Circadian rhythm evaluation and polysomnographic sleep tracking in cluster headache attacks.

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Part 1To determine if certain sleep stages (wake, REM, N1, N2, N3), and relatively high or low melatonin and cortisol levels, respectively, are associated with an increased or decreased instantaneous risk of cluster headache attacks in patients with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Headaches
Study type	Observational invasive

Summary

ID

NL-OMON56698

Source
ToetsingOnline

Brief title
Clock, sleep and cluster headache (CIESTA)

Condition

- Headaches

Synonym
clusterheadache, Trigeminal Autonomic Cephalalgias (TAC)

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Clock, Cluster headache, Sleep

Outcome measures

Primary outcome

Part 1:

The risk of the occurrence of a cluster headache attack depending on sleep stage, melatonin level, cortisol level and clock time (hazard ratio).

Sleep stage is defined as REM, N1, N2, N3 or wake. Melatonin and cortisol values will be defined as the relative increase or decrease compared to an individuals average value during the study period.

Part 2:

Difference in sleep stage distribution (percentage REM and non-REM), the average melatonin zenith (peak) and the average cortisol nadir (through) between ECH patients in bout versus ECH patients out of bout.

Secondary outcome

The secondary study parameters serve an exploratory character and will be addressed if possible.

Part 1

Sleep:

- The sleep stage (stage 1/N1, stage 2/N2, stage 3/N3 and REM) directly prior to attack onset. Results will be reported as a percentage of attacks per sleep

stage.

- The time between transition in sleep stage and attack onset, to determine whether transition between REM sleep and non-REM sleep precipitates an attack
- The time at which the first nocturnal attack occurs

Circadian rhythm markers:

- The average melatonin level at attack onset
- The average cortisol level at attack onset
- The average melatonin zenith and nadir
- The average cortisol zenith and nadir
- Average core temperature at attack onset
- Average proximal skin temperature at attack onset
- Time from core body temperature zenith and nadir to attack onset
- Time from skin temperature zenith and nadir to attack onset
- Sympathicovagal balance (heart rate variability) at attack onset

Part 2

To compare several characteristics of sleep and the biological clock in patients during an active cluster period versus remission, i.e.:

- The average sleep latency
- The average total sleep time
- The average sleep efficiency
- The percentage of REM sleep and non-REM sleep of total sleeping time
- The average REM latency

- The average REM density

- The REM fragmentation

- The gross motor activity as a measure for hypoarousability during REM sleep

- Average core body temperature

- Average proximal skin temperature

Study description

Background summary

The exact aetiology of cluster headache is still unknown. Several studies show a clear relationship between attacks, sleep and the circadian rhythm, indicating a pivotal role of the hypothalamus. However, results up until now have been inconsistent, mostly based upon single-night measurements in a hospital setting with a limited number of samples. We will use advanced ambulatory monitoring systems that have recently become available, allowing us to measure multiple consecutive nights of sleep and 24-hour tissue cortisol & melatonin rhythms (samples at 20 minute intervals). Unravelling the role of the hypothalamus and increased knowledge of sleep and clock rhythms in cluster headache will be of great value for follow-up studies on brain activity changes underlying attack susceptibility, to test treatment with medication targeting sleep and the biological clock, and to other researchers to investigate evolving hypotheses.

Study objective

Part 1
To determine if certain sleep stages (wake, REM, N1, N2, N3), and relatively high or low melatonin and cortisol levels, respectively, are associated with an increased or decreased instantaneous risk of cluster headache attacks in patients with either chronic or episodic cluster headache during the in bout phase.

Part 2
To determine if the sleep stage distribution (percentage REM and non-REM), and the average melatonin zenith (peak) and cortisol nadir (through) differ within patients with episodic cluster headache in bout versus out of bout.

Study design

A single centre, prospective cohort study consisting of a one-week baseline period, followed by 7 days of neurophysiological measurements during part 1 (CCH + ECH) and an additional 7 days of neurophysiological measurements during part 2 (only ECH).

Study burden and risks

Participating in the study includes 4-5 (CCH) of 8-10 (ECH) visits to the LUMC, filling out questionnaires, and 7 (CCH) or 14 days (ECH) of neurophysiological measurements. During the first visit, the subcutaneous microdialysis catheter will be placed. This can cause minor discomfort, but once the microdialysis pump is connected, the hormone sampling will happen automatically without any additional discomfort for the participant. All other measurements are non-invasive. The measurements will be performed at home, minimising the burden on participants, and risks are low. Participation in this study has no direct benefits. However, the results can lead to new insights and subsequently treatment options for cluster headache, and therefore indirectly benefit participants.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age >=18 and <70 years.
- Diagnosed with either chronic or episodic cluster headache according to the International Classification of Headache Disorders - third edition (ICHD-3) criteria.
o In case of episodic cluster headache: within 1 to 2 weeks from the start of the cluster episode, or in patients with a minimum of 4 expected weeks remaining in their cluster episode.
- >=5 nocturnal cluster headache attacks per week and no more than two nights without any cluster headache attacks during the one-week baseline period.
- On a stable regimen, or free of, cluster headache prophylactic therapy (including neuromodulation during the study period. Acute attack treatment with subcutaneous sumatriptan and/or 100% oxygen will be allowed and monitored.
- Regular sleep habits

Exclusion criteria

- Inability to use a Dutch electronic headache diary
- Other headaches if the patient cannot reliably distinguish them from attacks of cluster headache
- Current use of prophylactic medication for other headaches
- Diagnosis of a primary sleep disorder other than insomnia, including sleep apnoea syndrome
- Known pituitary disorder
- Pregnancy, lactation or trying to conceive (females)
- Use of opiates
- Estrogen containing oral contraceptive medication within the past 6 -weeks
- Use of melatonin within past 6 weeks
- Use of oral or parenteral glucocorticosteroids within past 3 months and/or use of oral, inhaled or parenteral glucocorticosteroids during the study period
- Use of medication that effects melatonin production, such as beta blockers.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-10-2024
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	10-04-2024
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	NL84386.058.23