Mitochondrial Capacity and Acylation in Young and Elderly Males

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

Summary

ID

NL-OMON45934

Source
ToetsingOnline

Brief title
MCAGE

Condition

- Other condition
- Muscle disorders

Synonym
Ageing, Sarcopenia

Health condition

Veroudering

Research involving
Human

Sponsors and support

Primary sponsor: Wageningen Universiteit
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Ageing, Mitochondrial capacity, Near-infrared spectroscopy, Post translational modifications

Outcome measures

Primary outcome

The main study parameter is mitochondrial capacity, measured as the rate of recovery of muscle oxygen consumption after exercise measured using NIRS in the vastus lateralis, gastrocnemius and tibialis anterior.

Secondary outcome

Muscle acylation status is analysed in muscle biopsies from the vastus lateralis. Physical activity is monitored using a wearable accelerometer over a period of seven days and a 24 hour urine is collected in order to analyse markers of mitochondrial function in urine. Blood is collected to analyse markers of mitochondrial function in plasma.

Study description

Background summary

Ageing is associated with a decline in muscle mitochondrial function. Measuring muscle mitochondrial function is challenging and to routinely assess mitochondrial function in response to exercise and dietary interventions, practical, non-invasive and robust measurements are needed. Near-infrared spectroscopy (NIRS) is a novel technique that allows to non-invasively measure mitochondrial capacity in the human muscle. Although the technique is promising for measuring mitochondrial function during ageing, it is yet be established how age-related changes in mitochondrial function differ between different

muscle types.

Apart from monitoring mitochondrial function non-invasively, there is a need to mechanistically understand the ageing process in the mitochondrion. The post-translational modification (PTM) of histones and other proteins by acylation has been identified to impact metabolism and gene transcription in the cell. Age-related changes in metabolism are likely to affect levels of acyl groups in the cell, hereby altering acylation patterns and regulating transcription and protein functionality. Sirtuins are a class of enzymes that exert deacylation activity and regulate acylation levels in the cell. Sirtuins are dependent on the cofactor nicotinamide adenine dinucleotide (NAD). Levels of NAD decline during ageing in humans, possibly further impacting acylation status in the cell. The reversible nature of PTMs suggests an interesting target for dietary and exercise interventions in vivo. Further research on how acylation is affected by age is needed, especially in apparently ageing tissues such as the skeletal muscle.

Study objective

The primary objective of this study is to measure mitochondrial capacity using NIRS in young and older healthy males in three different muscles (vastus lateralis, gastrocnemius and the tibialis anterior) to give insights on how age-related changes in mitochondrial function differ between different muscle types. The secondary objective is to analyse the effect of age on acylation status of the muscle. The relationship between mitochondrial function and acylation status will be explored. Furthermore, physical activity is monitored using accelerometry and plasma and 24-hour urine in collected to scan for markers of mitochondrial function.

Study design

Cross sectional study

Study burden and risks

No direct health benefits for the subjects are expected. The experimental procedures are safe, but can cause discomfort to a certain degree. The invasive measurements, blood sampling and muscle biopsy, can cause pain and local hematoma or bruising. Non-invasive measurement of mitochondrial capacity using NIRS makes use of arterial occlusions by external pressure, which can be painful or uncomfortable and possibly could bruise the site of the occlusion. Slight adjustments in daily life are asked from the subjects; e.g. the subject is asked to refrain from physical activity and alcohol before the test days and are expected to fast overnight. A financial compensation for the time investment of ¤75 is offered when completing the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Young
* Male, 19-25 years
* BMI 18.5-27 kg/m2
* Normal activity levels: 1-2 times per week engaged in a structured exercise session ;Elderly
* Male, 65-71 years
* BMI 18.5-27 kg/m2
* Normal activity levels: 1-2 times per week engaged in a structured exercise session
* Short physical performance battery score >6

Exclusion criteria

* (known symptoms of) Metabolic diseases, e.g. type I or II diabetes,
* Health concerns regarding respiratory and pulmonary diseases, e.g. COPD, (exercise induced) asthma and cardiovascular disease.
* Impaired physical performance (defined as short physical performance battery score < 6) (only for elderly)
* Contraindications for electrical stimulation, e.g. cardiac pacemaker
* Contraindications for muscle biopsy, e.g. usage of anticoagulants (low dose aspirin allowed)
* Regular smoker (defined as smoking >5 cigarettes per week)
* Vastus lateralis skinfold > 30mm (due to tissue penetration depth of near-infrared light)
* Haemoglobin concentrations below 8.0 mmol/L
* Usage of recreational drugs, e.g. marihuana, amphetamines and cocaine during the study (starting after first screening day)
* Recent usage (within four months) of supplements with suggestive training effects, e.g. creatine phosphate, EPO or anabolic steroids.
* Current or recent (< 2 weeks) participation in other clinical trials
* Employed or undertaking a thesis or internship at the department of Human and Animal Physiology

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-09-2018
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	13-08-2018
Application type:	First submission
Review commission:	METC Wageningen Universiteit (Wageningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 22045
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL65872.081.18
OMON	NL-OMON22045