

The role of hypocretin in food-related motivation and self-control: A fMRI study in narcolepsy patients

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To understand the neurocognitive mechanism underlying food-related motivation and control in patients with narcolepsy with cataplexy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Sleep disturbances (incl subtypes)
Study type	Observational non invasive

Summary

ID

NL-OMON38653

Source

ToetsingOnline

Brief title

Effect of hypocretin on motivation and control

Condition

- Sleep disturbances (incl subtypes)

Synonym

narcolepsy; disorder of excessive daytime sleepiness

Research involving

Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen

Source(s) of monetary or material Support: NWO

Intervention

Keyword: food, hypocretin, narcolepsy, obesity

Outcome measures

Primary outcome

We will assess the difference in performance (i.e. error rates and reaction times) and brain activity (using fMRI) in prefrontal cortex control (i.e. attentional bias to food-related words), and striatum (i.e. food and monetary reward cue responses).

Secondary outcome

NA

Study description

Background summary

Narcolepsy with cataplexy (NC) is caused by hypocretin deficiency. Patients with this disorder suffer from chronic daytime sleepiness and cataplexy (i.e. a sudden and transient episode of loss of muscle tone). The hypocretin system is crucial for arousal and maintenance of the waking state. Recently, hypocretin has also been shown to play an important role in reward and motivation. Hypocretin enhances dopamine signalling in the meso-limbic pathway that regulates reward processing and addiction. Animal studies have shown that when hypocretin is blocked in the meso-limbic pathway, addicted animals will stop drug-seeking behaviour. Furthermore, the meso-limbic pathway and its interaction with hypocretin has also shown to be important in regulating food-related motivation in rodents. There is clinical evidence that NC patients, who are lacking hypocretin, suffer from decreased general motivation and interestingly; despite the fact that narcoleptic patients are usually treated with amphetamine-like compounds they rarely develop drug dependency to their medication. Paradoxically, NC is associated with a global increased frequency of obesity and higher prevalence of eating disorders. Obesity is associated with an enhanced food-related motivation and diminished prefrontal control over food intake. What neuromechanisms contribute to abnormal food-related motivation and control in NC patients has not yet been studied. This study will test the neurocognitive mechanisms related to the disturbed

food-related motivation and control in NC by using behavioural and functional magnetic resonance imaging (fMRI) tasks.

Study objective

To understand the neurocognitive mechanism underlying food-related motivation and control in patients with narcolepsy with cataplexy.

Study design

We will use a cross sectional, patient-controlled design using a behavioral task and functional MRI experiments.

Study burden and risks

Both the patients groups will have to refrain from taking their medication (which usually consists of modafinil or methylphenidate). The severity of the sleep disorder will range considerable from mild; patients who do not need to take medication (use planned naps), to severe; with diminished functioning and in need of the maximum dosage of medication. In consultation with a treating physician, we expect that when patients are without medication, they will temporally experience the surfacing of their symptoms (such as sleepiness). After 1 week, the medication will directly relief the surfaced symptoms as it did previously (or work even better because of relieving tolerance effects), without any incubation time. The patient will make the decision whether he or she wants to go without medication for 1 week. We expect to mostly recruit less severe patients. On the day preceding each test day, subjects will have to adhere to some simple restrictions with respect to alcohol and drug intake. Also, subjects will also have to refrain from smoking on the test day itself, and from eating anything 5h before the appointment. Subjects will come to the lab for a test day which will take 3 hours.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Age: 18-60 years old
- Right-handed

Control group:

- No current sleep, neurological or psychiatric disorder

Patient groups:

- Narcolepsy with cataplexy, or narcolepsy without cataplexy or idiopathic hypersomnia (without long sleep time). All disorders should have been diagnosed according to the ICSD-2 criteria.
- All patients who take medications should be willing to withdraw from taking medication for 1 week.

Exclusion criteria

- Diabetes Mellitus
- (History of) clinically significant hepatic, cardiac, renal, cerebrovascular, endocrine, metabolic or pulmonary disease
- Uncontrolled hypertension, defined as diastolic blood pressure at rest > 90 mmHg or systolic blood pressure at rest > 160 mmHg
- (History of) clinically significant neurological or psychiatric disorders, and current psychological treatment other than narcolepsy (with/without cataplexy).
- Deafness, blindness, or sensori-motor handicaps
- History of taste or smell impairments

- Drug, alcohol or gamble addiction in the past 6 months
- Inadequate command of Dutch language
- Extreme restraint eating (i.e. score restraint eating ≥ 3.60 (females) or ≥ 4.00 (males) on the Dutch Eating Behavior Questionnaire; see also section 6.3.4)
- Current, strict dieting (i.e. specific diet and/or in treatment with dietitian)
- Food allergy to one of the ingredients used in the food rewards
- Contra-indications for MRI:
 - o Metal objects or fragments in the body that cannot be taken out
 - o Active implants in the body
 - o Using medical plasters
 - o Epilepsy
 - o Previous head surgery
 - o Pregnancy
 - o Claustrophobia

Study design

Design

Study type: Observational non invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Other

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 18-02-2014

Enrollment: 60

Type: Actual

Ethics review

Approved WMO

Date: 10-10-2013

Application type: First submission

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	12-12-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	
Date:	31-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	
Date:	21-05-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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: 27831
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL45550.091.13
OMON	NL-OMON27831