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

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Examine the effects of a single meal on BAT activation and intrinsic mitochondrial uncoupling in SM in lean and obese individuals, and define the role of the SNS within this response.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON38243

Source
ToetsingOnline

Brief title
Role of brown adipose tissue in meal induced thermogenesis.

Condition

- Other condition

Synonym
nvt

Health condition

Obesitas

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Adaptive thermogenesis, Brown adipose tissue, Mitochondrial uncoupling, Skeletal muscle

Outcome measures

Primary outcome

- Standard uptake value*s (SUV*s) of brown adipose tissue

- Skeletal muscle mitochondrial respiration/uncoupling

- Energy expenditure

Secondary outcome

- Body temperatures

- Skin perfusion

- Body composition

- Blood parameters

- UCP-1 and beta3-receptor polymorphisms

Study description

Background summary

Individual variation in adaptive thermogenesis (AT) can potentially be attributed to mitochondrial uncoupling in brown adipose tissue (BAT) and/or skeletal muscle (SM). Mitochondrial uncoupling in these tissues may be of metabolic significance, as well as to become pharmaceutically activated in efforts to combat obesity. Recent studies have shown the presence of BAT in human adults by exposing them to mild cold and subsequently measured them by FDG PET-CT imaging. BAT may thus be considered as an organ of physiological and pharmaceutical importance even in adults. Additionally, we recently showed that

mitochondrial uncoupling in human skeletal muscle tissue is related to adaptive thermogenesis after mild cold exposure.
Next to mild cold exposure, diet also induces AT by increasing BAT activity, probably wasting the excessive energy intake, as shown in animal overfeeding studies. Moreover, several rat studies have shown that even a single meal can stimulate brown adipose tissue activity mediated by the sympathetic nervous system (SNS). Finally, overfeeding induced adaptive thermogenesis and cold induced adaptive thermogenesis in humans seem to share common underlying mechanisms, both involving the SNS. Therefore it is hypothesized that a single meal is capable of increasing AT through mitochondrial uncoupling in BAT and SM, mediated by the SNS. Furthermore, it is expected that these responses will be blunted in obese people.

Study objective

Examine the effects of a single meal on BAT activation and intrinsic mitochondrial uncoupling in SM in lean and obese individuals, and define the role of the SNS within this response.

Study design

Three experiments will be conducted per individual. The first experiment will examine BAT activity (FDG PET-CT) after ingestion of a high caloric liquid meal (high in carbohydrates), whereas the second after ß-adrenergic stimulation by isoprenaline infusion. Finally, during the third experiment (positive control experiment) BAT activity will be measured after exposure to mild cold for 2 hours. Furthermore, energy expenditure by means of indirect calorimetry will be assessed and compared to BAT activity and to the intrinsic uncoupling capacity in SM. Therefore, mitochondrial uncoupling will be studied in a muscle biopsy taken prior to the experiment. Finally, body composition will be determined with a DXA scan, and skin perfusion and relevant body temperatures will be measured as well.

Intervention

Each individual will undergo three experiments with a different intervention. During the first experiment, the individual will receive a liquid meal containing 60% of their daily required energy intake. The meal will consist of nutridrink protein and nutrical, which is a protein rich and a carbohydrate rich drink respectively. The macronutrient composition is as follows: 10% protein, 78% carbohydrates, 12% fat.
The second experiment will consist of isoprenaline infusion in order to stimulate the sympathetic nervous system. This will be applied in three (incremental) doses (6,12 and 24 ng per kg fat free mass), of which each will last 30 minutes. Moreover, half of each group will ingest 250 mg of acipimox two hours before and at the onset of the experiment. This will supress

lipolysis resulting in lower FFA levels in the blood, subsequently stimulating glucose usage.
Finally, the positive control experiment will consist of exposure to mild cold (16 ºC) for two hours.

Study burden and risks

The isoprenaline infusion test contains relatively low doses (max 24 ng per kg of body weight), which will not be a serious risk for the patient.
The absorbed radiation dose from a FDG PET-CT scan after administration of 50 MBq of 18F-FDG is 1.8 mSv, which is considered as a low risk.
Finally, participants will be measured for just three mornings in total.

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

• Healthy lean and obese adults
• Age 18-30 years
• Gender: Male
• Lean: BMI 18.5-25 kg/m2;Obese: BMI >= 30 kg/m2
• Caucasians

Exclusion criteria

• Diabetes Mellitus
• Hyperthyroidism
• Cardiovascular and renal diseases
• Tachy-arrhythmias
• Asthma and other obstructive pulmonary diseases
• Hypertension (systolic/diastolic blood pressure >140/90)
• Hypotension (systolic/diastolic blood pressure <90/60)
• Elevated fasting blood glucose level (> 5.6 mmol/L)
• Medication: use of ß-blockers, tricylic antidepressants, MAO inhibitors
• Glaucoom: use of the medicine betamimeticum
• Individuen die al eerder mee hebben gedaan aan bruin vet onderzoek met een PET-CT scan of al een keer medische bestraling hebben gehad
• Jicht
• Lever insufficiëntie

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-09-2010

Enrollment:	34
Type:	Actual

Ethics review

Approved WMO Date:	28-05-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-10-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-12-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-04-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-02-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-06-2012
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
ISRCTN	ISRCTN21413505
CCMO	NL31762.068.10