The effect of cold acclimation on human brown adipose tissue and skeletal muscle mitochondrial uncoupling -a comparison in obesity and type 2 diabetes

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The primary objectives of this study are: (1) To establish the role of brown adipose tissue in cold-induced thermogenesis before and after a cold acclimation period; (2) to study the involvement of skeletal muscle mitochondrial uncoupling in cold-...

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

Summary

ID

NL-OMON40307

Source
ToetsingOnline

Brief title
Cold acclimation and brown fat - comparison in obesity and type 2 diabetes

Condition

- Other condition

Synonym
type 2 diabetes and overweight

Health condition

type 2 diabetes en overgewicht

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Brown adipose tissue, Cold acclimation, Obesity, Type 2 diabetes

Outcome measures

Primary outcome

1. To establish the role of brown adipose tissue in cold-induced thermogenesis

before and after a cold acclimation period

2. To study the involvement of skeletal muscle mitochondrial uncoupling in

cold-induced thermogenesis

3. To study the effect of chronic cold exposure on the white adipose tissue

depot

Secondary outcome

1. To study the effect of short-term and chronic cold exposure on relevant

blood parameters

2. To establish the effect of short-term and chronic cold exposure on body

temperatures and skin temperatures

3. To establish the role of polymorphisms in the UCP-1 and beta-3 receptor gene

on BAT activity and cold-induced thermogenesis.

Study description

Background summary

Upon mild cold exposure people can increase their energy expenditure. This is called non-shivering thermogenesis (NST). Moreover, during prolonged cold exposure NST can increase, this is called adaptive thermogenesis (AT). This metabolic reaction is subject to high inter-individual variability. These differences might be explained by the amount of active brown adipose tissue (BAT). Furthermore, a negative correlation between BAT activity and BMI was found and obese people show an impaired cold-induced thermogenesis. In addition, diabetic status has been associated independently with reduced BAT activity. In rodents, BAT and the skeletal muscle are mainly responsible for NST, and upon chronic cold exposure recruitment of BAT takes place. Recently, we showed that severe weight loss in obese subjects causes BAT recruitment, and BAT activity correlates with NST. Moreover, white fat cells can be converted into brown-like cells, called BRITE cell recruitment. Chronic cold exposure in healthy men showed a decrease in shivering with remaining elevated energy expenditure; this indicates that humans are also capable to increase NST.
It is hypothesized that upon chronic cold exposure in healthy obese adults, with or without type 2 diabetes, BAT and BRITE recruitment will take place. Furthermore, skeletal muscle mitochondrial uncoupling and adaptive thermogenesis will increase.

Study objective

The primary objectives of this study are: (1) To establish the role of brown adipose tissue in cold-induced thermogenesis before and after a cold acclimation period; (2) to study the involvement of skeletal muscle mitochondrial uncoupling in cold-induced thermogenesis and (3) to study the effect of chronic cold exposure on the white adipose tissue depot.

Study design

The volunteers will undergo two PET/CT-scans, in which cold-induced BAT activity will be measured before and after a cold acclimation period of 10 days. To investigate the role of the skeletal muscle mitochondrial uncoupling and BRITE cell recruitment a muscle and fat biopsy sample will be taken prior to the acclimation period and afterwards.

Intervention

Cold exposure. For 10 consecutive days the subjects will be exposed to cold (12 C).
To easily get used to this, exposure will be 2hours at the 1st day, 4hours at the 2nd day and day 3-10 6hours/day.

Study burden and risks

The risks of this study are low.

The total effective dose is low and will not give any risk to the subjects
The total absorbed radiation dose from two FDG-PET/CT-scans after administration of two times 75 MBq of 18F-FDG
is 4.6 mSv.
This is about three times the background radiation in the Netherlands and is below the criteria as stated in ICRP-60,
<10 mSv.

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

* Caucasians
* Age:
o Obese without type 2 diabetes: 18-65 years

o Obese with type 2 diabetes: 18-65 years
* BMI: 28-35 kg/m2
* Fat percentage: > 23%
* Gender: Male
* Specifically for obese subjects with type 2 diabetics:
o Diagnosed with type 2 diabetes at least 1.5 years before the start of the study
o Well-controlled type 2 diabetes: HBA1C < 8.5%
o Oral glucose lowering medication (metformin only or in combination with sulfonylurea agents)
o No signs of active diabetes-related co-morbidities like cardiovascular diseases, diabetic foot, polyneuropathy, retinopathy.
o No signs of active uncontrolled hypertension, liver of kidney malfunction
* Specifically for obese subjects without type 2 diabetes:
o Fasting blood glucose level <6.1 mmol/l
o No signs of active cardiovascular disease, uncontrolled hypertension, liver of kidney malfunction.

Exclusion criteria

* Participate in physical activity more than 2x/week
* Participation in earlier research that included a PET/CT-scan
* Radiation therapy due to medical treatment
* Unstable body weight (weight gain or loss > 5 kg in the last three months)
* Participation in another biomedical study within 1 month before the first screening visit;* Specifically for obese subjects without type 2 diabetes:
o Elevated fasting blood glucose level (> 6.1 mmol/L);* Specifically for obese subjects with type 2 diabetes:
o Impaired kidney- and/or hepatic function
o Diabetes related co-morbidities like cardiovascular diseases, diabetic foot, polyneuropathy, and retinopathy.
o Insulin dependent diabetic subjects

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-01-2014
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	27-11-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-03-2014
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	NL45645.068.13

Study results

Date completed:	23-02-2015
Actual enrolment:	21

Summary results
Trial ended prematurely