Sleep State Misperception Mispercieved?

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

Summary

ID

NL-OMON35484

Source
ToetsingOnline

Brief title
Sleep State Misperception Mispercieved?

Condition

- Sleep disturbances (incl subtypes)
- Sleep disorders and disturbances

Synonym
Paradoxical insomnia, Sleep state misperception

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Onderzoeks budget afdeling Slaap & Cognitie;Nederlands Instituut voor Neurowetenschappen;KNAW

Intervention

Keyword: Consciousness, Electroencephalography (EEG), Insomnia, non-repetitive), Sleep, Transcranial Magnetic Stimulation (TMS

Outcome measures

Primary outcome

This project will apply analysis tools for ERP, functional connectivity for

resting state EEG, resting state fMRI and task-related fMRI, single and double

pulse TMS (no repetitive TMS).

Main study parameter is the pattern of neural synchronization as measured using

EEG (sleep & wake)

Secondary outcome

In addition we will determine

-patterns of power spectra topography as measured using EEG (sleep & wake).

-Subjective to objective sleep duration discrepancy as measured using sleep

logs, actigraphy and EEG.

-ERP latency and amplitude (topography).

-Blood oxygenation level dependent (BOLD) response in SSM versus PI versus

controls during oddball task and resting state; regression of BOLD response on

latency and amplitude of ERP.

-Resting state functional connectivity in SSM versus PI versus controls

-Structural abnormalities in SSM versus PI versus controls, using voxel-based

morphometry (VBM) to measure regional volumetry and diffusion tensor imaging

(DTI) to measure structural connectivity

-Cortical excitability as assessed using TMS.

Study description

Background summary

Primary insomnia, or psychophysiological insomnia is a poorly understood condition that affects a considerable percentage of the population up till about 40% of the elderly population. Chronic insomnia increases the risk of physical and mental health problems, and is a major factor affecting quality of life (Van Someren, 2000). Polysomnography, i.e. the continuous overnight recording of electroencephalography (EEG), electromyography (EMG) and electrooculography (EOG) may reveal a reduced total sleep duration, decreased slow wave sleep, and increased fragmentation and interruptions by wakefulness. However, a considerable number of subjects that seek treatment for their subjective poor sleep do not show any objective sleep disturbance according to standardized polysomnographic scoring rules (Rechtschaffen and Kales, 1968). Subjects with such discrepancy between objective and subjective sleep disturbances are diagnosed with *Sleep State Misperception*, a term that strongly suggests that they do indeed sleep sound and have no reason to complain. None of subjects suffering from this condition agree, even after showing them polysomnographic data in the morning or waking them up during the night (Mercer et al., 2002). They*re convinced that these records may show anything but their sleep. And, importantly, their misperception is not without consequences for daytime functioning. Most striking is the finding that subjective rather than objective sleep complaints are negatively correlated with daytime performance on memory acquisition during the Selective Reminding Test (Buschke and Fuld, 1974; Szelenberger and Niemcewicz, 2000; 2001). Of note, this very test has in longitudinal aging studies shown to be one of the most sensitive tasks for quantifying age-related memory decline (Small et al., 1999) and risk of dementia (Grober et al., 2000). This suggests the possibility that the brain in fact suffers from its *misperception* of sleep. A recent unpublished observation (C. Bastien, personal communication) moreover indicates alterations in the amplitude (larger) and phase (advances) of event related potentials N2, P2 and N350 during an auditory oddball task; another sign of altered brain function.
We recently found insomniacs to respond differently on transcranial magnetic stimulation (Biol Psychiatry 2010). Because this reaction, the cortical excitability is highly heritable (Pellicciari et al, J Neurosci 2009) we may have discovered the first *endophenotype* of insomnia. We would like to immediately follow up on the finding by including the measurement in our ongoing protocol.
We aim to gain insight in the brain processes associated with sleep state misperception.

Study objective

We aim to establish whether our judgment of *misperception* is really doing justice to the condition paradoxical insomniacs suffer from. We should keep in mind that our present definition of sleep, based on the standardized polysomnographic scoring rules, by no means mirrors all the details of the cortical activities that occur during the night. If we would allow the possibility that the polysomnographic scoring rules may miss the very neuronal activity patterns that we all subjectively experience as sleep, the sleep clinician might turn out to be the one misperceiving the condition of sleep state misperception.
We are not aware of any previous study that has specifically focused on EEG markers of sleep state misperception, other than a reported trend towards an increase in average EEG power in the 14-35 Hz range (Perlis et al., 2001), which has on the other hand been reported to be a generic finding in insomnia (Merica et al., 1998), i.e. not specific to the sleep state misperception variant. In the present study we specifically address the hypotheses that nocturnal synchronization of oscillations is essential to the experience of sleep. We focus on synchronization of oscillations during slow wave sleep, when cortically generated slow oscillations increase the spatiotemporal coherence over widespread cortical areas (Steriade, 1999; Steriade and Timofeev, 2003). A recent unpublished observation (C. Bastien, personal communication) indicates alterations in the amplitude (larger) and phase (advances) of event related potentials N2, P2 and N350 during an auditory oddball task assessed during wakfulness in subjects suffering from sleep state misperception. We would therefore like to include both ERP and an fMRI study in order to evaluate brain activation related to auditory stimulation. The MRI session will also include a structural scan in order to allow for voxel-based morphometry - we recently found a reduction in orbitofrontal grey matter volume in elderly insomniacs without significant misperception - as well as a resting state fMRI recording - in the same insomniacs, we recently found a reduction in perfusion assessed using arterial spin labeling in areas that are part of the *default network*.

Study design

In brief, we will apply a cross-sectional case-control design using actigraphy, high-density EEG and ERP, resting-state fMRI and task-related fMRI. The first phase covers baseline actigraphy and sleep log measurements, meant to verify previous diagnoses of primary insomnia with and without sleep state misperception, and to verify normal sleep in control subjects.
Sub-classification of SSM:
SSM insomnia sufferers have to show on four out of seven actigraphic recording nights:
a) a Total Sleep Time (TST) > 380 minutes or a Sleep Efficiency (SE) >= 80%, as well as
b) using sleep logs and actigraphy, an overestimation >= 60 minutes of Sleep Onset Latency (SOL), an underestimation >= 60 minutes of TST or >= 15% underestimation of their SE.
For definite confirmation and inclusion in analyses SSM insomnia sufferers have

to show on two consecutive PSG recording nights (one available from history, two assessed in the present study):
a) a TST > 380 minutes or a SE >= 80%, as well as
b) an overestimation >= 60 minutes of SOL, an underestimation >= 60 minutes of TST or >= 15% underestimation of their SE.

The second phase covers one fMRI scan and two nights of high-density EEG recording, with an interval ranging between at least one day and at most one week. The fMRI study will evaluate (1) brain activation related to auditory stimulation (same oddball task as the subsequent oddball task with ERP recording) (2) a structural scan in order to allow for voxel-based morphometry and (3) resting state BOLD fluctiations. EEG will be recorded using a Micromed LDM-64 ambulatory recorder and a dedicated Easycap 61-channel equidistant electrode cap with 61 flat equidistant EEG electrodes and additional electrodes to record EMG and EOG. Participants have the choice of either being recorded in an apartment at the Boelelaan, or - distance allowing - at home. The cap will be affixed during the early evening. A wake resting state and alpha attenuation task (eyes open and closed) will be recorded at application of the montage in the late afternoon, as well as an auditory oddball task. The motor evoked potential (MEP) response on single and double-pulse transcranial magnetic stimulation is being measured, which lasts at most half an hour including preparation.

Study burden and risks

Participants keep a sleep diary and wear a wrist-watch-sized activity logger or one week, without behavioral restrictions. For nocturnal EEG recording, participants wear a 64-channel EEG-cap and a recorder all night, and have the choice of either being recorded in an apartment at the Boelelaan, or - distance allowing - at home. Two nights will be recorded, of which the first acts as adaptation night. EEG montage takes place in the late afternoon or early evening. EEG removal takes place the next morning. On each of the days, eyes closed and eyes open rest-EEG will be recorded, as well as an auditory oddball ERP task, concertedly lasting no more than 15 minutes. On one of the two days, an MRI scan lasting 60 minutes at most will be recorded. The motor evoked potential (MEP) response on single and double-pulse transcranial magnetic stimulation is being measured, which lasts at most half an hour including preparation.No risk is associated with any of the procedures.

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

Diagnosis of primary insomnia
20-70 years old
informed consent

Exclusion criteria

psychotropic medication (exclusion if not at least 4 weeks off medication)
metal in body
severe claustrophobia
major somatic disorder
psychiatric disorder

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2009
Enrollment:	36
Type:	Anticipated

Ethics review

Approved WMO Date:	26-03-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-05-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-01-2011
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

No registrations found.

In other registers

Register	ID
CCMO	NL26924.029.09