

The effect of a high caloric meal on brown fat activity and the role of the sympathetic nervous system in brown fat activation

Submission date 24/02/2012	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 02/03/2012	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 28/07/2014	Condition category Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Brown adipose tissue (BAT) is a type of fat tissue that is different from white adipose tissue, which stores calories as fat. Instead of storing calories, BAT is capable of generating heat from calories and thereby producing heat. It acts like a furnace and is an import organ, particularly in hibernating animals, to maintain a stable body temperature. It has been long known that human newborns and infants possess BAT, which helps them to maintain their body temperature. However, it was thought that BAT disappeared during the aging process. Surprisingly, this was not the case and recently it was discovered that BAT is still present in human adults, and that lean young people have the largest amounts of BAT. Interestingly, obese people have less BAT and it is now thought that there is link between BAT and obesity. It is also thought that BAT could be involved in maintaining energy balance and could thus be important in weight loss. It is known from animal studies that BAT is involved in maintaining energy balance, as it is capable of wasting excessive energy intake. In the current study we would like to gain more insight into the function of BAT with respect to this energy balance function. Furthermore, we are very interested in how BAT can be activated in humans. We know from animal studies that the sympathetic nervous system drives this tissue, but no clear evidence is yet available from humans. In this study we are investigating the role of the sympathetic nervous system in activating brown fat in lean human adults. We are also examining the role of BAT in burning off calories during high caloric intake. With this study we hope to find out more about the way BAT can be activated in humans. Finally, we are also interested in the intrinsic capacity of the skeletal muscle to generate heat in each subject. Next to BAT, skeletal muscle is a likely contributor to generate heat during cold exposure and/or other stimuli.

Who can participate?

Healthy young lean human adults aged 18-30. You must have a BMI between 18-25 kg/m2.

What does the study involve?

The study includes three experiments which all last one morning. The first experiment is a mild cold experiment in which you will be measured during 2 hours of cold exposure. We measure energy expenditure, body temperatures, and your BAT activity. This will be done in a PET-CT

scanner. The second experiment will be the isoprenaline experiment, in which we measure the same parameters but then during the infusion of isoprenaline (ISO). This substance activates the beta-adrenergic part of your sympathetic nervous system. You will notice this by an increased heart rate and contraction power of the heart. Finally, the third experiment will be similar to the previous two, but now you will eat a high calorie meal and we will measure you again for two hours. On a separate occasion, you will be asked for a muscle biopsy, in which we will take a small part of your leg muscle. This will not affect your muscle function.

What are the possible benefits and risks of participating?

There are no direct benefits for the participants. Hopefully, this study will help us to understand BAT in humans and eventually support the quest to tackle the obesity problem and its related metabolic diseases. The risks are minimal for this study. The isoprenaline infusion test involves relatively low doses, which will not be a serious risk for the patient. The absorbed radiation dose from a FDG PET-CT scan is considered as a low risk.

Where is the study run from?

This study will be conducted at Maastricht University in the Netherlands. The experiments take place at the Department of Nuclear Medicine in the academic hospital in Maastricht (MUMC).

When is the study starting and for how long is it expected to run?

The study started in September 2011 and will finish in April 2012.

Who is funding the study?

The Dutch Government funds this study: TOP subsidies (Netherlands Science Foundation ZonMw), which are (partly) financed by the Netherlands Organization for Scientific Research (NWO).

Who is the main contact?

Maarten Vosselman

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

NL 31762.068.10

Study information

Scientific Title

Role of brown adipose tissue in meal-induced thermogenesis and the involvement of the sympathetic nervous system

Study objectives

Aim:

Study the effects of isoprenaline and food intake on brown fat activity compared to brown fat activity during cold exposure (control experiment)

Hypotheses:

1. A single high-caloric, carbohydrate-rich meal will increase energy expenditure and is related to brown adipose tissue (BAT) activity and intrinsic mitochondrial uncoupling in skeletal muscle in lean human males
2. Sympathetic stimulation via isoprenaline infusion will increase energy expenditure and is related to BAT activity and intrinsic mitochondrial uncoupling in skeletal muscle in lean human males

Ethics approval required

Old ethics approval format

Ethics approval(s)

Medical Ethical Commission, Maastricht University, 28/05/2010, ref: 10-3-027

Study design

Single-center intervention study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Other

Study type(s)

Screening

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Obesity and its related metabolic diseases such as type 2 diabetes

Interventions

Each subject will undergo three experiments:

Experiment 1: mild cold experiment, in which the participants will be subject to mild cold exposure via air conditioning until they start shivering. Then the temperature will be increased by two degrees to avoid further shivering. This intervention will only be done one morning during this experiment.

Experiment 2: ISO experiment, in which isoprenaline (sulphate) will be intravenously infused with increasing dosages (6, 12, 24 nanogram per kilogram of fat free mass) for 30 minutes during dose 1 and 2 and for 55 minutes during dose 3. Then the infusion will be stopped. This intervention has to be completed one time.

Experiment 3: Meal experiment, in which each participant will be asked to ingest a high caloric carbohydrate-rich meal (10% protein; 78% carbohydrates; 12% fat; around 1500 kcal) which has been individually adjusted to 50% of their total daily required energy intake. The meal consists of Nutrical (Nutricia, the Netherlands) and Nutriprotein (Nutricia, the Netherlands). This intervention has to be done one morning only during the experiment.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

1. Standard uptake values (SUVs) of brown adipose tissue - skeletal muscle mitochondrial respiration/uncoupling
2. Energy expenditure

Secondary outcome measures

1. Body temperatures - Skin perfusion
2. Body composition - Blood parameters

Overall study start date

01/09/2010

Completion date

01/04/2012

Eligibility

Key inclusion criteria

1. Healthy lean and obese adults
2. Age 18-30 years
3. Male
4. Lean: BMI 18.5-25 kg/m² or obese: BMI \geq 30 kg/m²
5. Caucasians

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Upper age limit

30 Years

Sex

Male

Target number of participants

32

Key exclusion criteria

1. Diabetes mellitus
2. Hyperthyroidism
3. Cardiovascular and renal diseases
4. Tachy-arrhythmias
5. Asthma and other obstructive pulmonary diseases
6. Hypertension (systolic/diastolic blood pressure >140/90)
7. Hypotension (systolic/diastolic blood pressure <90/60)
8. Elevated fasting blood glucose level (> 5.6 mmol/L)
9. Medication: use of β -blockers, tricyclic antidepressants, MAO inhibitors
10. Glaucoma: use of the medicine betamimeticum

Date of first enrolment

01/09/2010

Date of final enrolment

01/04/2012

Locations**Countries of recruitment**

Netherlands

Study participating centre

Maastricht University

Maastricht

Netherlands

6229 ER

Sponsor information

Organisation

Maastricht University (Netherlands)

Sponsor details

P.O. Box 616
Maastricht
Netherlands
2509 AC

Sponsor type

University/education

Website

<http://www.maastrichtuniversity.nl/>

ROR

<https://ror.org/02jz4aj89>

Funder(s)

Funder type

Research organisation

Funder Name

Netherlands Science Foundation (Netherlands) ref: TOP 91209037

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
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Results article	results	01/12/2012	Yes	No
Results article	results	01/07/2013	Yes	No