Brown adipose tissue activity and bile acids

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23736

Source
Nationaal Trial Register

Brief title
Bile acids and BAT

Health condition

Healthy young men and women

Sponsors and support

Primary sponsor: W.D. van Marken LichtenbeltMaastricht University, Dept of Human Biology
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Source(s) of monetary or material Support: NWO TOP

Intervention

Outcome measures

Primary outcome

- Energy expenditure

- Brown adipose tissue activity

Secondary outcome

- Skin temperature
- Core temperature
- Body composition
- Skin perfusion

Study description

Background summary

Rationale: It has long been known that brown adipose tissue (BAT) activity is responsible for the major part of non-shivering thermogenesis in rodents. Recently functional BAT has been discovered in adult humans. The negative correlation that exists was between body mass index (BMI) and BAT activity in humans, suggests that BAT might play a significant role in the development and/or sustainability of obesity. Therefore, it could be a target for the therapy of obesity and it's accompanying metabolic diseases. Recent studies have shown that bile acids (BAs) induce D2 activity within rodent BAT and human skeletal myocyte cultures, which promotes the conversion of the inactive thyroid hormone thyroxine (T4) into the active 3-5-3` triiodothyronine (T3). T3, in turn, stimulates energy expenditure in both BAT and muscle. Human evidence for this suggestion is still limited and only a few studies have investigated the relationship between BAs and energy expenditure (EE) in humans. It is hypothesized that higher levels of circulating BAs will result in increased BAT activity.
Objectives: The primary objectives are: 1) to determine the effect of bile acids on glucoseuptake in brown adipose tissue; 2) to determine the effect of bile acids onwhole body energy expenditure and 3) to determine the effect of bile acids on skeletal muscle mitochondrial uncoupling and how this is related to non-shivering thermogenesis.
Study design: Three PET-CT scans will be performed in each subject, in which BAT activity will be measured, once under thermoneutral conditions after oral ingestion of chenodeoxycholic acid (a synthetic bile acid), once under thermoneutral conditions without ingestion of chenodeoxycholic acid, and once after cold-exposure.
Study population: Healthy, lean (BMI 18-25 kg/m2) male and female volunteers aged between 18-30 years.
Intervention: The intervention will consist of administration of 15 milligrams of chenodeoxycholic acid per kilogram bodyweight per 24 hours in one gift.
Main study parameters/endpoints: The main study parameters are BAT activity, which will be measured by means of PET-CT scanning, and (non-shivering) thermogenesis, which will be measured by means of indirect calorimetry. In addition, skeletal muscle mitochondrial uncoupling capacitywill be determined as well.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The total absorbed radiation dose from the three PET-CT scans included in this study, after administration of three times 50 MBq of 18F-FDG is 7.45 mSv. This is considered

as low risk.

Study objective

Human brown adipose tissue activity and energy expenditure will increase in the presence of bile acids

Study design

1
2
3

Intervention

The study will include three laboratory visits for each individual, in which BAT activity will be measured. During one visit BAT activity and EE will be determined after administration of CDCA. On another visit subjects will receive placebo and similar measurements will be performed. Finally, a positive control study will be done in which BAT activity will be determined after mild cold-exposure. CDCA will be given as oral administration of 15 mg/kg bodyweight in tablets of 250 mg each chenodeoxycholic acid in one gift during the 24 hours preceding the day of the scan. Participants will stay in the respiration chamber for 24 hourspreceding the PET/CT to guarantee controlled administration of CDCA/placebo and for determination of energy expenditure during administration of the drug/placebo. The morning of the scan subjects will receive the same dose of 15 mg/kg bodyweight CDCA or placebo again. This first PET/CT scan will be performed under thermoneutral conditions. The third and control visit will only include a PET-CT scan after mild cold-exposure, to ensure maximal BAT activity. For this, subjects will come to the lab after an overnight fast. All three scanning protocols consist of a static PET/CT scan. To investigate the role of bile acids on mitochondrial respiration/uncoupling in skeletal muscle, and to compare the results to the thermoneutral condition without intervention, muscle biopsies will be taken in both thermoneutral conditions. Thermogenesis will be measured using indirect calorimetry and the insulative response will be determined by means of thermometry and skin perfusion.

Contacts

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Eligibility criteria

Inclusion criteria

-Caucasians

-Age: 18-30 years

-Gender: male and female (females only on a specific oral contraceptive pill; microgynon 30 or levonorgestrel/ethinylestradiol)

-BMI: 18-25 kg/m2

-Good general health

Exclusion criteria

-Psychologically unstable subjects (as judged by the treating medical specialist)

-Subjects with mental retardation (as judged by the treating medical specialist)

-Subjects with severe behavior disorders (as judged by the treating medical specialist)

-Pregnancy or lactation

-The use of the following medication one month before the study is an exclusion criterium; ß-blockers, ursodeoxycholic acid, bile acid sequestrants and antacida

-Participation in an intensive weight-loss program or vigorous exercise program during the last year before the start of the study

-Abuse of drugs and/or alcohol

-Severe diabetes which requires application of insulin or patients with diabetes-related complications

-Surgery of the gastro-intestinal tract (only appendectomy is allowed)

-Previous ERCP with papillotomy

-History of cholesystectomy or disease of the gallbladder, biliary system and/or liver

-Hyperthyroidism or hypothyroidism

-BMI > 25 kg/m2

-Participation in earlier research or medical examinations that included PET/CT scanning

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Non controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2013
Enrollment:	18
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 38439
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL4108
NTR-old	NTR4253
CCMO	NL44774.068.13
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON38439

Study results

Summary results
N/A