The effects of intravenous TRH administration on brown adipose tissue activity in healthy, lean men.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON41582

Source
ToetsingOnline

Brief title
BATman-study

Condition

- Other condition
- Endocrine and glandular disorders NEC

Synonym
Obesity

Health condition

Obesitas

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Adipose tissue, brown, Positron-emission tomography, Thyroid hormones, Thyrotropin-releasing hormone

Outcome measures

Primary outcome

The degree of 18F-FDG uptake in BAT, skin temperature, blood pressure, heart

rate, and serum TSH, T3, T4, FT4, norepinephrine and normetanephrine after TRH

administration, compared to saline administration;

Secondary outcome

The association between BAT acitvity and changes in blood pressure, heart rate,

and serum TSH, T3, T4, FT4, norepinephrine and normetanephrine.

Study description

Background summary

Brown adipose tissue (BAT) is a well known major site of non-shivering thermogenesis in most mammals. It was only recently found to be present and active in human adults. Several studies have shown that BAT activity is increased in adult humans during cold exposure. Animal experiments show that heat production by BAT in response to cold is centrally regulated via cold-sensitive TRH-neurons in hypothalamus and hindbrain, which in turn activate sympathetic neurons in the spinal cord projecting to BAT. In animals, TRH plays a major role in the central regulation of BAT. Hence, central and systemic TRH administration causes a rise in BAT activity, an increase in body temperature and sympathetic tone.
Data suggests that human BAT participates in the control of energy expenditure and adiposity, making it an interesting potential new target for treatment of obesity and diabetes. Whether TRH plays a role in BAT activation in response to cold in humans, is unknown.

In this study, we aim to determine whether TRH administration stimulates BAT activity and sympathetic tone in adult humans.

Study objective

To investigate whether BAT tissue can be activated by intravenous administration of TRH. Secondary objectives are to determine whether intravenous TRH increases the degree of cardiovascular sympathetic stimulation and the response of skin temperature, and whether there is a correlation between the BAT-activity and these changes.

Study design

A double-blind, randomized, placebo-controlled cross-over study.

Intervention

Intravenous TRH administration.

Study burden and risks

Subjects will be invited to the hospital twice with an interval of minimally 7 days. Subjects will be asked to refrain from exercise and to fast 6 hours prior to study participation.
During the study, subjects will receive an intravenous cannula, through which they receive infusions of 18F-FDG, TRH and saline, and from which 7 blood samples will be collected. Placement of the intravenous cannula can be an unpleasant experience. There is a small chance of developing phlebitis.
Subjects will be exposed to a mild cold (18C) for one hour.
Subjects will undergo dynamic PET-CT imaging, cardiovascular monitoring and temperature monitoring. Side effects after intravenous TRH administration are minimal, and may include nausea, flushing, urinary urgency and changes in blood pressure. The total resulting dose from the whole-body 18F-FDG PET/CT examinations is 7.2 mSv, which is less than 3 times the annual natural background radiation exposure in the Netherlands. There are no further risks or benefits associated with participation.

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

Male sex
Age between 30 and 50 years old
BMI range 19 to 25 kg/m2

Exclusion criteria

Treated or untreated hypo- or hyperthyroidism
Renal dysfunction (eGFR >60)
Use of any medication known to affect thyroid hormone metabolism or the autonomic nervous system
Any cardiovascular disease
Recent stay of >2 weeks in the tropics within the last 6 weeks
The desire to conceive within 1 month

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-06-2014
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	15-04-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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: 23019
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL45656.018.13
OMON	NL-OMON23019