Stress response in narcolepsy type 1

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To investigate in people with NT1 and matched controls, after an experimentally induced social stress test:Primary:- Direct HPA activation (plasma cortisol).Secondary: - Direct autonomic stress response (ACTH and HR). - HPA activity and autonomic...

Ethical review	Approved WMO
Status	Completed
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON53558

Source
ToetsingOnline

Brief title
Stress response in NT1

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy type 1; narcolepsy with cataplexy

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Epilepsie Instellingen Nederland
Source(s) of monetary or material Support: EpilepsieNL

Intervention

Keyword: Corticotrophin-releasing hormone (CRH), Cortisol, Narcolepsy type 1 (NT1), Trier Social Stress Test for Groups (TSST-G)

Outcome measures

Primary outcome

Difference between patients with NT1 and matched controls in the mean plasma cortisol levels after stress exposure (T1), adjusted for baseline plasma cortisol level (T0).

Secondary outcome

- Differences between patients with NT1 and matched controls in the plasma cortisol levels after recovery (T2 and T3), adjusted for baseline plasma cortisol level (T0).
- Differences between patients with NT1 and matched controls in their plasma ACTH levels after stress exposure (T1) and recovery (T2 and T3), adjusted for baseline ACTH levels (T0).
- Differences between patients with NT1 and matched controls in HR during all time points of the experiment.
- Differences in subjectively experienced stress between patients with NT1 and matched controls at all time points of the experiment.
- Differences between patients with NT1 and matched controls in the association between objective and subjective stress parameters, and their relationship with any of the background variables, during all time points of the experiment.

Study description

Background summary

Narcolepsy type 1 (NT1) is a very disabling sleep-wake disorder caused by a cerebral deficiency of hypocretin (Hcrt, also known as orexin). A recent

post-mortem brain study of the hypothalamus in NT1 not only showed a major reduction of Hcrt cells, but also a 88% reduction of corticotrophin-releasing hormone (CRH)-positive neurons (Shan et al., 2022) in the paraventricular nucleus (PVN). CRH in this nucleus is known for its role as hypothalamic-pituitary-adrenal (HPA) axis activator. This matches with the earlier finding of reduced basal pituitary adrenocorticotropic hormone (ACTH) secretion in patients with NT1 (Kok et al., 2002). Therefore it is expected that patients with NT1 have a lowered cortisol (stress) response compared to matched controls. Better understanding of the HPA activity in patients with NT1 may give better insights in the effects of lost CRH-positive cells in this population. This knowledge may contribute to greater understanding of the etiology of the disease and the development of potential novel treatments in the future.

Study objective

To investigate in people with NT1 and matched controls, after an experimentally induced social stress test:

Primary:
- Direct HPA activation (plasma cortisol).

Secondary:
- Direct autonomic stress response (ACTH and HR).
- HPA activity and autonomic stress after a recovery time (plasma cortisol, ACTH and HR).
- Subjectively experienced stress directly after the stress test and after recovery time.
- The association between subjective and objective stress markers, and their relationship with any background variables.

Study design

A quasi-experimental case-control intervention in n=12 patients with NT1 and n=12 controls matched for age and sex. All participants will be exposed to the Trier Social Stress Test for Groups (TSST-G) in six groups of four participants each. Before the TSST-G (T0), directly after (T1), after a 15-minute recovery period (T2) and after a second 15-minute recovery period (T3), we will assess: plasma ACTH and cortisol and subjective stress. Heart rate (HR) will be measured continuously.

Intervention

The TSST-G is an effective stress intervention, where participants are instructed to give a public speech, followed by a mental arithmetic task, before a non-supportive jury while thinking they are being videotaped. This

test has shown in previous studies to effectively induce psychophysiological stress and activate the HPA axis (Von Dawans, Kirschbaum & Heinrichs, 2011).

Study burden and risks

Participants visit the research center once for about 4 hours in total. Participants are told that they participate in a study about social competence and resilience. During their visit they will be exposed to a stress test (TSST-G). In total, four blood samples will be taken via a cannula to avoid the stress of multiple punctures, which may be unpleasant and induces a regular (small) risk of local hemorrhage. The subjective questionnaires will take about 15 minutes each time, inducing minimal burden. Potential negative feelings regarding the TSST-G will be taken away as much as possible during an extensive debriefing. The TSST-G is a validated test which does not lead to extreme perceived anxiety levels or burden. Participants will not personally benefit from this study. They will be compensated with ¤50 for participation. Patients with NT1 will have the opportunity to take a nap at the research center after the experiment.

Contacts

Public
Stichting Epilepsie Instellingen Nederland

Achterweg 3
Heemstede 2103SW
NL
Scientific
Stichting Epilepsie Instellingen Nederland

Achterweg 3
Heemstede 2103SW
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age 18-64 years.
- For patient group: a diagnosis of narcolepsy type 1 following the ICSD-3 criteria.

Exclusion criteria

- For control group: any sleep-wake disorder or use of sleep medication
- Any other disease that may affect HPA activity
- History of anxiety disorders, panic attacks, cardiac disease or hypertension, epilepsy or Cushing*s disease
- Mental retardation
- Current depressive disorder
- Current use of antidepressants (not being low dose for cataplexy)
- Present use of benzodiazepines or any hormonal treatment (other than oral contraceptives)
- Pregnant or lactating
- Smoking > 5 cigarettes a day
- Excessive alcohol consumption (women >14, men >21 units a week)
- Lack of fluency in the Dutch language or speech impairments
- Experienced public speaker
- Psychologist or study/specialisation psychology

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	24-02-2023
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	12-10-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-03-2023
Application type:	Amendment
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	NL82071.058.22

Study results

Date completed: 30-06-2023

Results posted: 05-08-2024

Actual enrolment: 26

First publication
24-06-2024