The role of bile acids in human brown adipose tissue metabolism

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON38439

Source
ToetsingOnline

Brief title
Brown adipose tissue activity and bile acids

Condition

- Appetite and general nutritional disorders

Synonym
bile acids, brown adipose tissue

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Bile acids, Brown adipose tissue, Obesity

Outcome measures

Primary outcome

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 capacity will be determined as well.

Secondary outcome

Body temperature distribution, body composition and skin perfusion.

Study description

Background summary

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.

Study objective

The primary objectives are: 1) to determine the effect of bile acids on glucose uptake in brown adipose tissue; 2) to determine the effect of bile acids on

whole 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.

Intervention

The intervention will consist of administration of 15 milligrams of chenodeoxycholic acid per kilogram bodyweight per 24 hours in one gift (usually in non-obese subjects 1000 mg chenodeoxycholic acid per day).

Study burden and risks

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 7.05 mSv. This is considered as low risk.

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

- 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:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-11-2013
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Steripet
Generic name:	fludeoxyglucose
Product type:	Medicine
Brand name:	Xenbilox
Generic name:	Chenodeoxycholic acid

Ethics review

Approved WMO Date:	23-10-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-11-2013

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

ID: 23736
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-002512-27-NL
CCMO	NL44774.068.13
Other	NTR volgt
OMON	NL-OMON23736