The effect of acute whole-body heat exposure on liver insulin sensitivity and substrate metabolism

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To gain insight into the full spectrum of temperature-induced changes in glucose homeostasis, the present study will be aimed at assessing the effect of acute whole-body heat exposure on liver insulin sensitivity, substrate oxidation and plasma...

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

Summary

ID

NL-OMON47966

Source
ToetsingOnline

Brief title
Heat and hepatic insulin sensitivity

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Glucose metabolism, suger metabolism

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ZonMW/PTO

Intervention

Keyword: Heat exposure, Hepatic insulin sensitivity, Substrate utilisation, Thermoregulation

Outcome measures

Primary outcome

Assess the effect of acute, passively administered whole-body heat exposure on

* hepatic insulin sensitivity

* whole-body substrate oxidation

* plasma metabolites.

Secondary outcome

Assess the effect of acute, passively administered whole-body heat exposure on

* measures of thermophysiology,

* cardiovascular parameters

* thermal perception (thermal sensation and comfort)

Study description

Background summary

In a recent study, for the first time it has been shown that repeated exposure to heat beneficially affects liver metabolism and induces a change in whole-body substrate use. After 10 days of mild heat acclimation (6h per day, 10 consecutive days), rate of [glucose] disappearance (Rd) and endogenous glucose production (EGP) were reduced in a fasted state, indicating improved glucose homeostasis. Additionally, fat oxidation was increased after acclimation. Importantly, although it has been shown that parameters of liver metabolism improve after repeated whole-body heat exposure, it is unknown what the acute effects of whole-body heat exposure are on the hepatic insulin sensitivity. In order to get a superior understanding of the underlying mechanisms and relationships between heat and metabolism, and how acclimation effects build up and are established, the present study aims to assess the effect of acute whole-body heat exposure on hepatic insulin sensitivity,

substrate use and related blood parameters in healthy obese volunteers.

Study objective

To gain insight into the full spectrum of temperature-induced changes in glucose homeostasis, the present study will be aimed at assessing the effect of acute whole-body heat exposure on liver insulin sensitivity, substrate oxidation and plasma metabolites in healthy overweight adults between 45 and 65 years, a population group at risk for development of metabolic disorders.

Study design

The study will be set up in a randomised cross-over design. The study will consist of 2 test days in which the test subjects will be exposed to heat on one day and to a neutral temperature on the second day. The two conditions will be offered in random order

Intervention

Heat exposureby means of a water-perfused suit. Water temperature during heat exposure will initially be set at 39*C and adjusted as the test subject's core temperature changes. In the neutral condition, the water temperature will be set to 32*C.

Study burden and risks

We will take frequent blood samples, which can be dangerous in case of anemia. This is why people with a low Hb will be excluded from participation. The total amount of blood that will be taken in 2 days is maximal ~210mL (2x ~100mL during clamp and 10ml during the screening). Blood sampling itself and the infusions can cause bruises. Subjects that use anti-coagulants are excluded from the study. Infections or continued bleeding are very rare. Hyperinsulinemic-euglycemic clamping is a procedure we perform routinely in our laboratory without notable complications. In rare occasions, subjects exhibit symptoms of hypoglycemia (even if their blood glucose levels are still above 3 mmol/L). After successfully performing the clamp, blood glucose values will be monitored for an additional 30-60 minutes with glucose infusion stand-by if glucose levels happen to drop. Solid food and sugar-drinks will be provided directly after finishing the clamp, to avoid the experience of hypoglycemia.

Heat exposure might be perceived as uncomfortable. Especially during the heat condition, core temperature will be closely monitored during the procedures, as described under 6.3.2 of the protocol C1. Maintaining core temperature at a certain level (also called core temperature clamping) has been applied in many previous studies, and has been reported as being a useful and safe tool for standardization of a thermal strain in humans. Investigators will communicate

with the participants throughout the procedures to check comfort and well-being of the participants. It will be ensured that a potential fluid dysbalance cause by sweating during the measurement procedures will be compensated by isotonic fluid intake during and after the clamp.

The Blanketroll ® III system, as described in section 7 of the study protocol C1., is widely used in daily clinical routine to control body temperature and/or maintain a desired temperature. The system works through conductive heat transfer. Investigators involved in the study have obtained sufficient (year-long) experience, with the Blanketroll ® III Hyper-Hypothermia system, which means they can safely use and control it. By closely monitoring the participant*s core temperature as described under 6.3.2 and section 7 of the protocol C1., the risk for hyperthermia above the desired level of mild hyperthermia of ~37.5*C should be negligible.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
* Signed informed consent
* Men and women
* Caucasian / white western European
* Aged 45-65 years at the start of the study
* Body mass index (BMI) 27-35 kg/m2
* Stable dietary habits (no weight loss or gain of more than 5 kg in the past 3 months
* Stable sedentary lifestyle (not more than 2 hours of sports per week)
* Women after their menopause, meaning cessation of menses for at least 24 months) and only if they are not under hormonal treatment
* Suitable veins for cannulation or repeated venapuncture
* Generally healthy, no medication use that interferes with metabolism, no signs of active cardiovascular disease, liver or kidney malfunction. If volunteers need medication, it will be reviewed with the dependent physician on individual basis.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

* Type 2 Diabetes
* Men Haemoglobin <8.4mmol/L, women haemoglobin <7.8 mmol/L
* Signs of active uncontrolled hypertension, liver or kidney malfunction
* Cardiac problems and cardiovascular diseases, such as congestive heart failure, angina pectoris, cardiac infarction and arrhythmias
* Any medical condition requiring treatment and/or medication that might interfere with the investigated parameters. All medical conditions/medications will be reviewed with the dependent physician and in-/exclusion will be decided on individual basis
* Unstable body weight (weight gain or loss >3kg in the past three months)
* Participation in another biomedical study within 1 month prior to screening visit
* Participants, who do not want to be informed about unexpected medical findings, or do not wish that their treating physician will be informed, cannot participate in this study
* Blood donation three month prior to study and three month after finishing study
* Alcohol consumption of >2 servings per day for men and >1 serving per day for

women
* Smoking in the past 6 months

A medical doctor will judge participation eligibility based on the medical history questionnaire, medication use and fasting blood parameters. If the medical doctor advises that someone cannot participate, they will be excluded from enrolment.

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):	30-11-2020
Enrollment:	14
Type:	Actual

Medical products/devices used

Generic name:	Blanketrol® III Model 233 Hyper-Hypothermia System
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	19-09-2019
Application type:	First submission
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	NL70732.068.19
Other	NL7829