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The impact of the circadian clock on retinal function

Submission date 23/03/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 28/03/2024	**Overall study status** Completed	
Last Edited 19/06/2025	**Condition category** Eye Diseases	

Plain English summary of protocol

Background and study aims
Previous research indicates that visual functions vary throughout the day, likely due to natural body rhythms. However, it is unclear whether these changes are driven by the body's internal clock (circadian rhythm) or other factors. To understand this better, this study aims to separate the effects of circadian rhythms and other processes on retinal function. The research will focus on how the eye responds to light and perceives images. By studying these responses, the researchers hope to gain insights into how light affects the internal body clock and vice versa, potentially leading to refinements in our understanding of circadian rhythms.

Who can participate?
Adult healthy volunteers aged from 18 to 35 years old

What does the study involve?
Participants will spend 40 hours in a controlled environment, with alternating periods of wakefulness and sleep in dim or no light. During wakeful periods, they will undergo tests to assess their ability to see patterns and how their pupils react to light. Retinal sensitivity is expected to change depending on the time of day.

What are the possible benefits and risks of participating?
Participants in this study will play a crucial role in the advancement of scientific knowledge, with no immediate personal advantage or benefit. The study design ensures no long-term negative impacts on physical health or mental well-being. All necessary precautions will be taken to ensure participant comfort and engagement throughout the study, including measures to address any discomfort or difficulties experienced during the various procedures. The main experiment in this study consists of a 40-hour sleep-wake protocol, involving strict adherence to a predetermined sleep-wake schedule. Although participants may find it difficult to adjust to this schedule, the risks associated with the protocol are considered minimal. Temporary disruptions to circadian rhythms may occur as a consequence, leading to changes in sleep quality, mood, and overall well-being, similar to experiencing “jet lag” when traveling across time zones. However, participants will be closely monitored, and steps will be taken to ensure their comfort and well-being throughout the study. During certain psychophysical and pupillometric measurements, participants may experience strain and discomfort. To minimize these effects,

participants will have an opportunity to familiarize themselves with the visual tasks and tests before committing to the experiment. Throughout the study, the study team will closely monitor participant well-being and intervene if any participants report feeling uncomfortable. Before entering the main study, participants will provide blood samples. The process of drawing blood, while generally safe, carries some potential risks including discomfort, bruising at the puncture site and in rare cases, the possibility of permanent nerve damage. Additionally, there is a small chance of infection or allergic reactions to disinfectants, adhesive materials, or bandages used during the procedure. These risks will be managed through properly trained personnel, adherence to sterile techniques, and prompt attention to any adverse reactions. Participants in this study are required to adhere to a regular sleep-wake cycle for the whole study period of 3 weeks, which some individuals may find challenging. Through our screening methods, the study team will identify individuals who are likely to have no difficulties in maintaining a regular sleep-wake cycle. Additionally, participants will be required to abstain from caffeine and alcohol during the study, which may pose some difficulty for some individuals. During the screening process, the study team will select participants who have low to moderate consumption and are comfortable abstaining from these substances for the duration of the study. They are also asked to wear an actigraph tracker, which is no larger than a wristwatch, during this time. While some participants may find wearing the device intrusive or challenging, it provides valuable data for the research. In summary, the challenges and discomfort associated with this study are considered minor, as they are outweighed by the potential for significant advancements in fundamental biological and biomedical knowledge. The insights gained from this research will contribute to a better understanding of the interaction of visual processing of light and circadian signals. The study team will be committed to prioritizing participant well-being, maintaining their comfort, and ensuring their understanding and informed consent throughout the research process.

Where is the study run from?
Max Planck Institute for Biological Cybernetics

When is the study starting and how long is it expected to run for?
June 2023 to October 2024

Who is funding the study?
Max Planck Society for the Advancement of Science

Who is the main contact?
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Contact information

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Additional identifiers

Study information

Scientific Title
Within-subjects ultra-short sleep-wake protocol for characterising circadian variations in retinal function

Acronym
CiViBe

Study objectives
The circadian clock affects retinal function and sensitivity

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/10/2023, Medical Ethics Committee of the Technical University of Munich (Ismaninger Straße 22, Munich, 81675, Germany; +49 (0)89 4140 7737; ethikkommission@mri.tum.de), ref: 2023-369-S-SB

Primary study design
Interventional

Study design

Single-blinded interventional trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Circadian modulation of retinal function

Interventions
Ultra-short sleep-wake cycle intervention:
All participants undergo the same protocol and there are no study arms. The intervention is geared to decouple circadian from homeostatic parameters. Participants will stay in a controlled time-isolating environment under dim light conditions and adhere to an ultra-short sleep-wake cycle, alternating between 2h30m of wake time in dim light and 1h15m hour of sleep in no light.

Intervention Type
Behavioural

Primary outcome(s)
1. Pupil responses to silent-substitution modulations (L-M, S, L+M+S, Mel) are measured once using a Maxwellian multi-primary pupillometer during each ultra-short sleep-wake cycle
2. Psychophysical thresholds to silent-substitution modulations (L-M, S, L+M+S) are measured once using the Metropsis stimulus system during each ultra-short sleep-wake cycle

Key secondary outcome(s)
1. Core body temperature is measured using telemetry pills continuously during the entire experiment.
2. Distal-proximal temperature measured using skin temperature sensors continuously during the entire experiment.
3. Rest-activity cycles are measured using actigraphs continuously during the entire experiment.
4. ECG is measured using a heart rate monitor continuously during the entire experiment.
5. Glucose concentrations are measured using a CGM continuously during the entire experiment.
6. Ocular structures are measured using OCT once per ultra-short sleep-wake cycle
7. Salivary cortisol concentrations are measured using Salivette and later ELISAs every 45 minutes during each ultra-short sleep-wake cycle
8. Salivary melatonin concentrations are measured using Salivette and later ELISAs every 45 minutes during each ultra-short sleep-wake cycle
9. Intraocular pressure is measured using a tonometer once per ultra-short sleep-wake cycle
10. Psychomotor vigilance is measured using the Psychomotor Vigilance Test (PVT) once per ultra-short sleep-wake cycle
11. Blood pressure is measured using a wearable blood pressure monitor every 45 minutes per ultra-short sleep-wake cycle

Completion date
31/10/2024

Eligibility

Key inclusion criteria

1. Good physical health
2. Good mental health
3. Good ocular health
4. Normal or corrected-to-normal vision
5. Normal colour vision

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
35 Years

Sex
All

Total final enrolment
13

Key exclusion criteria
1. Too low (<18.5) or too high (>25) BMI
2. Alcohol abuse (AUDIT >7)
3. Self-report of depressive symptoms
4. Self-report of history of anxiety disorder
5. Extreme chronotype
6. Any use of medications (except for hormonal contraception)
7. Smoking
8. Photosensitive epilepsy
9. Shift work
10 . Transmeridian travel
11. Pregnancy
12. Endocrine alterations
13. Drug use during the study
14. Alcohol use during the study

Date of first enrolment
01/01/2024

Date of final enrolment
30/09/2024

Locations

Countries of recruitment
Germany

Study participating centre
Max Planck Institute for Biological Cybernetics
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Sponsor information

Organisation
Max Planck Institute for Biological Cybernetics

ROR
https://ror.org/026nmvv73

Funder(s)

Funder type
Research organisation

Funder Name
Max-Planck-Gesellschaft

Alternative Name(s)
Die Max-Planck-Gesellschaft, Max Planck Society for the Advancement of Science, Max-Planck-Gesellschaft zur Förderung der Wissenschaften, Max Planck Society, MPG

Funding Body Type
Government organisation

Funding Body Subtype
Research institutes and centers

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and analysed during the study will be published as a supplement to the results publications. All data will be available on our GitHub (https://github.com/tscnlab) repository and/or FigShare under an open-access license.

IPD sharing plan summary

Stored in publicly available repository, Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol (preprint)		02/03/2024	28/03/2024	No	No