Studienprotokoll

Titel der Studie:

Impact of everyday light exposure patterns on metabolic, cardiovascular and psychological health in younger and older adults
Akronym: AgeLight

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Projektleiter:

Dr. Jan-Frieder Harmsen

Lehr- und Forschungsgebiet Healthy Living Spaces
Institut für Arbeits-, Sozial- und Umweltmedizin
RWTH Aachen - Universitätsklinikum
Pauwelsstraße 30
D-52074 Aachen

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0. Deutsche Synopse

Menschen verbringen die meiste Zeit in Innenräumen unter suboptimalen Lichtverhältnissen, was zunehmend als Risikofaktor für die steigende Häufigkeit von Herz-Kreislauf-, Stoffwechsel- und psychischen Erkrankungen in der alternden Gesellschaft angesehen wird. Lichtexposition kann den Blutzucker, den Blutdruck und das psychische Wohlbefinden beeinflussen. Daher können schlechte Lichtverhältnisse im Alltag zu der zunehmenden Belastung des Gesundheitssystems im Zusammenhang mit einer alternden Bevölkerung beitragen. Außerdem ist bekannt, dass die Lichtempfindlichkeit im Alter abnimmt (z. B. aufgrund der altersbedingten Degeneration der Augenstrukturen), was positive gesundheitliche Auswirkungen von Licht abschwächen kann. Derzeit ist jedoch weitgehend unbekannt, wie sich die Lichtexpositionsgewohnheiten und die Sensitivität gegenüber den gesundheitlichen Auswirkungen von Licht mit dem Alter verändern. Ebenso ist unklar, inwieweit Unterschiede in der Lichtempfindlichkeit von der Degeneration der Linse und der Netzhaut abhängen. In dieser Studie sollen alltägliche Lichtverhältnisse jüngerer und älterer Erwachsener charakterisiert und im Zusammenhang mit kardiovaskulärer, metabolischer und psychischer Gesundheit betrachtet werden. Konkret wird ein ambulanter Erhebungsansatz über 12 Tage angewendet, bei dem physiologische Parameter und alltägliche Gedanken, Verhaltensweisen und Erfahrungen verschiedener Altersgruppen mit Hilfe von tragbaren Technologien (z. B. Lichtsensoren, Aktivitäts-Tracker, kontinuierliche Blutzuckermessgeräte) und Smartphone-basierten Selbstberichten (z. B. Stimmung, Vitalität) gemessen werden. Zu Beginn der Studie wird die Degeneration der Linse und der Netzhaut der Teilnehmenden durch Augenärzte objektiv quantifiziert. An den letzten zwei Tagen werden die Teilnehmenden in randomisierter Reihenfolge einen Arbeitstag bei schwachem und einen weiteren bei hellem Licht unter demselben Messprotokoll wie zuvor verbringen, sodass jede Person sowohl einen Bürotag bei schwachem Licht und einen Tag bei hellem Licht verbringt (randomisiertes Cross-over Design). Auf diese Weise wird die individuelle Lichtempfindlichkeit und deren gesundheitliche Auswirkungen experimentell bewertet. Die Teilnehmenden erhalten als Aufwandsentschädigung nach Beendigung der Studie 200 € und bekommen zudem Rückmeldung über ihre alltäglichen Blutzucker- und Blutdruckwerte, sowie eine detaillierte Augenuntersuchung. Dieses Projekt wird dazu beitragen, den Einfluss von Licht auf Gesundheitsparameter im Alltag besser zu verstehen und langfristig gesunde Beleuchtungskonzepte in verschiedenen Gebäudetypen für unterschiedliche Altersgruppen zu ermitteln.

1. Background

Within a day, the Earth rotates once around its own axis, causing predictable changes in light conditions throughout the day. In this context, humans have developed the ability to synchronize their physiological processes to a period length of around 24 hours, adapting to these recurring fluctuations. Our ambient light hence has a major influence on our physiology and psychology depending on the time of day. However, over the last century our relationship to light has drastically changed: our current "indoor society" spends about 90% of awake time indoors exposed to lower light intensities (e.g. up to 300 lux for typical electric office lighting) than outside in natural daylight (e.g. up to 100,000 lux on a sunny day), along with excessive exposure to artificial light during the evening beyond sunset. Yet, studies on the impact of daytime light exposure patterns are limited (Fleury et al., 2020). A chronic lack of daylight in combination with excessive light in the evening is increasingly being considered as a risk factor in the aging society's rising incidence of cardiovascular, metabolic, and psychological disorders. For example, experiencing darker days and brighter nights was associated with a higher risk for the onset of several psychological disorders such as depression or psychosis (Burns et al., 2023). In terms of short-term effects on potential mediating mechanisms, Harmsen et al. previously showed that bright light during office hours induced mostly favorable acute effects on glucose control and thermoregulation in older insulin-resistant volunteers compared to dim light (Harmsen et al., 2022) and that natural office lighting through windows improved glucose control in older type 2 diabetes patients (Harmsen et al., 2022). Similarly, when workers were exposed to higher levels of light during their workday, they reported increased vitality and lower depressive symptoms (Mariana G. Figueiro et al., 2017; Nagare et al., 2021). However, to date, there is only limited data on how light exposure patterns differ across the lifespan (Scheuermaier et al., 2010) and how aging may affect the influence of light on our physiology and psychology. First findings indicate that younger and older adults show different emotional effects of exposure to blue light (Sletten et al., 2009), but these differences have so far not been addressed in daily life.

Growing evidence suggest that the effects of light on health parameters vary dramatically across individuals, yet recommendations for appropriate light exposure in real-life settings rarely take these individual differences into account (Chellappa, 2021). In this context, age has been identified as a moderator of light sensitivity (Chellappa, 2021), but the underlying mechanisms remain elusive. Therefore, this interdisciplinary project will for the first time explore the contribution of aging processes within the eye to an individual's sensitivity to light and its health effects. The degeneration of the lens associated with cataract is a natural aging process that affects the amount of light that can reach the retina. Cataract affects around 17% in the general population worldwide and up to 54% in the over-60 age group (Hashemi et al., 2020). Replacing the lenses of the eye by surgery largely restores light transmission and has been shown to improve the sleep-wake rhythm, the release of the sleep hormone melatonin, light sensitivity, and sleep quality (Brøndsted et al., 2017; Giménez et al., 2016). Depending on how far the degeneration of the lens and retina have progressed and/or whether surgical intervention has taken place, large individual differences in sensitivity to different ambient light can therefore be expected. However, this aging process is ignored by most previous attempts to study the physiological and psychological health effects of light.

2. Aim of the study

With the primary hypothesis of this study being that younger and older individuals differ in their light exposure patterns in everyday life, the two main goals of the AgeLight study are to:

- characterize light exposure patterns in younger and older adults and their link to cardiovascular, metabolic, and psychological health
- identify determining factors of an individual's sensitivity to light and its health effects (such as degeneration of the lens and retina)

3. Study design

This study is designed as an observatory field study of characterizing younger and older adults' everyday life in terms of light exposure patterns as well as cardiovascular, metabolic and psychological health parameters over 10 days continuously through wearables and smartphone-based self-reports (ambulatory assessment period). On the first day of data collection, each participant will undergo an eye examination at the Institute of Ophthalmology. Thereafter participants start wearing the wearable sensors and instructions on how to complete the smartphone-based self-report forms are provided. Data will be collected from the first evening onwards (ca. 18:00 h). After the ambulatory assessment period under free-living conditions, participants will spend the 11^{th} and 12^{th} day in a controlled office room environment from 08:30 to 17:00 h. In a randomized cross-over design, the 11^{th} and 12^{th} day will be spent in either bright (1250 lux) or dim office lighting (10 lux). On these days, participants will continue to wear the wearables and complete the same smartphone-based self-reports as over the 10-day ambulatory assessment period. Between day 11 and 12, participants will leave controlled conditions from 17:00 h on day 11 to 08:30 h on day 12. On day 11 and 12, participants will receive a standardized fluid meal for breakfast and a bread-based meal for lunch, and are otherwise instructed to avoid any food, caloric or caffeinated beverages between 08:30 and 17:00 h. After removing all wearables on day 12, the study ends at 17:30 h. Over these 12 days of data collection, participants will be asked to keep their bedtimes at home as consistent as possible between days, and on day 11 and 12 they will be instructed to come to the office facilities fasted without any caloric intake after 22:00 h on the previous evening of day 10 and 11, respectively.

To minimize the burden on participants in this study, we use mobile and user-friendly devices for data collection and give clear instructions for data collection. We keep individual assessments short, limit the study duration to 12 days and provide incentives for participation (up to €200 reimbursement). On day 11 and 12, participants are mostly free to do whatever they like to do while being in the office environment (e.g. watching movies, paperwork, reading, video-meetings etc.).

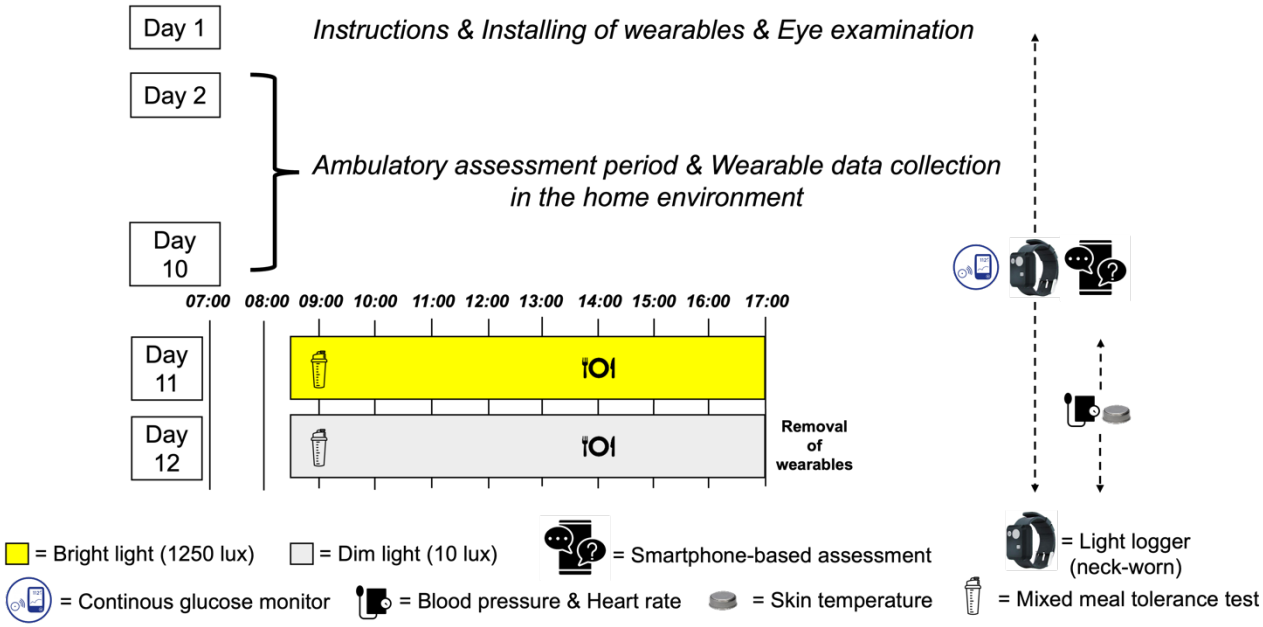


Fig.1. Overview of study design.

4. Responsibilities

4.1. Involved centres

The AgeLight study is led by the Institute for Occupational, Social and Environmental Medicine at the University Hospital RWTH Aachen in collaboration with the Institute of Ophthalmology (also Faculty 10), and the Institute of Psychology (Faculty 7).
The responsible entity is:

1. University Hospital RWTH Aachen
   Institute for Occupational, Social and Environmental Medicine
   Teaching and research area Healthy Living Spaces
   Pauwelsstr. 30 | 52074 Aachen

And partners are:

2. Institute of Ophthalmology
   Faculty 10 (Medicine)
   Pauwelsstr. 30 | 52074 Aachen
3. Institute for Psychology
   Faculty 7 (Philosophy)
   Dennewartstr. 25 – 27 | 52068 Aachen

4.2. Involved researchers

Main responsible:
Dr. Jan-Frieder Harmsen, Institut für Arbeits-, Sozial- und Umweltmedizin

Leading researchers:
Prof. Dr. Marcel Schweiker, Institut für Arbeits-, Sozial- und Umweltmedizin

Dr. Anna Jori Lücke, Institut für Psychologie
Prof. Dr. Andreas Neubauer, Institut für Psychologie
Prof. Dr. Peter Walter, Klinik für Augenheilkunde
Dr. Sabine Baumgarten, Klinik für Augenheilkunde
Prof. Dr. Thomas Kraus, Institut für Arbeits-, Sozial- und Umweltmedizin

4.3. Financing

The project is funded by the Federal Ministry of Education and Research (BMBF) and the Ministry of Culture and Science of the State of North Rhine-Westphalia (MKW) as part of the Excellence Strategy of the Federal and State Governments, supplemented by funds from the LuF Healthy Living Space (basic funding of the endowed professorship funded by VILLUM FONDEN, Tobaksvejen 10, DK-2860 Soborg, Denmark, (https://veluxfoundations.dk/en) a Danish foundation.

4.4. Registration

The study will be registered on osf.io.

5. Participants

30 healthy younger adults and 30 healthy older adults.

5.1. Inclusion Criteria

- Age: 18-35 or 60-80 years old
- Voluntary participation, signed consent form
- Owns an Android or iOS Smartphone compatible with the m-Path App
- Generally healthy (self-reported)
- Non-smoker for at least 12 months (self-reported)

5.2. Exclusion criteria

- Pregnancy (for female participants) (self-reported)
- Night-shift worker
- Eye diseases (e.g. glaucoma, age related macular degeneration, diabetic retinopathy conditions after retinal detachment / retinal blood vessel occlusions)
- Pseudophakic eyes
- Psychological disorders: insomnia, depression, bipolar disorder and generalized anxiety disorder
- Wearing specially-filtered glasses

5.3. Scheduling

The 12 days of testing will take place after an initial phone call screening. Participants can leave the study at any time for any reason if they wish, without any consequences. The investigator may decide to remove a participant from the study for urgent medical reasons. Participants may be removed from the study if they do not adhere to the study procedure. After elimination, there is no follow-up examination of the participant. In case of withdrawal due to medical complications, the participant is referred to a general practitioner.

5.4. Recruitment

Participants are recruited via advertisements on billboards at the RWTH Aachen University Hospital and in newspapers as well as websites.

6. Methods

6.1. Study Timeline

The study will be conducted between November 2024 and May 2025.

6.2. Participants and Groups

The two comparative groups formed in this study consist of 30 younger adults (18-35 years) and 30 older adults (60-80 years), both females and males will be included, and the aim is to match both groups with respect to sex (i.e. ideally 15 women and 15 men per group). The age contrast in the two groups is chosen, as substantial differences in degeneration of the lenses and retina within the eye can be expected.

For the sample size calculation of n = 30 per group, we refer to Zauner et al. (Zauner et al., 2023), who created a procedure to calculate statistical power and required sample size for wearable light-logging data. For most light-logging metrics, their approach shows that for strong differences in light exposure patterns (i.e., winter vs. summer) even smaller samples are sufficient (n = 3-24). We do not expect that differences between age groups are that strong as seasonal differences. However, we are confident that effects of about d = 0.7 could be detected with our design (n = 30 per group).

6.3. Study Components

6.3.1. Phone call screening

The phone call screening will take place after participants have received the participant information. During the phone call screening process, potential participants will receive a short overview of the study and have a chance to raise questions. Once all questions have been answered, several key factors will be assessed to determine participants' eligibility by both the inclusion and exclusion criteria. Additionally, more comprehensive information will be gathered that is required for a smooth execution of the upcoming experiment.

1. Date of birth, including age, year, and month, but excluding the specific day.
2. Gender. ☐Female ☐Male ☐Diverse ☐Do not want to answer
3. Body weight in kg.
4. Height in m.
5. Healthy in general? ☐Yes ☐No
6. Any heart or vascular disease[1]? ☐Yes ☐No
7. Take any medication[2]? · ☐Yes ☐No
   - 7.1. If yes: Has any change in the intake[3] in the last 3 months? ☐Yes ☐No
   - 7.2. If so, which ones, how often, since when and in what dosage?

[1] e.g. high blood pressure, heart failure, diabetes, ...
[2] e.g. painkillers, beta-blockers, thyroid medication, insulin, ADHD medication
[3] dosage, frequency

8. Drink alcohol? ☐Yes ☐No
   8.1. If so, how many units[4] per week?
9. Take drugs? ☐Yes ☐No
10. For female participants: pregnant or breastfeeding? ☐Yes ☐No
11. Hours of work each week.
12. Did you have cataract surgery? ☐Yes ☐No
13. Have you been diagnosed with any eye disease? ☐Yes ☐No
14. Have you been diagnosed with any psychological disorder? ☐Yes ☐No
15. Do you have sleep problems? ☐Yes ☐No
16. Involved in shift work? ☐Yes ☐No
17. Wearing specially-filtered glasses? ☐Yes ☐No
18. Do you possess a smartphone? ☐Yes ☐No

Once participants are eligible based on the phone call screening, they will be invited for an initial visit at the University Hospital to sign the informed consent form, perform the eye examination, fill out questionnaires, and provide them with the wearable sensors and instruct them on how to complete the smartphone-based self-report forms over the data collection period.

6.3.2 Eye examination

For the eye examination, participants pass different stations on day 1:

1) Objective refraction
Participants sit in front of the autorefractor and an automated assessment of the refraction (sphere, cyclinder, axis) is performed.

2) Testing Visual acuity (distance visual acuity)

sc (sine correctione)
Firstly, visual acuity is tested "uncorrected", which is without glasses or contact lenses. Participants are positioned in a well-lit area in the standard distance from the visual acuity chart (with Landolt rings). The testing distance is typically 6 meters but it may vary, for example in smaller spaces. Here, mirrors can be used to achieve the required distance. The participant is instructed to cover one eye with the hand or an eye patch, and thereafter are asked to read the Landolt rings on the chart. The smallest line they can read correctly is recorded. The process is repeated with the other eye covered.

ccs (cum correctione sine)
The above-mentioned procedure for testing sc visual acuity is repeated, however with the participant's own glasses (if applicable). Each eye is tested separately.

[4] glasses

cc (cum correctione)
Participants are comfortably seated and positioned correctly in front of the phoropter. The height of the phoropter is aligned with the participant's eyes. The phoropter is set to its default position, with the lenses set to zero (no correction). Participants look at the visual acuity chart and different lenses are presented in order to find the lens combination that brings the best visual acuity. In this way best subjective spherical and cyclindrical refraction are determined and documented for each eye. Values are compared to objective refraction and checked for plausibility.

3) Slit lamp examination
Participants are seated comfortably in front of the slit lamp. Height and position of the slit lamp are adjusted to participant's eyes. Pupils are not dilated with mydriatic eyedrops. The eyes are examined starting with the anterior segment. Especially the lens is investigated for its transparency and any signs of cataracts. Lens opacities are documented concerning the *lens opacities classification system III (LOCS III).*
For posterior segment examination, additional lenses are used (90D) with the slit lamp to view the posterior segment of the eye. Any opacities of vitreous or floaters are recorded and retina, optic disc, macula and retinal vessels are inspected. All findings are documented and any abnormalities are evaluated for potential exclusion criteria.

4) OCT (Optical coherence tomography) examination of the retina
Participants are positioned in front of the OCT machine. Chin rest and forehead strap are adjusted so that the participant's head is stable and comfortable. The participant is asked to look straight ahead at the fixation target inside the machine. The focus of the OCT machine is adjusted until a clear image of the retina is visible on the screen. The image is captured and screened for any artifacts or distortions and is repeated if necessary.

5) Foveal reflectance analyzer
Participants will be seated with both forehead and chin supported. They will be instructed to look straight forward onto a bright white spot. The macular pigment reflectometer will record the difference between the light entering and leaving the eye across the visual spectrum. The participant will not notice any of this. Spectral analysis of the reflected light provides an adequate estimate of the yellowing of the intra-ocular lens.

6.3.3 Questionnaires

At the beginning of the study on day 1, participants will complete established questionnaires characterizing their typical behaviour and personality traits that may be relevant to better understand their light exposure and impacts thereof in daily life. These questionnaires will be implemented using the tool SoSci Survey and can be filled out with any device connected to the internet. The full list of questionnaires can be found in Table 1.

Table 1. List of questionnaires included in the study.

Questionnaire	Reference
Pittsburgh Sleep Quality Index (PSQI)	(Buysse et al., 1991)
Light Exposure Behaviour Assessment (LEBA)	(Siraji et al., 2022)
Munich Chronotype Questionnaire (MCU)	(Roenneberg et al., 2003)
BFI-K	(Rammstedt & John, 2005)
Subjective Vitality Scales (trait)	(Bertrams et al., 2020)
Satisfaction with Life Scale	(Diener et al., 1985)
Sensorische Verarbeitungssensitivität	(Satow, 2022)
Assessment of Sleep Environment (ASE) questionnaire	(Grandner et al., 2022)

6.3.4 Smartphone-based ambulatory assessment

The ambulatory assessment will be conducted via the m-Path app installed on the participants' own smartphones. The app is available for Android and iOS smartphones. It will prompt participants to fill out a short questionnaire six times per day by sending a push-notification. And participants will be asked to take pictures of every food or drink (except of water) and upload these pictures through the m-Path app. Data from the assessments is saved encrypted on a secure GDPR-compliant server in the EU and will be matched to the other collected data using a pseudonymized alpha-numeric code.

Table 2. Measures applied in the ambulatory assessment phase.

All beeps		References
Affective well-being	MOOD-zoom + extra items??	
Vitality	Subjective Vitality Scales (state)	(Bertrams et al., 2020)
Alertness	Karolinska Sleepiness Scale	(Akerstedt & Gillberg, 1990)
Daily Experiences	Stressor Occurrence	
	Uplift Occurrence	
Current Situation	Place	
	Activity	
	Social contact	
	Light sources	
	Perception of current light	(M. G. Figueiro et al., 2021)
Morning only		
Sleep parameters	CONSENSUS sleep diary	(Carney et al., 2012)
Sleep quality	Adapted PROMIS sleep disturbance short form	
Evening only		
Cognitive Function	2-back task	As already implemented in m-Path
Health	Self-Rated Health	
	Physical Symptoms	(Larsen & Kasimatis, 1991)

6.4 Measurement devices

All measurements within the framework of the research project are non-invasive, except for placing a continuous glucose monitor on the non-dominant forearm of participants from day 1 of the data collection period onwards.

Table 3 shows the different types and respective resolutions of the recorded data.

The continuous glucose monitor and the light sensor will be worn throughout the 12 days of the study, while the thermal skin sensors and the ambulatory blood pressure device will only be worn on day 11 and 12, between 08:30 and 17:00 h respectively.

Table 3. Data collected, methods and resolution.

Data	Unit	Device name	Frequency
Skin temperature	°C	iButtons	1 min
Interstitial glucose	mmol/L	Abbott Freestyle Pro IQ	15 min
Illuminance	Lux Melanopic EDI	Actlumus	1 min
Blood pressure	mmHg	ECGpro Holter-RR USB	15 min

6.4.1 Actlumus wearable light sensor

Participants will wear a light logger around the neck like a pendant to log daily light exposure levels. The light logger is only worn during the day and taken off at night, or when participants get in contact with water (e.g. showering or swimming). We will be using the ActLumus by Condor Instruments, which is an actimeter with integrated light logger. The logger estimates melanopic EDI and photopic lux through several light channels. The logger is very lightweight (12-31 g) and can be clipped to the collar, cloth or worn around the neck or clipped onto glasses to measure light at eye-level. Data will be read locally using a cable and transferred to our computers (no cloud or external server involved) and analysed with a locally installed software from Condor Instruments called ActStudio.

Fig.2. Actlumus wearable light-logger

6.4.2 Continuous glucose monitoring

From day 1 to day 12, participants will wear a continuous glucose monitor device on the non-dominant upper arm. The FreeStyle Libre Pro iQ (Abbott) is a system that can measure blood glucose profiles reliably over a period of up to 14 days; it is a standard technique in daily diabetes practice. A needle-shaped sensor will be inserted subcutaneously in the skin of the arm. Glucose concentrations will be measured every 15 minutes in the interstitial fluid of the subcutaneous tissue. These values will be sent to a monitor via a transmitter.

After collecting all the data, blood glucose profiles will be examined for readings that deviate from the normal range. If any abnormalities are detected, participants will be notified while maintaining rigorous medical confidentiality.

Fig. 3. Continuous glucose monitor

6.4.3 ECGpro Holter-RR USB

The AMEDTEC Holter ECG (Fig. 4) constitutes a comprehensive long-term ECG system designed with an optimal workflow. It efficiently delivers swift and precise analysis of Holter

ECG recordings, available in either 3 or 12-channel modes. Thanks to the device's Auto-Feedback Logic (AFL), participants experience minimal discomfort. It is capable of recording data for multiple days (up to 72 hours) and can store up to 300 measurements. Furthermore, it enables the definition of various day and night intervals.

Fig.4. ECGpro Holter-RR USB

The ambulatory blood pressure monitoring (ABPM) system AMEDTEC ECGpro Holter-RR, created from the ABPM software Holter-RR, manufacturer: AMEDTEC Medizintechnik Aue GmbH, CE 0494, and the ABPM recorder device Holter-RR, manufacturer: I.E.M. GmbH, CE 0044, is a system according to Directive 93/42/EEC, article 12, and complies with the essential requirements of MDD 93/42/EEC as well as the regulations of the Medical Devices Act.
AMEDTEC Medizintechnik Aue GmbH maintains a certified quality management system according to DIN EN ISO 13485 and a certificated quality assurance system according to MDD 93 / 42 / EEC, Annex II.
The Holter-RR NIBP device complies with the requirements of the ESH (European Society of Hypertension) and has a BHS (British Society of Hypertension) A/A grading. AMEDTEC ECGpro Holter-RR is a medical device of risk class IIa by MDD 93/42/EEC, annex IX. The device complies with the requirements of the applicable standards,
particularly

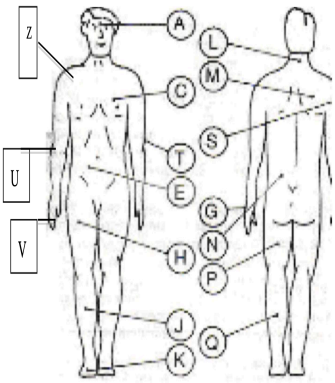
- DIN EN ISO 80601-2-30 „Medical electrical equipment –Part 2-30: Particular requirements for the basic safety and essential performance of automated type non-invasive sphygmomanometers“,
- DIN EN 60601-1 „Medical electrical equipment – Part 1: General requirements for basic safety and essential performance“ and

- DIN EN 60601-1-2 „Medical electrical equipment – Part 12: General requirements for basic safety and essential performance – Collateral standard: Electromagnetic disturbances – Requirements and tests“.

After collecting all the data, the heart rate and blood pressure data will be examined for readings that deviate from the normal range. If any abnormalities are detected, participants will be notified while maintaining rigorous medical confidentiality.

6.4.4 iButton thermal skin sensor

A wireless temperature system for human skin temperature measurements is described, i.e. the iButton (type DS1921H; Maxim/Dallas Semiconductor Corp., USA). The iButton is a small (16×6mm2), rugged self-sufficient system that measures temperature and records the results in a protected memory section. Afterwards time and temperature data can be transferred directly to a computer for data analysis. Four iButtons will be worn by participants on day 11 and 12 from 08:30 to 17:00 h, respectively. The four iButtons will be placed on the right foot, left hand, left chest and neck, as shown in Figure 5 below. They will be attached with self-adhesive tape.



14-point scale	
A	Forehead (middle)
C	Chest (left)
E	Abdomen (right, 4 cm under the belly button)
G	Wrist (left, dorsal)
H	Upper leg (font, right, middle)
J	Shin (right, middle)
K	Foot (right, middle)
L	Neck (middle)
M	Shoulder blade (right)
N	Lower back (left)
P	Upper leg (back, left, middle)
Q	Calf (middle)
S	Shoulder/upper arm (right on m. Deltoideus)
T	Elbow/upper arm (left, outer side)
Extra	
U	Under arm (right, inner side)
V	Middle finger (right, palmary)
Z	Supraclavicular

Fig.5. iButton thermal skin sensors

All sensors that will be applied to the participants (i.e., ActLumus, FreeStyle Libre Pro iQ, iButtons, ECGpro Holter-RR) are CE-certified and will be used only for their intended purpose.

6.5 Flowchart and Schedule

After a person expressed interest in participation, researchers will reply by sending the information letter and consent form via email. Subsequently, researchers will schedule a phone call during which they will provide a brief overview of the key aspects of the experiment and address any questions or concerns which participants may have. Additionally, this phone call will serve as an opportunity to evaluate participants' eligibility based on the inclusion and exclusion criteria (see 6.3.1. phone call screening).

Following the phone call and scheduling the participation days, participants will sign the informed consent form during the first visit at the University Hospital.

On day 1, each participant will undergo an eye examination and thereafter starts wearing the wearable sensors and receives instructions on how to complete the smartphone-based self-report forms are provided. After the ambulatory assessment period in participants' everyday life (days 2-10), participants will spend the 11^{th} and 12^{th} day in a controlled office room environment from 08:30 to 17:00 h. Between day 11 and 12, participants will leave controlled conditions from 17:00 h on day 11 to 08:30 h on day 12.

Throughout these 12 days, the sensors continuously record data until they are removed at the end of day 12. Flowchart 1 illustrates this 12-day study period.

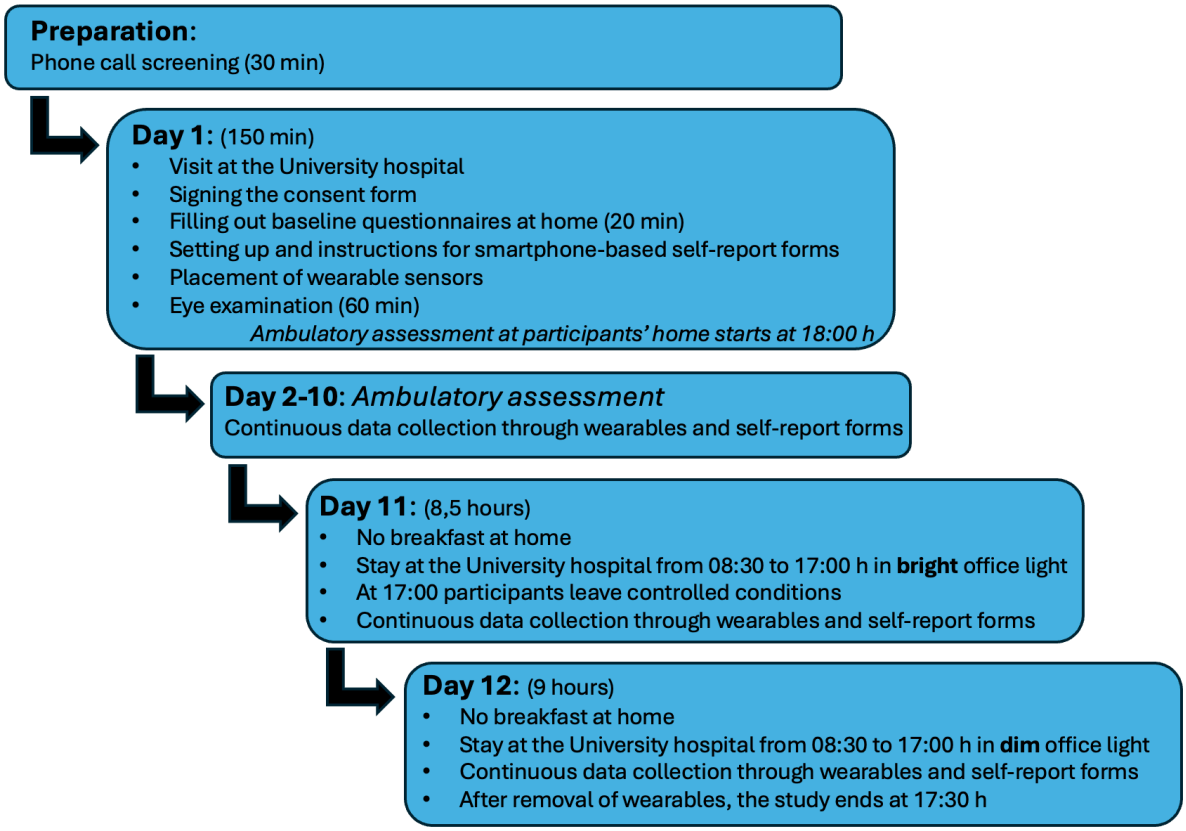


Fig.6.: Flowchart of chronological events of participants enrolment in the study.

7 Risks

Overall, the study ensures that participants are exposed to conditions within the naturally occurring limits of daily life. We do not expect any risks from participating in the ambulatory assessment with previous research showing high acceptability and no noteworthy reactivity to measurement in participants' behavior. Nevertheless, on day 11 and 12 participants may be exposed to light conditions that could be perceived as uncomfortable compared to their preferences.

Blood pressure measurements will be performed on day 11 and 12 by means of an automatic inflatable cuff. These measurements might feel a bit uncomfortable, but do not induce negative health effects. After wearing the continuous glucose monitor for 12 days, skin irritation can occur from where the sensor wire is inserted.

The eye examinations bring no special risks for participants. Individuals might feel dazzled for a few seconds after the slitlamp examination, especially after retinoscopy.

In summary, there are no side effects, exposures, or complications associated with this study.

Medical benefits. The study has no direct medical benefit to the participants. However, the results form the basis for suggesting improvements in light exposure behaviour for health purposes and thus provide a basis for aspects of disease prevention and health promotion. In addition, if something abnormal is noted with respect to the eye examination, daily blood

sugar levels and blood pressure, participants will be informed and advised to seek a medical health professional.
Unexpected medical findings. With wearing the continuous glucose monitor and the blood pressure cuff as well as eye examinations, there is a small risk of unexpected medical findings. These unexpected findings could be revealed based on abnormal blood sugar levels (i.e. indicative of type 1 or 2 diabetes mellitus, and hypoglycemia, respectively), or abnormal blood pressure levels (i.e. indicative of cardiovascular issues), or eye degeneration (i.e. for which surgery could be recommended). In case of such unexpected findings, a physician (Institute of Ophthalmology) will inform the individual participant and discuss further steps. Prior to such a conversation, the right of the participant not to know is taken into account.

Dealing with COVID-19-related risks. According to WHO, there is no pandemic situation (*Statement on the Fifteenth Meeting of the IHR (2005) Emergency Committee on the COVID-19 Pandemic*, n.d.).

8 Statistical analysis

8.3 Descriptive statistics

Statistical analysis will be performed using the statistical computer programs SPSS for Mac OS (version 25, IBM) and R Studio for Windows. Descriptive statistics will be reported for all data parameters and will be reported as minimum, maximum, mean, standard deviation (SD) and intraindividual standard deviation (iSD) for data assessed in daily life, and/or standard error of the mean (SEM). As a measure of dispersion, SD will be used for descriptive statistics of the assessed data, while the SEM will additionally be reported for the results of the primary and secondary outcomes.
In case of non-normality, values will either be transformed using log transformation or non-parametric tests will be used. In addition, Pearson correlation coefficients will be computed to correlate parameter values. The unpaired Students t-test will be used to compare outcome measures between the young and old group. Due to the randomized cross-over design, to compare outcomes between the bright and dim office light condition irrespective of age (secondary outcome), a paired t-test will be conducted. Differences will be considered statistically significant when tested two-sided $p < 0.05$. Missing values will not be replaced. We will apply a full information approach using all available data from all participants.

8.4 Primary and secondary study parameters

As the primary hypothesis of this study is that younger and older individuals differ in their light exposure patterns in everyday life, the primary outcome of this study is melanopic equivalent daylight illuminance (M-EDI) quantified in lux by the Actlumus wearable light sensor. M-EDI may differ between groups with respect to overall daily levels, exposure levels at different times of day (work-day vs. weekend-day), and the difference in exposure levels between work-days and weekend-days. Therefore, M-EDI will be statistically analysed between groups in the following three ways:

1. Compare the area under the curve (AUC) of M-EDI from day 1 to day 8 between young and old (unpaired t-test)

2. Averaging exposure levels over work-days and weekend-days in 1-hour time intervals over 24 hours and compare the two average 24-hour M-EDI patterns between young and old (2-way repeated measures ANOVA, factor 1 (between-subjects) group, factor 2 (within-subjects) time)
3. Averaging the onset of M-EDI in the morning hours and the offset in the evening over work-days and weekend-days and calculate the difference in onset and offset between the averaged work-day and weekend-day between groups (unpaired t-test)

The secondary hypotheses are that light exposure patterns in everyday life are linked to daily metabolic, cardiovascular and psychological outcomes, and that this link is stronger in individuals displaying less degeneration of eye structures.

Accordingly, mixed effects regression analyses will be performed to assess the relationship between different aspects of daily light exposure (momentary M-EDI, average daily exposure level, onset/offset; independent variables) and each of the daily health parameters (metabolic, cardiovascular, psychological functioning, and sleep; dependent variables). To evaluate the role of the degree of eye degeneration, an interaction term between light exposure and eye degeneration will be added to the regression models.

9 Ethics

The study must be approved by the Ethics Committee of RWTH Aachen University. The study is carried out in accordance with the Declaration of Helsinki (the latest version, established in Fortaleza, Brazil, 2013) and the Law on Medical Research involving Human Beings (WMO) and the General Data Protection Regulation (GDPR or GDPR).

9.3 Recruitment and Consent

Participants are recruited via advertisements on billboards of the University Hospital RWTH Aachen, public buildings in Aachen, the HLS mailing list, and social media such as LinkedIn and Facebook. Potential participants will be informed in writing and orally during an informational phone call about the study protocol by the coordinating investigators, and participants can contact the researchers at any time if questions arise. Participants who have already participated in previous studies and have given written consent to be contacted again for future studies (HLS mailing list) will be informed by e-mail. Subsequently, potential interested participants will receive participant information documents by email. After at least one day, participants can contact the research team by phone, email or in person if they would like to participate in the study. During their first visit at the hospital, participants will be asked to provide written informed consent after the lead investigator has verified that participants have understood the study information and that any open questions have been clarified. Participants can terminate their participation in the study at any time without giving a reason for their decision.

9.4 Safety Reports

According to § 10 para. 4 of the WMO, the Principal Investigator will interrupt the study if there are reasonable grounds for the continuation of the study to endanger the health or safety of the participants. The Principal Investigator shall immediately inform the accredited Ethics Committee of any temporary interruption, including the justification for such action. The study will be suspended until a further positive decision is made by the accredited ethics committee. The research team ensures that all participants are informed.

9.4.2 Adverse events (AEs)

Adverse events are defined as any adverse experience that occurs for a participant during the study, whether or not it is considered to be related to the experimental intervention. All adverse events spontaneously reported by the participant or observed by the investigator or his staff are recorded.

9.4.3 Serious adverse events (SAEs)

A serious adverse event is any adverse medical event or effect that

- Leads to death;
- Is life-threatening (at the time of the event);
- Requires hospitalization or the extension of an existing inpatient hospital stay;
- Results in persistent or significant disability or inability;
- Is a congenital anomaly birth defect; or
- Any other important medical event that did not result in any of the results listed above as a result of a medical or surgical procedure, but could have occurred at the reasonable discretion of the investigator.

Elective hospitalization is not considered a serious adverse event.

The principal investigator shall report to the accredited ethics committee that approved the protocol any occurrence of an SAE within 7 days of the first notification for SAEs resulting in death or life-threatening, followed by a maximum period of 8 days to complete the initial preliminary report. All other SAEs shall be reported within a maximum period of 15 days after the first knowledge of the serious adverse events by the principal investigator.

9.4.4 Follow-up of adverse events

All SARs are tracked until they subside or until a stable situation has been reached. Depending on the event, follow-up may require additional tests or medical procedures if indicated and/or a referral to the general practitioner or a specialist. SAEs must be reported by the end of the study as defined in the protocol.

10 Data protection

The privacy of the participants participating in the study will be protected. This means that the study results are associated with a code/number and not with the name of the participant. Apart from the research team, only control bodies and the monitoring team have access to the research data.
The key document is secured and password protected; only the Principal Investigator (Dr. Jan-Frieder Harmsen) and three other Co-Investigators (Dr. Anna Jori Lücke, Prof. Dr. Marcel Schweiker and Prof. Dr. Andreas Neubauer) can access the key document. The data are stored

on servers of the University Hospital RWTH Aachen. Anonymized data will be passed on to project partners of RWTH Aachen University. Anonymized and partially aggregated date will later be deposited in a research data repository.

Participants will receive information about the overall results of this study. This information shall be provided orally or in writing. The retention period for the research data will be 10 years and only the researchers directly involved in the research will have the opportunity to access this data.

11 Insurance

We do not foresee any additional risks for the participants, as the exposures do not exceed naturally occurring daily exposures, so we do not consider subject insurance necessary. For the insurance of the way to and from the laboratory, we have provided a route accident insurance ("Wege-Unfall-Aufenthaltsversicherung") under policy number … (will be added later).

12 Costs, incentives and loss of earnings

For most of the duration of the study, the participants can pursue their everyday life tasks. Each participant completing the 12 study days will receive up to 200 € for carrying out the entire study. The expense allowance will start at €155 if all parts of the 12-day study are completed. Participants receive a bonus of €20 if they answered at least 80% of the six daily questionnaires via their smartphone, and another €20 if they answered 90%. If they recruit other participants for this study through their social network, they receive another €5.

13 Signature

Aachen, 09.10.2024

Dr. Jan-Frieder Harmsen

14 References

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