Effect of sodium oxybate on brown adipose tissue activity in narcolepsy

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Primary objective:1. To assess the effect of SXB treatment on cold-induced BAT volume and activity in narcolepsy type 1 patients.Secondary objectives:1. To assess the effect of SXB treatment on thermoneutral BAT volume and fat fraction, lipoprotein...

Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON48148

Source
ToetsingOnline

Brief title
Sodium oxybate and brown adipose tissue in narcolepsy

Condition

- Other condition
- Hypothalamus and pituitary gland disorders
- Lipid metabolism disorders

Synonym
hypersomnia, narcolepsy

Health condition

hypersomnieën

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,UCB,UCB Pharma

Intervention

Keyword: Brown adipose tissue, Narcolepsy, Sodium oxybate

Outcome measures

Primary outcome

Cold-induced BAT volume and activity: measured by individualized cooling followed by 18F-FDG PET-CT scan in healthy controls and in narcolepsy type 1 patients before and after 3 weeks of SXB treatment.

Secondary outcome

- Resting energy expenditure: measured by indirect calorimetry in healthy controls and in narcolepsy type 1 patients before, after 1 day and after 3 weeks of SXB treatment.
- Skin temperature: measured by wireless iButtons in healthy controls and in narcolepsy type 1 patients before, after 1 day and after 3 weeks of SXB treatment.
- Thermoneutral and cold-induced lipoprotein dynamics in healthy controls and in narcolepsy type 1 patients before and after 3 weeks of SXB treatment.
- Fat/lean mass loss: measured by bioelectrical impedance analysis measurement.
- Thermoneutral BAT volume and fat fraction: measured by MRI scan in thermoneutral condition in healthy controls and in narcolepsy type 1 patients before and after 3 weeks of SXB treatment.

Study description

Background summary

From as early as the 1930s, it has been reported that obesity is more prevalent in patients with the sleep-wake disorder narcolepsy than in healthy controls. Recent observations show that narcolepsy type 1 patients lose weight when using sodium oxybate (SXB). A mean loss of 5.1 kg has been reported in several studies. The underlying mechanism is unclear. Based on the available animal studies and one human study that shows an increase in sympathetic activity after SXB administration [4], we hypothesize that activation of energy-combusting brown adipose tissue (BAT) via enhanced sympathetic innervation by SXB might be crucial in mediating the weight loss in narcolepsy type 1 patients after initiation of SXB treatment.

Study objective

Primary objective:
1. To assess the effect of SXB treatment on cold-induced BAT volume and activity in narcolepsy type 1 patients.

Secondary objectives:
1. To assess the effect of SXB treatment on thermoneutral BAT volume and fat fraction, lipoprotein dynamics, resting energy expenditure and skin temperature in narcolepsy type 1 patients.
2. To assess differences in cold-induced BAT volume and activity, thermoneutral BAT volume and fat fraction, resting energy expenditure, skin temperature and cold-induced lipoprotein dynamics between narcolepsy type 1 patients and healthy controls.
3. To correlate weight and fat/lean mass loss in narcolepsy type 1 upon SXB treatment initiation with observed BAT activity changes.

Study design

Prospective observational study.

Study burden and risks

The 18F-FDG tracer that is used in the 18F-FDG PET-CT-scan for brown adipose tissue measurement is radioactive. The end-products of metabolizing this tracer are not. All radioactivity of 18F-FDG decays with a half-life of 110 minutes (just under 2 hours). Thus, within 24 hours (13 half-lives), the radioactivity in the patient and in any initially voided urine after the PET exam, will have decayed to 2*13 = 1/8192 of the initial radioactivity of the dose. In this study, 74 MBq 18F-FDG will be administered intravenously. Using a conversion

factor of 1.9x10-2 mSv/MBq, this amounts to an effective radiation dose of 1.40 mSv. A low dose CT scan (30 mA) will be used for attenuation correction and localization of the 18F-FDG uptake sites, with an effective radiation dose of 2.60 mSv. The resulting total effective radiation dose from the CT scan and FDG will be 4.00 mSv in healthy controls and 8.00 mSv in patients (2 18F-FDG PET-CT-scans). The effective dose is between 1-10 mSv and therefore comes within category IIb according to the risk categorization based on ICRP-62 (following the LUMC complex license of May 20th 2010, paragraph VIII), which involves a risk for the irradiated individual in the order of one in ten thousand, which is considered low and does not present any danger to the environment as recently described. Furthermore, the above described 18F-FDG PET-CT-scan protocol is a standard procedure performed at the University of Maastricht and the LUMC in research with (young) healthy volunteers. In accordance with this low risk category, our research findings may have the potential to
exert important beneficial effects concerning future therapeutic strategies targeting the obesity epidemic.
An allergic reaction to 18F-FDG is extremely rare and usually mild. We will monitor the subject during the study day to see if any allergic symptoms occur, such as shortness of breath, skin reactions or nausea.
Subjects with contraindications for MRI will be excluded. There are no known risks known associated with the use of MRI.
It is important to state that the risks of sodium oxybate are not added risks to this study, since sodium oxybate treatment is not influenced by this study.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients:
1. Narcolepsy type 1 based on ICSD-3 criteria.
2. *18 and <40 years of age.
3. White Caucasian descent.
4. Clinical indication for sodium oxybate treatment.
5. BMI * 27 kg/m2, Healthy controls:
1. Age-, gender- and BMI-match with patient.

Exclusion criteria

Patients and healthy controls:
1. Smoking.
2. Renal, hepatic or endocrine disease.
3. Previous use of sodium oxybate.
4. Use of medication known to influence glucose and/or lipid metabolism or brown adiposue tissue activity (e.g. *-adrenergic receptor blockers).
5. Participation in an intensive weight-loss program or vigorous exercise program during the year before the start of the study.
6. Contraindications for sodium oxybate treatment.
7. Contraindications for undergoing an MRI scan:
- Presence of non-MR safe metal implants or objects in the body.
- Pacemaker, neurostimulator, hydrocephalus pump, drug pump, non-removable hearing aid, large recent tattoos.
- Claustrophobia
- Tinnitus or hyperacusis

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Ethics review

Not approved

Date:	20-09-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL67755.058.18