The effect of cold exposure on glucose and fat metabolism

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

Summary

ID

NL-OMON47478

Source ToetsingOnline

Brief title The effect of cold exposure on glucose and fat metabolism

Condition

• Glucose metabolism disorders (incl diabetes mellitus)

Synonym Diabetes, type2diabetes

Research involving Human

Sponsors and support

Primary sponsor: Universiteit Maastricht Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cardiovascular disease, cold exposure, fat metabolism, insulin sensitivity

Outcome measures

Primary outcome

* Meal test: metabolism of triglyceride, cholesterol and lipoproteins after a

meal

* Insulin senstivity as determined by hyperinsulinemic euglycemic clamp.

Secondary outcome

* Pulse Wave Velocity: to measure arterial stiffness

* Retina photography: central retinal arterial equivalent (CRAE), central retinal vein equivalent (CRVE) and arteriovenous ratio (AVR).

* Muscle biopsy: molecular analysis of insulin signalling and analysing an

insulin independent pathway causing GLUT4 translocation. Primary myotubes

obtained from the muscle biopsies will be cultured to investigate the

underlying molecular pathway. Skeletal muscle lipid accumulation is measured by

immunofluorescence microscopy.

* Intrahepatic lipid content measured non-invasively with H-MRS

* iButtons: to measure skin temperature during cold exposure

* Bloodsamples: HBA1C, Endothelial/inflammatory markers and energy metabolism markers

* Questionnaires: Thermal sensation and comfort

* Energy expenditure: measured with indirect calorimetry

Study description

Background summary

The number of people with type 2 diabetes is increasing. This metabolic disorder is characterised by failing insulin secretion relative to the body's requirement for insulin, which is typically increased. Diabetes patients are among others at increased risks for cardiovascular disease. Recently it has been suggested that brown adipose tissue may play a role in the etiology of diabetes. To test this hypothesis, we used cold acclimation for 10 days (in order to stimulate brown adipose tissue) to investigate insulin sensitivity in diabetic patients. Very interestingly, we found very pronounced effects of cold acclimation on insulin sensitivity, which could not be explained by BAT, but were associated with an increased GLUT4 translocation in skeletal muscle cells in fasting state, which might indicate that cold acclimation affects muscle (Hanssen et al., Nature Medicine, in press). Given this large effect of cold acclimation on insulin sensitivity, it is very interesting to investigate if cold acclimation will also have beneficial effects on cardiovascular risk factors. The main focus will be on lipid metabolism and vascular function. Furthermore, we want to investigate if the effect will sustain for a longer period of time.

Study objective

The primary objectives of this study are: 1. To examine the effect of cold acclimation on cardiovascular risk parameters in type 2 diabetic patients. 2. To study if the previously observed effect of cold acclimation on insulin sensitivity in type 2 diabetic patients is sustained for a longer period of time. As secondary objectives we will study the underlying mechanism for improved insulin sensitivity due to cold exposure.

Study design

In this study, type 2 diabetic subjects will be exposed to cold for 10 days. These subjects will undergo the following measurements before and immediately after the intervention: hyperinsulinemic euglycemic clamp, muscle biopsies, high fat-meal test in combination with vascular tests and energy expenditure measurements, and a proton magnetic resonance spectroscopy of the liver. These tests will be performed in two experimental days (both before and after the intervention). Between the two experimental days after the intervention, the subjects will be exposed to cold for two other days. In addition, a third hyperinsulinemic euglycemic clamp will be performed 10 days after the intervention to investigate the long-term effect on insulin sensitivity. Furthermore, 64 days after cold acclimation a fasting blood sample will be taken to measure markers for glucose homeostasis.

Intervention

The intervention consists of a 10-day cold acclimation period (the 1st day 2 hours, the 2nd day 4 hours and day 3-10 6 hours).

Study burden and risks

Due to the many actions and measurements during this study the strain for the subjects is substantial. Although complications are rare, each measurement involves some risks. During hyperinsulinemic euglycemic clamp subjects might exhibit symptoms of hypoglycaemia. Muscle biopsies might be complicated by bleeding, infection or nerve damage. After the anesthetics wore off, subjects might exhibit pain. The intravenous canula used during the clamp and meal test may cause a haematoma. The effective dose of the DXA-scan is 1-7 microSievert and this is considered as a low risk.

Contacts

Public Universiteit Maastricht

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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: 45 * 70 years
- * BMI: 27-35 kg/m2
- * Gender: male or female
- * Women should be postmenopausal
- * Diagnosed with type 2 diabetes at least 1.5 years before the start of the study
- * Relatively well-controlled type 2 diabetes: HbA1c < 8.5%
- * Oral glucose lowering medication (metformin only or in combination with sulfonylurea agents)

* No signs of active diabetes-related co-morbidities like active cardiovascular diseases, active diabetic foot, polyneuropathy, retinopathy.

* No signs of active liver or kidney malfunction.

Exclusion criteria

I* Participate in physical activity more than 2x/week

- * Unstable body weight (weight gain or loss > 5 kg in the last three months)
- * Participation in another biomedical study concerning brown adipose tissue within 1 month before the first screening visit
- * Insulin dependent type 2 diabetes patients
- * Smoking
- * Men: HB <8.4 mmol/L, Women: Hb <7.8 mmol/l

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):	16-03-2016
Enrollment:	16
Туре:	Actual

Ethics review

Approved WMO	
Date:	23-12-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	
Date:	20-04-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	
Date:	27-06-2016
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO	
Date:	30-08-2017
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

ССМО

ID NL54084.068.15