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# 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

**Registration date**
02/03/2012

**Overall study status**
Completed

**Last Edited**
28/07/2014

**Condition category**
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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
Dr Wouter van Marken Lichtenbelt

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# Additional identifiers

### Protocol serial number
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

## Study type(s)
Screening

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

### Key secondary outcome(s))
1. Body temperatures - Skin perfusion
2. Body composition - Blood parameters

### 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 ≥ 30 kg/m2
5. Caucasians

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Upper age limit
30 years

### Sex
Male

### 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 ß-blockers, tricylic antidepressants, MAO inhibitors
10. Glaucoom: 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
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6229 ER

## Sponsor information

### Organisation
Maastricht University (Netherlands)

### ROR
https://ror.org/02jz4aj89

## Funder(s)

### Funder type
Research organisation

**Funder Name**
Netherlands Science Foundation (Netherlands) ref: TOP 91209037

# Results and Publications

## 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? |
|---|---|---|---|---|---|
| Results article | results | 01/12/2012 | | Yes | No |
| Results article | results | 01/07/2013 | | Yes | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |