Day-night rhythm in muscle metabolism of prediabetic subjects

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The main objective is to investigate the presence of a day-night rhythm in skeletal muscle mitochondria of participants with prediabetes. Secondary objectives include linking this rhythm to variations in whole body energy consumption and exploring...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON46463

Source
ToetsingOnline

Brief title
Day-night rhythm in muscle metabolism of prediabetics

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
n.v.t.

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Cardiovasculair Onderzoek Nederland (CVON)

Intervention

Keyword: Circadian rhythm, Day-night rhythm, metabolism, Skeletal muscle

Outcome measures

Primary outcome

The main end-point is a day-night variation/rhythm in skeletal muscle mitochondrial function.

Secondary outcome

Secondary study parameters are day-night variations/rhythms in whole-body energy metabolism, skeletal muscle mRNA and protein levels and liver triglyceride concentration.

Study description

Background summary

Many processes in the body are synchronised to a day-night rhythm, mastered centrally in de hypothalamus. However, in our 24/7 culture, we often do not obey to the day-night cycle imposed upon us by nature. Recent evidence from both observational and experimental studies indicates that this behaviour negatively influences our metabolic and cardiovascular health, possibly leading to obesity and type 2 diabetes mellitus (T2DM). An important hallmark of obesity and T2DM is a decreased skeletal muscle mitochondrial function, which can be restored by activating the AMPK, SIRT1 pathway. Interestingly, recent research indicates that also AMPK and SIRT1 are under the influence of a day-night rhythm, suggesting that this rhythm would also be present in skeletal muscle mitochondrial function. However, to date, no information is available on a day-night rhythm of mitochondrial function in human skeletal muscle of subjects with prediabetis. Yet, this information is important: if mitochondrial metabolism is indeed regulated in a day-night rhythm it may open opportunities for of the timing of (drug) treatment to improve mitochondrial metabolism, thereby opening new leads for therapeutic interventions in T2DM.

Study objective

The main objective is to investigate the presence of a day-night rhythm in

skeletal muscle mitochondria of participants with prediabetes. Secondary objectives include linking this rhythm to variations in whole body energy consumption and exploring day-night differences in liver triglyceride content.

Study design

In this observational study, subjects are asked to adhere to a normal lifestyle 1 week prior to the test period, with standardized eating and sleeping time, validated by diaries and accelerometry. During the test period, subjects remain at the research center for 44 hours, with standardized meals, eating time, mild exercise (walking) and sleeping time. In the evening of day 1 and the morning of day 2, subjects will undergo an MRS scan of the heart. Furthermore, during the second test day and night, five muscle biopsies are performed at different time points, combined with blood draws and indirect calorimetry.

Study burden and risks

Subjects will report to the university four times and will spend in total about 48 hours at the university (3 short screening and pre-test visits and 1 test period of 44 hours). Subjects will be asked to fill in 2 questionnaires and 1 food and sleep diary. Furthermore subjects are asked to adhere to a standardized lifestyle 1 week before the test period. During the test period subjects will undergo five muscle biopsies and 15 blood draws (from i.v.catheter). Muscle biopsies may be unpleasant and there is a risk of hematoma. The risk of infection or prolonged bleeding is low due to state of the art technique and sterility measures.

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

* Caucasian
* Healthy (as determined by dependent physician based on medical questionnaire)
* Male
* Age: 40-75
* Overweight: BMI 25 * 35 kg/m2
* Prediabetic based on one or a combination of the following criteria:
o Impaired Glucose Tolerance (IGT): plasma glucose values * 7.8 mmol/l and * 11.1 mmol/l 120 minutes after glucose drink consumption during OGTT in screening.
o Impaired Fasting Glucose (IFG): Fasting plasma glucose * 6.1 mmol/l and * 6.9 mmol/l.
o Insulin Resistance: glucose clearance rate * 360 ml/kg/min, as determined using OGIS120.
o HbA1c of 5.7*6.4%.;* Regular sleeping time (normally 7 * 9h daily)
* Stable dietary habits: no weight gain or loss > 3kg in the last three months

Exclusion criteria

* Use of anticoagulants
* Fasting plasma glucose * 7.0 mmol/l
* Haemoglobin < 7.8 mmol/l
* Previously diagnosed with type 2 diabetes
* Any medical condition and/or medication that might interfere with the investigated parameters as judged by study physician.
* Current alcohol consumption > 20 grams alcohol/day
* Subjects who do not want to be informed about unexpected medical findings during the screening /study, or do not wish that their physician is informed, 1 month prior to the screening visit
* Any contra-indication to Magnetic Resonance Imaging (MRI) scanning:
o Any implant or prosthesis that is contra-indicated for MRI (e.g. cardiac pacemaker,

defibrillator, neural stimulator and other)
o Metal containing foreign bodies in the eye or brain
o Any other metal containing objects contra-indicated for MRI scanning (e.g. certain prosthetic limbs, certain tattoos or certain permanent eyeliner*)
o Claustrophobia
o Epilepsy
* Any contra-indication to the Equivital telemetric pill:
o Known or suspected obstructive disease of the gastrointestinal tract
o History of disorders or impairment of the gag reflex
o Previous gastrointestinal surgery
o Felinization of the esophagus
o Hypomotility disorders of the gastro-intestinal tract
* Implanted electromedical device
* Extreme early bird or extreme night person (score *30 or *70 on MEQ-SA questionnaire, document F1-2)
* Heavily varying sleep-wake rhythm
* Nightshiftwork during last 3 months
* Travel across > 1 time zone in the last 3 months
* Engagement in exercise > 2 hours total per week
* Significant food allergies/intolerance (seriously hampering study meals)
* Participation in another biomedical study within 1 month before the first study visit
* Using > 400mg caffeine daily (more than 4 coffee or energy drink)
* Smoking
* Any acute condition, exacerbation of chronic condition, or medical history that would in the investigator*s opinion interfere with the study

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):	17-05-2018
Enrollment:	60

Type:	Actual

Ethics review

Approved WMO Date:	29-03-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-08-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL64753.068.18