Narcolepsy - a functional MRI study

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This study aims to further clarify the pathophysiological mechanisms underlying the decreased vigilance, sleep/wake lapses, and the emotional processing leading to cataplexy.

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

Summary

ID

NL-OMON31921

Source
ToetsingOnline

Brief title
NFM

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy (no synonym available)

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Interne financiering

Intervention

Keyword: cataplexy, EEG, fMRI, Narcolepsy

Outcome measures

Primary outcome

The intensity of the Blood Oxygenated Level Dependent (BOLD)-signal, obtained

with a 3 T MRI-scanner as well as the simultaniously registered EEG-signal of

62 electrodes placed on the scalp.

Secondary outcome

None

Study description

Background summary

Narcolepsy is a primary sleep disorder, with an estimated prevalence of 5-6 per 10,000 in the Western population. The main symptoms are excessive daytime sleepiness and attacks of muscle weakness called cataplexy, but other features like fragmented nocturnal sleep, decreased vigilance and memory deficits are very often present. It is a disabling disease: somnolence and decreased vigilance interfere with work and education. Patients have an increased risk of accidents and tend to avoid social gatherings because of the embarrassment caused by cataplexy and sleep attacks. Not even optimal therapy can abolish such problems, so narcolepsy presents a large burden for patients as well as their relatives.

Cataplexy is defined as a sudden and transient loss of muscle tone, triggered by emotion. The spectrum of muscle weakness ranges from mild buckling of the knees to generalized paralysis of all striated skeletal muscles, sometimes lasting minutes. Consciousness is completely preserved, showing that only motor systems are affected. One of the most puzzling features of cataplexy is its induction by emotions or situations associated with emotions. Laughter is undoubtedly the most frequent trigger.

Less thoroughly explored symptoms of narcolepsy include decreased vigilance and impaired nocturnal sleep. Patients often fall asleep quickly, but awake frequently during the night. The total sleep time over a 24-hour period is not increased in comparison to healthy subjects despite their daytime naps. Although impaired night sleep may contribute to a decreased vigilance during the day, nocturnal sleep disturbances do not explain vigilance problems during the day sufficiently, as their treatment does not solve the problem 6.

The vast majority of patients with narcolepsy-cataplexy lack the neurotransmitter hypocretin (also called orexin). This peptide is found only in the lateral hypothalamus, a structure that is not directly involved in either motor control or the regulation of emotions. However, the hypocretin neurons project widely throughout the brain. How a loss of hypocretinergic cells leads to the different symptoms of narcolepsy, is still unknown.

Study objective

This study aims to further clarify the pathophysiological mechanisms underlying the decreased vigilance, sleep/wake lapses, and the emotional processing leading to cataplexy.

Study design

In this comparative study, will use simultaneous electro-encephalography (EEG) and functional Magnetic Resonance Imaging (fMRI) recordings to analyse brain activity in narcoleptics and healthy controls under three different circumstances:

1. During a presentation of emotional stimuli (funny and non-funny pictures)

2. During an attention task (the Sustained Attention to Response Task)

3. During quiet resting state (ultimately leading to sleep).

Study burden and risks

Subjects are not allowed to take medication with influence on the central nervous system two weeks prior to and during the study. We will try to recruit narcoleptic patients without medication preferentially, but may have to take recourse to ask patients to stop their drugs temporarily for the purpose of the study. Withdrawal from anti-narcoleptic medication may lead to an increase in daytime sleepiness and cataplexy during this period. However, the symptoms are reversible when medication is restarted. We will guide patients during this period and they are free to withdraw their consent any time, without any negative consequences for present or future treatment.

Considering the possibility of asymptomatic intracranial abnormalities in this study, two different issues should be addressed. In the first place, fMRI scans use other settings than regular diagnostic scans. As a consequence, there is a possibility that an actual abnormality may not come to light. In other words, the absence of abnormalities on our scan doesn*t exclude their presence. Subjects will be informed accordingly.
Furthermore, there is a possibility of detecting relevant abnormalities not (yet) causing complaints, even with the settings of scientific scans. These

findings must be anticipated. Part of the informed consent is that such clinical relevant findings will be reported to the subject. When subjects refuse to be informed about possible incidental findings on their scan, they will not be included in this study.

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

Patients: Age 18-65 years, narcolepsy with cataplexy according to ICSD-2
Healthy controls: Age 18-65 years

Exclusion criteria

Unwillingness or inability to sign informed consent
Presence of (other) sleep disorders
Structural brain lesion and/or any other disease of the central nervous system, including psychiatric disorders
Use of any medication influencing the central nervous system 2 weeks prior to the study;MRI-related:
Pacemaker
Intracranial metal objects (e.g. clips, prosthesis etc.)
Pregnancy
Claustrofobia
Piercings that cannot be removed

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2008
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission

Review commission: METC Leids Universitair Medisch Centrum (Leiden)

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	NL20360.058.07