and V*O2max will be assessed via an incremental exercise test. DmO2 will be assessed via NIRS and 31P-MRS-derived [phosphocreatine] recovery kinetics will be used to validate NIRS-based assessment of DmO2. Skeletal muscle biopsies will be obtained from the vastus lateralis muscle of the quadriceps to assess mitochondrial respiration, morphology, and the concentrations of proteins involved in mitochondrial dynamics.

Study burden and risks

Participants in this study will be asked to perform physical exercise tests, give a muscle biopsy, fingertip blood samples (three times), and undergo a series of brief (5-10 s) intermittent arterial occlusions as well as a prolonged (120 s) arterial occlusion. There is some extent of burden and risk associated with obtaining muscle biopsies, however, this will be mitigated by the fact that these procedures will only be carried out by highly trained physicians.The risks of the physical exercise measurements and fingertip blood

samples are negligible. The arterial occlusion procedures are uncomfortable, however they are not associated with any adverse effects and are regularly used and well-tolerated in our laboratory.
There is a significant time investment on behalf of the participants, since participants are required to visit the laboratory on six occasions for a total of 8 hours. Participants will receive compensation for parking, travel costs, and will receive 100 Euros upon completion of the study. However, there are no direct benefits related to participating in this research. The findings of this research will provide insight into the skeletal muscle ageing process and the mediating influence of exercise.

Contacts

Public
Vrije Universiteit

Van der Boechorststraat 7
Amsterdam 1081BT
NL
Scientific
Vrije Universiteit

Van der Boechorststraat 7
Amsterdam 1081BT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, young sedentary participants must meet all of the following criteria:
• Aged between 18-30 years
• Male or female
• Not currently engaging in any formal exercise training or competitive sports
• No chronic health conditions likely to affect exercise tolerance or the physiological responses to exercise

In order to be eligible to participate in this study, young trained participants must meet all of the following criteria:
• Aged between 18-30 years
• Male or female
• Currently engaging in formal training (at least 3 times per week) in competitive endurance sports
• No chronic health conditions likely to affect exercise tolerance or the physiological responses to exercise

In order to be eligible to participate in this study, older sedentary participants must meet all of the following criteria:
• Aged between 50-65 years
• Male or female
• Not currently engaging in any formal exercise training or competitive sports
• No chronic health conditions likely to affect exercise tolerance or the physiological responses to exercise

In order to be eligible to participate in this study, older trained participants must meet all of the following criteria:
• Aged between 50-65 years
• Male or female
• Currently engaging in formal training (at least 3 times per week) in competitive endurance sports
• No chronic health conditions likely to affect exercise tolerance or the physiological responses to exercise

Exclusion criteria

• Age that falls outside of 18-30 years (young groups) or 50-65 years (middle-aged groups)
• Inability to provide informed consent
• History of claustrophobia
• Ineligibility to perform the exercise test described in this study protocol or follow instructions

• Contraindication for MRI (e.g. pacemaker, claustrophobia; see F1 vragenlijsten screening MRI Amsterdam)
• Being under investigation for non-diagnosed disease at the time of investigation
• Risk factors for exercise testing registered by a Dutch version of the pre-participation questionnaire (American college of sports medicine and American Heart association). Possible risk factors will be discussed with a medical specialist or general practitioner before a subject can be included
• BMI >30 due to adiposity, since this is known to cause difficulties in obtaining muscle biopsies and NIRS measurements
• Vastus lateralis adipose tissue thickness >10 mm due to difficulties in obtaining high quality NIRS data
• Pregnancy
• Are current smokers or have been a regular smoker within the last 12 months

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-03-2024
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	24-01-2024
Application type:	First submission

Review commission: METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85101.018.23