Conditioning of the Cortisol Awakening Response (CAR)

Published: 03-04-2018
Last updated: 12-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50199

Source
ToetsingOnline

Brief title
CAR Conditioning

Condition

- Other condition

Synonym
Not applicable

Health condition

Het onderzoek wordt bij gezonde mensen uitgevoerd. Uitkomsten uit deze lijn van onderzoek bieden nieuwe handvatten voor therapeutische interventies voor patiënten met verlate slaap-fase syndroom of seizoensgebonden depressie.

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: NWO onderzoektalentbeurs

Intervention

Keyword: Circadian rhythms, Conditioning, Cortisol, Sleep

Outcome measures

Primary outcome

The main study parameter is change in the CAR (evocation measurement compared

to baseline measurement) in the experimental compared with the control group.

Secondary outcome

Secondary outcomes are physiological parameters (e.g. HR), and psychological

parameters (e.g. affect).

Study description

Background summary

Preliminary evidence suggests that endogenous hormone secretion, such as cortisol or insulin, might be behaviorally conditionable in humans. With regard to conditioning of physiological circadian reactions, preliminary evidence is available in rodents only. It is currently unclear whether it is possible to condition circadian reactions in humans, but if proven possible, this approach might be used as a new and minimally invasive treatment method for patients suffering from dysregulated circadian rhythms, such as delayed-phase sleep disorder and seasonal affective disorder.

Study objective

The primary objective is to investigate the effect of olfactory conditioning during sleep on the circadian-related cortisol awakening response (CAR). Secondarily, we will investigate the effect of the conditioning on physiological parameters (e.g. heart rate (HR)) and psychological parameters (e.g. affect). We will also explore the impact of personality and several sleep parameters (sleep quality and sleep duration) on the conditionability of the

CAR, since these parameters have been shown to affect the size of the CAR.

Study design

A previously validated two-phase randomized controlled conditioning paradigm will be applied in the home environment of participants. After being screened, eligible participants will fill in several questionnaires. Participants will be randomized to either the experimental or the control group on the basis of a random number sequence, generated before the start of the study. During the first week of the study all participants will be required to fill in a short (max 5 minutes) daily diary, assessing among other things sleep parameters. Besides the diary, participants* sleep-wake cycle will be objectively monitored during the 1st and 2nd week of the study using the MotionWatch8. As a baseline measurement for primary and secondary outcome parameters, on Friday morning of the first week, after regular awakening via an alarm clock, participants will start with collection of saliva from awakening up to 45 minutes after awakening, by means of 4 non-invasive cotton sampling measures. They will also fill in several short questionnaires and they will sleep with an HR sensor for assessment of the physiological secondary outcomes. In the second week, all participants are again required to fill in a short daily diary. Moreover, the first three days (association phase; Monday until Wednesday night), participants are exposed to a distinctive scent (conditioned stimulus, CS;) by means of a controlled scent delivery system from thirty minutes before awakening up to their regular awakening time (via an alarm clock), in order to associate this scent to the natural steep rise in cortisol levels before awakening (unconditioned stimulus, US). On Thursday night - one week after the baseline CAR-assessment to control for weekly activity patterns - participants will set their alarm clock four hours earlier than their regular awakening time and either be exposed to the CS (experimental group) or a different distinctive scent (non-CS; control group) (evocation phase). At this time, their CAR is again measured in 4 saliva samples. Again, they will also fill in several short questionnaires. After the last saliva measurement they are allowed to go back to sleep. During the nights in the association phase and evocation phase, participants will sleep with an HR sensor for assessment of the physiological secondary outcomes. In Figure one, a schematic overview of the design is presented (see section Study Design of the METC protocol).

Intervention

The intervention consists of a conditioning paradigm, in which as association is learned between a scent and the circadian CAR. See Study design of the summary for the description of this paradigm.

Study burden and risks

Risks associated with the study protocol are minimal. Participants will report

to university once, after which the remainder of the protocol will be carried out at home. Participants will be asked to set an alarm clock on their regular awakening time on four days, and will be woken up four hours before their regular awakening time during the evocation phase. After the saliva measurements in the evocation phase, participants will be allowed to sleep again after 45 minutes. Potential risk of this early awakening (evocation phase) could be somewhat more fatigue than on other days. The scents are hypoallergenic and all measures are non-invasive. The controlled scent technology delivery systems (Air/Q-100 & Air/Q-160, Prolitec Inc., Milwaukee, WI, US) have received CE-marking. Participants can stop the study at any time for any reason. Participation entails an approximate total time investment of five hours. Studying the effects of conditioning of the cortisol awakening response will shed more light on the possibilities and boundaries of conditioning circadian-related endocrine parameters. This approach could be used to potentially shift circadian rhythms, and thus could lead to a new, minimally invasive treatment for patients suffering from dysregulated circadian rhythms.

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

* Male gender
* Aged between 21 and 34 years of age
* Good understanding of written and spoken Dutch.

Exclusion criteria

* Refusal to give written informed consent
* Severe somatic or psychiatric conditions that would adversely affect participant*s safety or that might interfere with the study protocol
* Olfactory impairments
* Known sensitivity or hypervigilance to one of the ingredients of the scents used in this experiment
* Heavy use of (illegal) drugs including cannabis and habits of heavy drinking
* Irregular sleep pattern or sleep problems
* Use of medication that interferes with the study protocol
* Factors known to influence the CAR:
o Having an acute illness, or experienced an illness in the past seven days (e.g. influenza, common cold)
o Experienced jet lag or shift work in the past seven days
o Use of (oral) glucocorticoid medication
o HPA-axis related endocrine disorders (e.g., Cushings disease or Addisons disease)
o Brain damage, particularly hippocampal brain damage
o Obesity

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-04-2018
Enrollment:	88
Type:	Actual

Ethics review

Approved WMO Date:	20-04-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
Approved WMO Date:	11-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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	NL62812.058.17