Mitochondrial Coupling Efficiency, Respiration and Vitamin B2 status in Untrained and Endurance-trained Young Females

Published: 05-08-2019
Last updated: 19-03-2025

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

Summary

ID

NL-OMON48355

Source
ToetsingOnline

Brief title
B-MCORE

Condition

- Other condition

Synonym
metabolism, vitamin B2 status

Health condition

metabolisme

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Metabolism, Mitochondrial respiration, Training status, Vitamin B2 status

Outcome measures

Primary outcome

The main study parameters are mitochondrial function in PBMCs measured using the Seahorse XFe96 analyser, expressed as mitochondrial oxygen consumption (pmol O2/min), and vitamin B2 status, measured using the erythrocyte glutathione reductase (GR) activity coefficient (EGRAC) combined with plasma and urine vitamin B2 and derivative analysis.

Secondary outcome

Subjects will be screened for VO2max, measured using an incremental exercise protocol on a bicycle ergometer. Sixteen endurance-trained and sixteen untrained subjects will be included based on their VO2max. These subjects are invited to the two study days, in a fasted state. The two study days will take place on two consecutive days. Blood samples will be collected during both study days to analyse mitochondrial respiration, vitamin B2 status, and markers of mitochondrial function, metabolic health and immune function. In addition, 24-hour urine will be collected to analyse vitamin B2 status and markers of mitochondrial function and metabolism. Muscle mitochondrial function will be assessed in the gastrocnemius and flexor digitorum superficialis using

transient arterial occlusions and NIRS measurements. Subjects will conduct an exercise protocol on a bicycle ergometer for 60 minutes at 70% of their VO2max. Subjects will be asked to adhere to dietary guidelines to standardize their intake of vitamin B2, and to record their food intake during the first study day. Physical activity is monitored using a wearable accelerometer in the period between the two study days.

Study description

Background summary

Extensive endurance training puts a high energy demand on the human body. Macronutrient as well as micronutrient requirements should be met to support the generation of energy. Mitochondria generate energy by the oxidation of macromolecules, and vitamins and minerals are essential to support mitochondria during substrate oxidation. Although all B-vitamins are involved in mitochondrial function, vitamin B2 is of particular interest as it is directly involved in energy generation and ROS production. Furthermore, in human studies, exercise was negatively associated with vitamin B2 status and trained individuals have been reported to have poor vitamin B2 status. Previously, we observed compromised mitochondrial function in PBMCs from endurance-trained individuals. We now want to address the role of vitamin B2 in endurance-trained individuals, and its role in supporting mitochondrial PBMC function as well as other cellular function. Since we previously demonstrated that muscle mitochondrial recovery constants, as measured by NIRS, are excellent non-invasive markers of mitochondrial capacity in muscle, we will use NIRS to characterize muscle mitochondrial capacity in our participants, and study the association with vitamin B2 status.

Study objective

The primary objective of this study is to measure mitochondrial function in PBMCs from endurance-trained and untrained young females and link it to vitamin B2 status. Secondary objectives are to compare basal and exercise-stimulated mitochondrial function in PBMCs and vitamin B2 status, to understand how exercise impacts PBMC metabolism and vitamin B2 status and to study whether this differs between endurance-trained and untrained individuals. Characterization of muscle mitochondrial capacity will be measured using NIRS to study the association between vitamin B2 status and muscle mitochondrial

function. Furthermore, markers of mitochondrial and metabolic health will be analysed to investigate the mechanistic link between mitochondrial function in PBMCs and vitamin B2 status

Study design

Observational study

Study burden and risks

No direct health benefit for the subjects is expected. The experimental procedures are safe, but can cause discomfort to a certain degree. The exercise test could lead to muscle fatigue and soreness afterwards. Blood sampling can cause 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 adhere to dietary guidelines, refrain from physical activity and alcohol before the test days and is expected to fast overnight. Also, the participant is asked to fill out questionnaires. 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

* 18-28 year old female
* BMI 18.5-25 kg/m2
* VO2max * 37 mL/kg/min or VO2max * 47 mL/kg/min

Exclusion criteria

* Health concerns regarding respiratory and pulmonary diseases, for example COPD or (exercise induced) asthma;
* (Known symptoms of) chronic diseases, for example cardiovascular disease and cancer;
* (Known symptoms of) metabolic diseases, for example type I or II diabetes or hyperthyroidism;
* (Known symptoms of) inborn metabolic diseases, for example glucose-6-phosphate dehydrogenase (G6PD) deficiency;
* (Known symptoms of) hematological disorders, for example anemia or disturbed red blood cell formation;
* Haemoglobin concentrations below 7.5 mmol/L;
* Regular smoker (defined as smoking >5 cigarettes per week);
* Lactating or pregnant;
* Following a veganistic lifestyle, i.e. excluding the consumption of animal or animal-derived food products. Vegetarians are allowed to participate in the study;
* Usage of hormonal contraceptive medication other than the birth control pill Microgynon 20/30 or a generic variant containing 0.02/0.03 mg ethinylestradiol and 0.10/0.15 mg levonorgestel. Examples include IUD contraceptives or contraceptive rings. The use of condoms or pessaria is allowed;
* Recent use (within four months) of supplements with suggestive training effects, for example creatine phosphate, EPO or anabolic steroid;
* Recent daily usage (within four weeks) of supplements containing vitamin B2 (including multivitamin supplements) and usage of vitamin B2 supplements during the study;

* Usage of recreational drugs, for example marihuana, amphetamines and cocaine during the study (starting after first screening day);
* Suffers from (sport) injury that hampers maximal exercise performance;
* Blood donation during the previous 2 months or during the course of study;
* Current participation in other clinical trials;
* Not subscribed to a general practice (GP) practice;
* 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:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-10-2019
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO

Date:	05-08-2019
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: 24874
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL70136.081.19
Other	Wordt nog toegekend door het Nederlands Trial Register
OMON	NL-OMON24874