The post-illumination pupil respOnse and its relation with Sleep quality and skin temperature in patients with a history of optic Chiasm Compression

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational non invasive

Summary

ID

NL-OMON47454

Source
ToetsingOnline

Brief title
Out-of-SynCC

Condition

- Hypothalamus and pituitary gland disorders
- Nervous system neoplasms benign
- Sleep disturbances (incl subtypes)

Synonym
optic chiasm compression; compression of the eye nerve

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Optic chiasm, Pupillary light response, Retinohypothalamic tract, Suprachiasmatic nucleus

Outcome measures

Primary outcome

Difference in PIPR after a blue-light stimulus between the two groups;

expressed in two parameters:

- PIPR-mm = baseline pupil diameter (mm) * post-blue pupil diameter (mm)

- PIPR-% = 100 x PIPR-mm/baseline pupil diameter (mm)

Secondary outcome

* Differences in questionnaire results on sleep quality, chronotype, fatigue

and depression (MCTQ, HDSQ, PSQI, ESS, ISI, BQ, MFI-20, HADS)

* Differences in polysomnography, actigraphy & sleep diary results

* Differences in skin temperature results

* Correlations between parameters of PIPR, sleep, sleep-wake rhythm and skin

temperature

Study description

Background summary

A history of optic chiasm compression is associated with altered circadian rhythmicity with complaints of disturbed sleep and daytime fatigue, despite adequate hormonal substitution in case of hypopituitarism. Compression of axons of special intrinsically photosensitive retinal ganglion cells (ipRGCs) that

form the retinohypothalamic tract (RHT) and mediate photoentrainment of the suprachiasmatic nucleus (SCN) could be a causal factor. Similar ipRGCs control the pupillary light reflex through projections to the olivary pretectal nucleus (OPN). The post-illumination pupil response (PIPR) after blue light is regarded as an unique indicator of melanopsin-mediated ipRGC function. We hypothesize that hypopituitarism patients with a history of optic chiasm compression due to a sellar tumour have a reduced PIPR as a result of dysfunctional ipRGC transduction, and that a reduced PIPR is related to disturbed sleep and altered thermoregulation in these patients.

Study objective

Our main objective is to assess the difference in PIPR after a blue-light stimulus between hypopituitarism patients with and without a history of CC. Secondary objectives include differences in subjective and objective sleep quality, sleep-wake disturbances and skin temperature between groups and correlations between these parameters and to the PIPR.

Study design

Observational study, comparing two predefined groups from one historical cohort of patients suffering from pituitary insufficiency. Duration: 8 days per patient, 1 or 2 study visits.

Study burden and risks

A medical and ocular history is taken through an interview. Several questionnaires on sleep, fatigue and chronotype are filled out at home (60-75 minutes). For most patients there will be only one study visit. Visual acuity and colour vision are evaluated and then the PIPR assessment is performed using pupillometry. After dilatation of the pupil to achieve maximal illumination of the retina, the right eye is exposed to bright red and blue light stimuli with intensities well below safety recommendations. The pupil diameter of the left eye is continuously measured using an infrared camera. After the pupillometry the left pupil is dilated as well and an evaluation by an ophthalmologist follows, using slit-lamp biomicroscopy. The visit, including waiting time and explanation, will last half a day. Tropicamide side-effects are minor and include transient stinging and a dry mouth. The induced mydriasis affects visual acuity for several hours, so patients cannot drive during that time. The risk of inducing acute angle closure glaucoma with tropicamide is extremely low (0.006-0.03%). In the unlikely event of it occurring, rapid treatment is at hand. If the ophthalmological evaluation is unremarkable, ambulant study procedures follow. Patients receive an actigraph, to be worn continuously on the wrist for 7 days and causing no more discomfort than a wristwatch. They will also keep a sleep diary during this week. Furthermore, 5 small water-resistant temperature sensors are placed on different locations on the

skin for 3 days with either Velcro or adhesive tape. These can cause some minor discomfort. A 6th sensor is attached to the actigraph strap to record environmental temperature, causing no discomfort. The last procedure is an ambulant polysomnography during one night. Various electrodes and sensors are administered by a trained nurse on the head, chest and legs. The wires are connected to a portable recorder that is worn on the body with an elastic band. Patients can therefore move around normally. The various sensors and wires can be somewhat inconvenient during eating, drinking and other activities. After waking up the next day, they can remove the equipment return it by mail in a specially provided box.
The risks associated with participation in this study are negligible, and the burden is limited. The results of the study will aid in the understanding of ipRGC function and the association with disturbed sleep and thermoregulation after optic chiasm compression. This will lead to better information for patients and guide future research on the consequences of chiasm compression and on interventions to alleviate symptoms.

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

* > 18 years
* At least one impaired central endocrine axis
* Clearly documented cause of hypopituitarism
* Adequate replacement of hormone deficiencies
* Patients with history of chiasm compression: documentation of visual field defects or loss of visual acuity and a suprasellar extending tumour on MRI (before treatment)

Exclusion criteria

* Ocular pathology that could influence the PIPR
* Impaired colour vision
* Previous intra-ocular surgery
* Hypersensitivity to tropicamide
* Use of medicinal eye drops or systemic medication that can affect the pupillary response; assessed on an individual basis
* Pituitary surgery < 12 months prior to examination
* History of whole-brain radiation
* Shift work the month prior to examination
* Travel across >3 time zones the month prior to examination
* Pregnancy
* Other comorbidity that could interfere with the study procedures; assessed on an individual basis

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:	Recruitment stopped
Start date (anticipated):	27-03-2017
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	15-07-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-08-2018
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	NL57603.018.16