One night of partial sleep restriction: effects on metabolism, mood and stress responsiveness

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Research Questions: Primary:1. Does a single night of short sleep reduce metabolic flexibility following a mixed meal challenge?2. Does a single night of short sleep alter the responsiveness of the HPA-axis?3. Are the disturbances of a single night...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON43632

Source
ToetsingOnline

Brief title
Metabolism and stress after one night of partial sleep restriction

Condition

- Lipid metabolism disorders

Synonym
Lipid metabolism, obesity

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Metabolism, Mood, Sleep, Stress

Outcome measures

Primary outcome

The primairy study parameters are:

- Lipid metabolism by measurement of hormone and lipid concentrations in plasma

in response to a mixed-meal challenge

- Energy metabolism by measurement of indirect calorimetry

- HPA-axis responsiveness by hormone and blood pressure measurement during a

cold- feet pressor test

- Mood via short questionnaires (Profile of Mood States)

Secondary outcome

The secondairy study parameters are:

- Gene expression profiles and metabolomics in muscle and fat tissue and plasma

- Gene expression profiles in skin and hair samples

Study description

Background summary

In modern daily life, incidental short sleep duration has become a common feature. Chronic short sleep duration is associated with a many adverse health effects, including metabolic disturbances such as obesity, type 2 diabetes and cardiovascular diseases, as well as disturbances in the stress system, negative mood and tissue ageing. These associations may be explained by metabolic disturbances caused by repeated incidental short sleep duration. A single night of partial sleep restriction of 4 hours sleep in healthy individuals acutely induces insulin resistance with respect to glucose uptake. Furthermore, several nights short sleep impairs intracellular insulin signalling in white fat.
Insulin is produced upon glucose availability and is a signal for tissues to

switch from fat oxidation (during fasting) to glucose oxidation. The ability to switch between glucose and fat oxidation in response to insulin is called metabolic flexibility. Short sleep may therefore impair metabolic flexibility, predisposing to more insulin resistance.
Interestingly, insulin in the brain decreases the feedback of the hypothalamus-pituitary-adrenal (HPA) axis, thereby contributing to an increased cortisol response. Additionally, short sleep increases late afternoon cortisol levels. Disturbances in the HPA-axis are in turn related to mood and downstream effects on tissue aging as a result of cross-talk between the central HPA-axis and local HPA-axis equivalents are also implicated. Study in mice shows that cortisol produced by the central HPA-axis in response to chronic stress exerts negative feedback on the local HPA-axis equivalent in skin resulting in suppression of melanogenesis. Melanin production is an important defence mechanism against UV irradiation and it*s tissue ageing effects. Taken these data together, we hypothesize that short sleep reduces metabolic flexibility, increases insulin resistance and thereby reduces HPA-reactivity. Furthermore, we hypothesize short sleep will negatively affect mood and tissue ageing due to dysregulation of the HPA-axis. Since a higher BMI is correlated with metabolic inflexibility and insulin resistance, we hypothesize that higher BMI will enlarge the effects of short sleep on metabolism, HPA-axis reactivity and downstream effects.

Study objective

Research Questions:
Primary:
1. Does a single night of short sleep reduce metabolic flexibility following a mixed meal challenge?
2. Does a single night of short sleep alter the responsiveness of the HPA-axis?
3. Are the disturbances of a single night of short sleep dependent on BMI?
Exploratory:
4. Does a single night of short sleep negatively affect mood and accelerate tissue ageing?
5. Does a single night of short sleep disturb intracellular metabolic pathways in fat and muscle tissue?
6. Does a single night of short sleep affect circadian rhythms hormone levels and skin temperature?

Study design

We will investigate the effects of a single night of short sleep compared to normal sleep in 36 participants within a BMI range from 20-35 kg/m2 in a balanced cross-over intervention study.

Intervention

A single night of short sleep duration (4 hours) compared to a control condition of normal sleep duration (8 hours).

Study burden and risks

The study is composed of three components: a single screeningsvisit, two times a study day at our research facility and at-home measurements.

Time, Actions, Risks
Screening:
Time: ~ 1 hour.
Actions: height, weight, physical examination, bio-electrical impedance, 1 venapuncture.
Risks: local hematoma

Study day (2x):
Time: From 21.00 until 18.00 the following day, in our research unit.
Actions: intravenous catheter, short or normal sleep duration, two times isocaloric liquid mixed meal, indirecte calorimetry, muscle, fat and skin biopsy, hair samples, stress reactivity test.
Risks: local hematoma (from intravenous catheter), localized pain, swelling, hematoma and small scar (from biopsies).Transient localized pain from hair sampling. Transient physical discomfort from stress reactivity test (3 minutes of cold feet and several blood pressure measurements).

In-home measurements
Time: during one week prior to study day: ~15 minutes daily en 3 times 30 mintues. Once per study: 1 hour.
Actions: daily completion of diary (sleep, diet and physical activity), completion of 4 questionnaires concerning sleep habits. Collection of saliva following study day (3 times per studyday), by chewing on cotton collector.
Risks: none.

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

- Informed consent
- Caucasian men
- Age between 18 and 55 years
- BMI between 20 and 25 kg/m2 (equally divided over the range, so ideally n=12 in BMI categories 20 -25; 25 - 30; 30 - 35 kg/m2)

Exclusion criteria

Active endocrine disease (e.g. diabetes mellitus type 1 and type 2, thyroid disease, Cushing*s disease and lipid-associated disorders such as FH)
- Fasting glucose >7.0 mmol/L
- Severe chronic disease (e.g. chronic liver or kidney disease)
- Severe insomnia, sleep disorders or exceptional habitual sleep duration (<6 or >10 h).
- Medication use including the following: lipid lowering drugs, glucocorticoids, sleep medication, hormone replacement, glucose lowering drugs, insulin therapy (last 6 weeks), anticoagulants
- Recent time zone travel (last 6 weeks)
- Shift work (last 6 weeks)
- Severe alcohol use (>21 units/week)
- Psychiatric disease
- Drug abuse
- Recent participation to another nutritional or biomedical trial (last 6 weeks)
- Taking medication, which may interfere with study measurements, as judged by the

responsible physician
- Reported weight loss or weight gain (10%) in the last six months prior to the pre-study screening
- Clinically relevant abnormalities in clinical chemistry at screening (to be judged by the study physician)
- Reported use of any nicotine containing products in the six months preceding the study and during the study itself;
- Extreme strenuous exercise during last 3 months, as judged by responsible physician
- Excessive sunbathing during the last 3 months, as judged by responsible physician

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-06-2016
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO

Date:	29-03-2016
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	NL55111.058.15

Study results

Date completed:	01-07-2018
Actual enrolment:	33