international Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (iSPHYNCS): Dutch participation

Published: 13-09-2023
Last updated: 19-08-2024

The aim of this longitudinal study is to find new biological, clinical and/or electrophysiological biomarkers in order to define and differentiate individual diagnoses of NT1 and the NBL, and to find improved treatment targets and strategies.

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

Summary

ID

NL-OMON56089

Source
ToetsingOnline

Brief title
iSPHYNCS-NL

Condition

- Sleep disturbances (incl subtypes)

Synonym
Narcolepsy with or without cataplexy; Sleeping illness; Excessive daytime sleepiness

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Epilepsie Instellingen Nederland
Source(s) of monetary or material Support: Swiss National Science Foundation (vergelijkbaar met NWO)

Intervention

Keyword: Biomarkers, Idiopathic hypersomnia, Narcolepsy

Outcome measures

Primary outcome

The primary endpoints are clinical: the proportion of subjects with diagnosis of NT1 or other CDH diagnoses at follow up. Results from this study are expected to substantially improve (and revise) diagnostic criteria for NBL, which may result in identification of new treatment targets/strategies.

Secondary outcome

The secondary endpoints are biological determinants and biomarkers: the proportion of patients with autoreactive T-cell clones in NT1 and in some NBL subjects but not in controls, and the intestinal microbiome of NT1 and NBL in comparison to controls. The tertiary endpoints are Electrophysiological biomarkers and questionnaire outcomes for NT1 and NBL in comparison to controls.

Study description

Background summary

Narcolepsy type 1 (NT1) is a relatively well defined disorder with known specific and sensitive biomarkers and a suspected autoimmune pathology. All other central disorders of hypersomnolence (CDH) have ill-defined diagnostic criteria with overlapping signs and symptoms and little is known about their pathophysiology. In clinical practice excessive daytime sleepiness (EDS) without cataplexy remains the main diagnostic challenge: Often diagnostic criteria are only partly fulfilled and clinical signs and symptoms overlap within the different CDH, resulting in incorrect diagnoses or even no diagnosis can be made. As a result patients receive wrong or no treatment, even though effective therapeutic options would exist. Therefore, a better definition of

the disorders other than NT1, the so-called narcoleptic borderland (NBL), is urgently needed.

Study objective

The aim of this longitudinal study is to find new biological, clinical and/or electrophysiological biomarkers in order to define and differentiate individual diagnoses of NT1 and the NBL, and to find improved treatment targets and strategies.

Study design

A prospective, observational, longitudinal study with 3 years follow-up for patients and 1 year for controls. Initiated in Switzerland, with 8 Swiss participating sleep centres. This (initially Swiss) study has been expended internationally to Germany, Italy, and Netherlands. The Sleep-Wake Center of SEIN is the only participating Dutch site. The data and stool samples collected in the Dutch site are shared with the international study group. For the Dutch site, the collected blood and CSF samples that are necessary to answer the research questions, are collected and stored following the LUMC Narcolepsy Biobank protocol. The few participants that did not have blood sampling within their regular care, wil be asked to donate blood in the light on the current research. This will be also stored following the LUMC Narcolepsy Biobank protocol.

Study burden and risks

Biomaterial collection takes place during the regular visits in addition to the clinical workup. Following the already existing LUMC Narcolepsy Biobank protocol, blood and CSF that are collected within the routine clinical procedure are stored in the biobank. The few participants that did not have blood sampling within their regular care, wil be asked to donate blood in the light on the current research, which is also stored in the Narcolepsy Biobank following its protocol. For the current study, additional stool samples are collected twice: at baseline and at the 12 month follow-up. Participants are asked to wear a FitBit © on the wrist that monitors 24-hour activity patterns for the duration of one year. Participants fill out a set of questionnaires at various time points throughout their study participation, concerning disease symptoms, psychological health, quality of life and medication adherence. Questionnaire part A takes 5-10 minutes and is filled out 5 times (at baseline, and at 6, 12, 24, and 36 months follow-up). Part B takes 40-50 minutes and is filled out 3 times (at baseline, and at 12 and 36 months follow-up). A neuropsychiatric interview is assessed twice (at baseline and at 12 month follow-up), which takes 15-20 minutes. Patients who show signs and symptoms of depression or acute suicidality, are given the opportunity to further evaluate this issue during one of the clinical visits and are treated or referred if

needed. For visits which are only study-related, patients and controls will get their travel costs refunded. Healthy controls receive ¤150 (divided over four time points) for their study participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

All participants:
- Age 16-70 years
- Ability and consent to undergo electrophysiological routine assessment
- Ability to give informed consent

Patients:
- Subjective complaints of excessive daytime sleepiness (EDS) and/or

hypersomnolence (H) as defined in the protocol
- EDS and/or H present daily or almost daily for at least 1 month prior to the consultation

Healthy Controls:
- Proportionally age and gender matched healthy subjects

Exclusion criteria

All participants:
- Chronic infectious diseases (such as Hepatitis B/C, HIV)
- Chronic use of antibiotics
- Recent use (over 8 weeks) of immune-modulating drugs

Patients:
- The following disorders/conditions that on clinical grounds are considered to be the cause of EDS/H:
-- Other sleep disorders
-- Other neurological disorders
-- (Auto-)immune and systemic disorders
-- Malignancy (except: Status in Remission for over 10 years)
-- Instable psychiatric disorder
-- Active infectious disease at screening
-- Permanent medications/drugs
- Sleep disordered breathing (SDB): Presence of clinically significant and untreated obstructive (OSA) or central sleep apnea (CSA) as determined by the investigator or documented previously; or documentation of one of the following:
-- Apnea index (AI) over10 if on OSA treatment or untreated; or
-- Clinically significant hypoventilation; or
-- Noncompliance with primary OSA/PAP therapy in case of clinically significant OSA
-- except if NTI has been diagnosed including decreased or missing CSF hypocretin

Healthy Controls:
- Subjective complaints of EDS and/or H as defined in the protocol
- Epworth Sleepines Scale (ESS) over 10
- Polysomnography (PSG) with apnea index (AI) over10/h and/or periodic leg movement series (PLMS) Index over 30/h
- SDB: Presence of clinically significant and untreated OSA or central sleep apnea (CSA) as determined by the investigator or documented previously; or documentation of one of the following:
-- Apnea index (AI) over 10 if on OSA treatment or untreated; or
-- Clinically significant hypoventilation; or

-- Noncompliance with primary OSA/PAP therapy

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):	01-09-2023
Enrollment:	80
Type:	Anticipated

Ethics review

Approved WMO

Date:	13-09-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	25-07-2024
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	NL84710.058.23