Department of Electronics, Lighting Unit

Research methods and neurophysiological mechanisms behind the alerting effects of daytime light exposure

Emilia Rautkylä

Aalto University

DOCTORAL DISSERTATIONS

Aalto University publication series
DOCTORAL DISSERTATIONS 72/2011

Research methods and neurophysiological mechanisms behind the alerting effects of daytime light exposure

Emilia Rautkylä

Doctoral dissertation for the degree of Doctor of Science in Technology to be presented with due permission of the School of Electrical Engineering for public examination and debate in Auditorium S4 at the Aalto University School of Electrical Engineering (Espoo, Finland) on the 14th of October 2011 at 12 noon.

Aalto University
School of Electrical Engineering
Department of Electronics, Lighting Unit

Supervisor
Prof. Liisa Halonen, Aalto University, Espoo, Finland

Instructor
Dr. Marjukka Puolakka, Aalto University, Espoo, Finland

Preliminary examiners
Prof. Christian Cajochen, Centre for Chronobiology, PUC, Basel, Switzerland
Doc. Sami Leppämäki, Clinic for Neuropsychiatry, HUCH, Helsinki, Finland

Opponent
Prof. Emeritus Peter Boyce, Rensselaer Polytechnic Institute, Troy, USA

Aalto University publication series
DOCTORAL DISSERTATIONS 72/2011

© Emilia Rautkylä

ISBN 978-952-60-4249-7 (pdf)
ISBN 978-952-60-4248-0 (printed)
ISSN-L 1799-4934
ISSN 1799-4942 (pdf)
ISSN 1799-4934 (printed)

Aalto Print
Helsinki 2011

Finland

The dissertation can be read at http://lib.tkk.fi/Diss/

Author
Emilia Rautkylä

Name of the doctoral dissertation
Research methods and neurophysiological mechanisms behind the alerting effects of daytime light exposure

Publisher School of Electrical Engineering

Unit Department of Electronics

Series Aalto University publication series DOCTORAL DISSERTATIONS 72/2011

Field of research Illuminating Engineering

Manuscript submitted 28 April 2011 **Manuscript revised** 22 August 2011

Date of the defence 14 October 2011 **Language** English

☒ **Monograph** ☐ **Article dissertation (summary + original articles)**

Abstract

An important aim of today's lighting research is defining and quantifying the optimal parameters of light for maximal alerting response. They would be useful in various clinical and non-clinical applications. The debate has covered the light intensity, the spectral distribution, the duration of the light exposure, and the circadian phase in which the light is administered. However, no consensus over the optimal parameters has been found.

The thesis claims that the lack of consensus is due to three things. First, the terminology around alertness is confounding and alertness has not been defined properly. Second, the methods used to study light-induced alertness are not always optimal, because they do not consider the delicacy of the light stimulus nor are they based on the physiology of alertness. Third, the research has concentrated too much on effects instead of causes and therefore the mechanisms behind the alerting effects of light are not yet fully known.

The thesis addresses these problems. It begins by discussing the physiology and the terminology behind the term "alertness". On the basis of the discussion, it defines alertness as an activation state of the brain that is induced by stimuli and reduced by the lack of them. The thesis continues with an evaluation of the methods used to study light-induced alertness. First the methods are assessed theoretically and after that the practical testing of heart rate, skin conductance, pupil size and subjective sleepiness is reported. Together, the evaluations show that the methods based on the autonomic nervous system activity are good for detecting the effects. For investigating the causes behind these effects monitoring the central nervous system should be used. Brain imaging is highly recommended.

Further on the thesis discusses the neurophysiological mechanisms behind the light-induced alertness in daytime, which are less known than the night-time mechanisms. A new model of two separate pathways from the retina to the activation system is suggested. The new model links emotions to the alerting effects of light. The correlation of subjective mood and alertness is verified with a practical study. A test protocol to study the causal relationship of light, emotions and alertness objectively is also suggested.

In addition to the objectives, a few interesting observations from the practical studies are reported. First, exposure to blue-enriched white light was shown to help students to retain their alertness during the natural dip time in the afternoon in the autumn compared to exposure to normal white light. Second, changes in the light exposure were shown to induce greater alerting effects than a constant light exposure. These observations contribute to the search for the optimal parameters of light exposure.

Keywords light exposure, alertness, mood, circadian, limbic, amygdala, locus coeruleus

ISBN (printed) 978-952-60-4248-0 **ISBN (pdf)** 978-952-60-4249-7

ISSN-L 1799-4934 **ISSN (printed)** 1799-4934 **ISSN (pdf)** 1799-4942

Location of publisher Espoo **Location of printing** Helsinki **Year** 2011

Pages 103 **The dissertation can be read at** http://lib.tkk.fi/Diss/

Aalto-yliopisto

Tiivistelmä

Aalto-yliopisto, PL 11000, 00076 Aalto www.aalto.fi

Tekijä
Emilia Rautkylä

Väitöskirjan nimi
Tutkimusmenetelmät ja neurofysiologiset mekanismit päiväaikaisen valoaltistuksen aiheuttamien vireysvaikutusten taustalla

Julkaisija Sähkötekniikan korkeakoulu

Yksikkö Elektroniikan laitos

Sarja Aalto University publication series DOCTORAL DISSERTATIONS 72/2011

Tutkimusala Valaistustekniikka

Käsikirjoituksen pvm 28.04.2011 **Korjatun käsikirjoituksen pvm** 22.08.2011

Väitöspäivä 14.10.2011 **Kieli** Englanti

☒ **Monografia** ☐ **Yhdistelmäväitöskirja (yhteenveto-osa + erillisartikkelit)**

Tiivistelmä

Yksi tämän hetken tärkeimmistä valaistustutkimuksen tavoitteista on määritellä optimaaliset parametrit vireyttä edistävälle valaistukselle. Niillä olisi käyttöä useissa kliinisissä ja ei-kliinisissä sovelluksissa. Tutkimus on keskittynyt valaistusvoimakkuuteen, spektriin sekä valoaltistuksen kestoon ja ajoitukseen suhteessa vuorokausirytmiin. Vielä ei ole kuitenkaan päästy varmuuteen, millainen valo vaikuttaa eniten päiväaikaiseen vireyteen.

Väitöskirja esittää tämän johtuvan kolmesta syystä. Ensinnäkin vireys-termiä ei ole määritelty kunnolla ja vireyteen liittyviä termejä käytetään erilailla riippuen tutkimuksesta ja kielestä. Toisekseen vireydentutkimusmenetelmät eivät aina sovellu valaistustutkimukseen, koska ne eivät perustu fysiologiseen vireyteen ja ota huomioon, että valoärsyke jää herkästi muiden ärsykkeiden peittoon. Kolmanneksi, tutkimus on keskittynyt valoaltistuksen seurauksiin eikä syihin, ja siksi vireyden mekanismit ovat vain osittain tunnettuja.

Väitöskirja käsittelee edellä mainittuja ongelmia. Sen alussa keskustellaan terminologiasta ja fysiologiasta vireyden taustalla. Keskustelun perusteella ”vireys” määritellään aivojen aktivaatiotilaksi, joka aiheutuu ärsykkeestä ja laskee ärsykkeiden puuttuessa. Tämän jälkeen väitöskirjassa arvioidaan vireydentutkimuksessa käytettyjen menetelmien soveltuvuutta valaistuskokeisiin teoreettisen tarkastelun ja käytännön kokeiden avulla. Autonomisen hermoston toimintaa mittaavat menetelmien osoittautuvat soveltuvan hyvin valon vaikutusten mittaamiseen. Mekanismien selvittämiseen tarvitaan keskushermostoa tutkivia elektrofysiologisia menetelmiä. Erityisesti aivokuvantamista suositellaan.

Tämän jälkeen väitöskirja paneutuu neurofysiologisiin mekanismeihin päiväaikaista vireyttä kohottavan valoaltistuksen taustalla. Ne tunnetaan huonommin kuin yöaikaiseen vireyteen liittyvät mekanismit. Väitöskirjassa esitetään uusi malli kahdesta erillisestä polusta silmän retinasta aivojen aktivaatiojärjestelmään. Mallin mukaan on mahdollista, että valo vaikuttaa tunteisiin, ja muuttuva tunnetila saa aikaan virkistävän vaikutuksen. Työssä raportoidun käytännön koe mukaan subjektiivisesti mitattu mieliala ja vireys korreloivat positiivisesti. Kausaalisuuden tutkimista varten ehdotetaan testiprotokollaa.

Asetettujen tavoitteiden lisäksi väitöskirjassa esitetään muutama mielenkiintoinen huomio käytännön kokeista. Ensinnäkin syksyllä luonnollisen iltapäiväväsymyksen aikana kylmänsävyinen valkoinen valo auttoi opiskelijoita säilyttämään vireystasonsa paremmin kuin lämpimänsävyinen valkoinen valo. Toisekseen muutokset valoaltistuksessa osoittautuivat kohottavan vireyttä enemmän kuin jatkuva valoaltistus. Nämä huomiot tuovat lisätietoa optimaalisten valaistuksen parametrien määrittämiseen.

Avainsanat valoaltistus, vireys, mieliala, sirkadiaaninen, limbinen, mantelitumake

ISBN (painettu) 978-952-60-4248-0 **ISBN (pdf)** 978-952-60-4249-7

ISSN-L 1799-4934 **ISSN (painettu)** 1799-4934 **ISSN (pdf)** 1799-4942

Julkaisupaikka Espoo **Painopaikka** Helsinki **Vuosi** 2011

Sivumäärä 103 **Luettavissa verkossa osoitteessa** http://lib.tkk.fi/Diss/

PREFACE

The work presented in this thesis was conducted at the Lighting Unit of Aalto University School of Electrical Engineering. A part of the work was carried out in the project "Aktiivivalo" funded by the Finnish Funding Agency for Technology and Innovation (Tekes), Philips Oy Lighting, Helvar Oy, Senate Properties and the Finnish Work Environment Fund.

None of the three practical studies would have been possible without the voluntary subjects. Besides the study participants, I wish to thank my former colleague Petteri Teikari for his contribution on the design and implementation of Study II. I wish him all the success with his PhD studies in Lyon!

I am grateful to Dr Timo Partonen from the National Institute for Health and Welfare for all our inspiring conversations on the mechanisms behind the light-induced alertness. The employees of the Finnish Institute for Occupational Health, as well as the researchers in the Advanced Magnetic Imaging centre gave valuable insight on my studies.

I want to thank my supervisor Professor Liisa Halonen for her encouragement and unbelievable enthusiasm towards my work. I am thankful for Dr Marjukka Puolakka for her comments and support throughout the whole process. Professor Christian Cajochen from the Centre for Chronobiology, Psychiatric University Clinics in Basel, and Docent Sami Leppämäki from the Clinic for Neuropsychiatry, Helsinki University Central Hospital, did a great job in pre-examining my thesis. I would also like to thank Professor Emeritus Peter Boyce for agreeing to be my opponent in the defence.

It was not always clear that this thesis would see daylight. Years 2009-2010 were challenging with desperate nights and hardworking holidays. But you know me: I start, I finish. I am grateful to my boss Jussi for giving me the opportunity to take part-time leave from Philips to be able to complete the thesis in spring 2011. I wish to thank all my Philips colleagues for understanding the special arrangements, and especially Henri and Tarja for your great support and help whenever needed.

Ashley and Jaana, you rock! Thanks for proofreading my manuscripts for the publications. I am happy to say that the work was not done for nothing! Peppe, thanks for your insight and help with the mystical world of statistical analysis. I am also very grateful to my godfather Kalle and friend Mikko for giving me your time by reading and commenting on the final version of the thesis. You all helped me when I most needed it!

Finally, I want to acknowledge the huge role my family played in my doctoral thesis. The idea to get involved with lighting studies in 2004, as well as the push to continue towards the doctoral degree after having completed the master's degree in 2006, came from my dad Olli. What an interesting path it has been so far and it is still continuing! My mom Kati and brother Juuso showed great support during the process, just like they have always done in my life. Anni, your unbelievable determination with your Master's Thesis helped me to finish as well, thanks and congrats to us both!

Last but not least my deepest thanks goes to my wonderful boyfriend Eero who has not only put up with my bad mood and stress, but also helped in all means, by reading my thesis, by discussing about it, by cooking when I was too busy to do it and by taking me dancing, climbing, sailing or to some of our other hobbies when I needed a break from the thesis work. Thank you my love!!!

I would like to dedicate this work to my grandparents Mami, Pappa, Mummo and Ukki, who unfortunately are not with us anymore. I believe they would have been proud.

I have now reached the top of a small climbing rock, next the path goes out to the big mountains!

Helsinki, August 2011

Emilia Rautkylä

CONTENTS

LIST OF ABBREVIATIONS AND SYMBOLS

Abbreviations

ANS	autonomic nervous system
CCD	charge-coupled device
cd/m²	candela per square metre, unit of luminance
CFR	corticotrophin-releasing factor
CMOS	complementary metal oxide semiconductor
CNS	central nervous system
CO2	carbon dioxide
DALI	digital addressable lighting interface
DMH	dorsomedial nucleus of the hypothalamus
DR	dorsal raphe
ECG	electrocardiogram
EDA	electrodermal activity
EEG	electroencephalogram
EMG	electromyogram
EOG	electro-oculogram
fMRI	functional magnetic resonance imaging
GABA	gamma-aminobutyric acid
GHT	geniculohypothalamic tract
hbw	half-bandwidth
HF	high-frequency power
HR	heart rate
HRV	heart rate variability
Hz	herz, unit of frequency
IGL	intergeniculate leaflet
ipRGC	intrinsically photosensitive retinal ganglion cell
K	kelvin, unit of colour temperature
KSS	Karolinska sleepiness scale
LC	locus coeruleus
LDT	laterodorsal tegmental nucleus
LED	light-emitting diode
LF	low-frequency power

LHA	lateral hypothalamus
lx	lux, unit of illuminance
MEQ	Morningness-Eveningness questionnaire
mm	millimetre
MPON	medial preoptic nucleus
MRI	magnetic resonance imaging
NIF	non-image-forming
nm	nanometre
OX1R	orexin receptor 1
OX2R	orexin receptor 2
PET	positron emission tomography
PLR	pupillary light reflex
POMS	profile of mood states
ppm	parts per million, unit of concentration
PPT	pedunculopontine tegmental nucleus
PUI	pupillary unrest index
PVT	psychomotor vigilance test
RHT	retinohypothalamic tract
SCN	suprachiasmatic nucleus
SD	standard deviation
SEM	slow eye movements
SPSS	Statistical Package for the Social Sciences
TMN	tuberomamillary nucleus
VAMS	visual analogue mood scale
VAS	visual analogue scale
VLPO	ventrolateral preoptic nucleus
vSPZ	ventral subparaventrical zone
VTA	ventral tegmental area

Symbols

E	illuminance
λ_{max}	peak wavelength
T_{cp}	correlated colour temperature
R_a	colour rendering index
N	number of subjects
P_t	Probability value for Student's *t* test
P_f	Probability value for Fisher's exact test
P_{cs}	Probability value for Pearson's chi-square test
P_r	Probability value for Pearson's correlation
r	Pearson's correlation coefficient
ΔM	change in mood
ΔA	change in alertness

1 INTRODUCTION

1.1 Background and research problem

In 1980, Lewy and other investigators at the National Institute of Mental Health in Maryland, USA, reported that bright artificial light could suppress nocturnal melatonin production in humans [1]. This finding indicated that light can act as a cue to synchronise mammalian circadian rhythms. Therefore it led directly to the use of timed bright light exposure to study and treat disorders of human circadian rhythms.

In 1995 Campbell et al. [2] published a consensus report on the alerting and activating effects of light treatment for sleep disorders. They reported that exposure to bright light may be associated with enhanced subjective alertness. However, in the 1990s relatively little attention was paid to the alerting properties of light on the human brain [3]. In fact, only a few studies directly or indirectly examined the activating effects of light on alertness.

This all changed when in 2000 Provencio et al. [4] identified melanopsin in the novel, third-type photoreceptor that Foster, Provencio et al. [5] had discovered in the retina of mammals in 1991. Soon it became clear that melanopsin is the visual pigment of the intrinsically photosensitive retinal ganglion cells (ipRGC) that set the circadian clock and play an essential role in many of the non-visual effects that light has on human [6, 7]. Since then, various groups have investigated the relationship between artificial light and alertness with the aim of establishing the optimal parameters of light for the maximal sensitivity of melanopsin [8-10].

Today it is well established that both night-time and daytime light exposure induces acute alerting effects on humans (for a review, see [3]). The effects are often called “non-visual effects of light” because they are not related to vision but to a non-classical photoreceptor system that is distinct from rods and cones. It should, however, be noted that instead of non-

visual effects it is more appropriate to call the effects non-image-forming (NIF), because the visual system consists of an image-forming visual system, which enables us to detect and trace objects in the visual world, and a non-image-forming visual system, which synchronises the circadian clock [11]. Another essential difference between the image-forming and non-image-forming responses to light are that the former is time-locked to the stimulation, while the latter can last longer than the exposure [12].

Light exposure is used for the clinical treatment of sleep and mood disorders [13], but also to resolve the problems associated with intercontinental travel and shift work. Common to these problems is a misalignment between the circadian clock and the external environment and therefore help can be provided by shifting the circadian clock by means of light [14].

The lighting sector is interested in using knowledge about light and alertness to integrate the findings into the lighting recommendations for workplaces. The objective is to be able to design the lighting in such a way that besides maximising the visual performance, it would also maximise wellbeing and work performance. Therefore the recent research has aimed at finding out the parameters for optimal, alertness-ancillary lighting in terms of light intensity, spectrum, and correlated colour temperature, as well as the duration and timing of exposure [10, 15-19].

The original objective of this thesis was to contribute to the search for optimal parameters by studying which kind of light induces the greatest effects on human alertness. The research started in 2007 with a two-stage field study that investigated the effects of colour temperature and timing of light exposure on daytime alertness. The study collected important data on the effects and their dependency on the season and the time of the day. However, several deficiencies were also faced when comparing the results of previous studies.

First, it turned out that there is no coherent definition of alertness but it is defined and named differently, depending on the study and the research area [20-22]. Therefore it was not clear what alertness is, physiologically, and how it should be studied. Second, because of the diversity in methodology and test settings it was hard to verify observations and compare the results of different studies. Third, research had concentrated on effects instead of causes. The mechanisms behind the alerting effects of light were not known and therefore one could not be sure that one is measuring the alerting effects of light and not the effects of, for example, climatic factors such as noise or temperature [23].

It became clear that the deficiencies would need to be corrected before the parameters for optimal lighting could be established. This gave motivation to the work presented in the thesis and set new targets for the study.

The thesis is a monograph that is based on two published scientific papers [24, 25], one per-reviewed conference paper [26] and one study that has not been reported previously.

1.2 Aim of the work

The overall aim of the work was to increase the knowledge about the relationship between light and alertness from the perspective of lighting research and to give practical instructions for future studies.

The work had three objectives. The first objective was to form a definition of alertness in physiological terms. The second objective was to evaluate the methods currently used in alertness research and to give recommendations for methods to be used in studies on light and alertness. The third and final objective was to find out more about the neurological mechanisms behind light-induced daytime alertness.

The original objective of this thesis, to contribute to the search for optimal parameters for light, was discarded.

1.3 Research methods

The research for the thesis consisted of theoretical evaluations and analysis, as well as practical studies. The practical studies included two field studies and one laboratory study.

In the first field study (Study I) the effects of the colour temperature and the timing of light exposure on the daytime alertness of university students were investigated by questionnaires, including the Karolinska sleepiness scale (KSS). In the laboratory study (Study II) the usability of three methods commonly used in alertness research was evaluated by comparing their output to a subjective evaluation achieved with the KSS. The three methods were skin conductance, pupil size, and heart rate measurements. In the second field study (Study III) the correlation between alertness and mood in different lighting conditions was assessed by means of the KSS and a tailor-made mood scale.

The statistical analysis in each experiment was carried out with Statistical Package for the Social Science (SPSS).

1.4 Scope of the research

The thesis deals with the research methodology and the mechanisms of alertness. It does not propose optimal parameters for light exposure, nor can its results as such be used for lighting recommendations.

The research concentrates on ocular light exposure. It does not evaluate the methodology or impacts of light treatment directed to the brain via the ear canal [27] or the popliteal region behind the knee [28].

2 STATE OF THE ART

The activating effects of light on alertness have been studied over the past two decades. In 1991, Badia et al. [29] reported increased alertness, measured by human electroencephalogram (EEG) beta activity, under continuous bright light (5,000 lx, vertical illuminance at eye level) exposure compared to continuous dim light exposure (50 lx) during the night-time. During the daytime no significant differential effects between the two light intensities were detected. The findings of the study were justified by the ability of bright light to suppress melatonin release during the night-time [1]. No comments were, however, given on the relationship between light exposure and daytime alertness, leaving open the question of whether daytime alertness could also be enhanced by light.

Over a decade later Phipps-Nelson et al. [15] examined the effects of bright light (1,000 lx, vertical illuminance at eye level) exposure, as compared to dim light (< 5 lx), on daytime subjective sleepiness and salivary melatonin levels, as well as psychomotor vigilance and incidences of slow eye movements (SEM). In their study bright light exposure reduced subjective sleepiness, reduced SEMs, and improved psychomotor vigilance test (PVT) performance compared to dim light, but had no effect on salivary melatonin. The results broadened the knowledge about daytime alertness by indicating that light can have effects on daytime sleepiness, but that these effects are mediated by mechanisms that are separate from melatonin suppression. Therefore their study can be considered to have started the search for another mechanism than melatonin suppression underlying alertness, a search that is still going on today.

Cajochen has also studied light-induced alertness and referred to the possibility of another mechanism in addition to the melatonin pathway. He has contributed to alertness research, especially to knowledge about the physiology of alertness, concentrating, however, on night-time light exposures. In 2000 Cajochen et al. [30] communicated that alerting response

depends on the intensity of the light when the response is measured subjectively and objectively with an EEG. In their study half of the maximum alerting response to bright light at 9,100 lx (illuminance at eye level) was obtained with light of only 100 lx, indicating that ambient room light might also be used for improving alertness. Later, in 2005, Cajochen et al. [16] showed for the first time that human alertness could be sensitive to short-wavelength light. In their study 460-nm monochromatic light had a greater effect on alertness compared to 500-nm light, suggesting that the sensitivity of human alertness is blue-shifted. In the same year Lockley et al. [10] verified this by examining alertness with KSS ratings and auditory PVT and EEG recordings after continuous exposure to monochromatic 460-nm and 555-nm light.

In the next year Revell et al. [17] reported that alertness might be most sensitive to light of an even shorter wavelength than 460 nm. They examined subjective alertness after applying three short light pulses of different wavelengths (420 nm, 440 nm, and 470 nm) and one 4-hour-long light pulse of 600 nm and found that compared to 470 nm, alertness levels were significantly higher in 420-nm light and significantly lower in 600-nm light. However, Vandewalle et al. [9] showed contradictory evidence by reporting that functional magnetic resonance imaging (fMRI) showed increased brain activity under pulsed blue light (473 nm) compared to pulsed violet light (430 nm) while the subjects were performing a working memory task.

In 2007 Mills et al. [31] applied the knowledge about the effects of short wavelengths on alertness, but instead of monochromatic light they used blue-enriched white light with a continuous spectrum. The study concentrated on the effects of colour temperature on alertness in a real-life test setting by comparing office workers' response to 2,900-K light (128 lx, average vertical illuminance at eye level) with their response to 17,000-K (170 lx) measured with two questionnaires evaluating e.g. alertness, work performance, and daytime sleepiness. Their study suggested that high correlated colour temperate fluorescent light can improve wellbeing and productivity in office work, drawing attention to the practical implications of light-induced daytime alertness. However, their study can be criticised because in the control conditions of 2,900 K the effects were also positive.

In 2008 Viola et al. [32] continued using high correlated colour temperature 17,000-K light (310 lx, horizontal illuminance of the work plane) in an office environment, comparing it to 4,000-K white light (421 lx) with ques-

tionnaires and ratings scales assessing e.g. alertness, mood, and performance. This time the blue-enriched white light proved to improve all the above during working hours, while the control condition of 4,000 K did not.

As can be seen from the studies mentioned above, the aim of the research during the past two decades has been to define and quantify the optimal parameters of light for maximal alerting response. The debate has concentrated on light intensity (irradiance/illuminance), the spectral distribution or correlated colour temperature of light, the duration of the light exposure, and the circadian phase in which the light is administered [3]. However, no consensus regarding the optimal parameters has been found.

The lack of consensus can be explained by three things. First, the terminology around alertness is confounding and alertness has not been defined properly. As a result of that the research groups may end up studying something that is not alertness, but only similar to it. The terminology and physiology behind the term “alertness” will be further discussed in Chapter 3.

Second, as a result of the wide range of different methods used in the lighting studies, it is hard to compare the results. The methodology needs uniformity to allow repetition and dialogue between the studies. In the studies it is often forgotten what alertness is, physiologically, and therefore the methods used to study light-induced alertness are not always optimal. Finding proper methods is, however, challenging because light is a delicate stimulus and in lighting research papers the problems related to the usability of the study methods chosen are reported too seldom. These problems are addressed in Chapter 4.

Third, the research has concentrated too much on effects instead of causes and therefore the mechanisms behind the alerting effects of light on humans are not yet fully known.

It is known that the timing of sleep and waking are regulated by the circadian and homeostatic processes. According to the two-process model [33], the homeostatic process represents the natural drive for sleep that increases during wakefulness and decreases during sleep. The circadian process is cyclical and sleep-wake-independent and it represents the daily oscillations in the core body temperature, sleep propensity, and alertness [34]. The three-process model is an extension of the two-process model with a third process representing sleep inertia [35]. Because of these three processes, Cajochen has postulated [3] that light should have its strongest alerting action when the drive for circadian sleep is at its maximum, under high

homeostatic sleep pressure and during sleep inertia. In addition it has been suggested that emotional and cognitive inputs interact with the circadian and homeostatic processes taking part in the circadian modulation of alertness [36].

The free-running circadian period of a human is not exactly 24 hours but 24 hours and 11 minutes on average [37]. It means that internal and external cues are needed to synchronise humans to the earth's 24-hour light/dark cycle [38]. Light is the strongest such external cue [39]. Light adjusts the human circadian phase and suppresses melatonin secretion [1]. Melatonin is a sleep-inducing hormone produced in the brain by the pineal gland. The production of melatonin starts in the evening, and peaks between 2 and 4 in the morning. The secretion of melatonin is regulated by the suprachiasmatic nucleus (SCN), the brain's circadian clock. In addition to the sleep/wake rhytmn, the SCN controls many basic functions of the body, such as the core body temperature and the secretion of serotonin and cortisol, often referred to the "mood hormone" and "stress hormone" respectively.

Melatonin suppression caused by light exposure has not been observed when the eyes are covered [40]. However, light has elicited activating effects in blind people [8, 40, 41] indicating that the non-image-forming pathway is formed by other photoreceptors than rods and cones. Today it is well established that the intrinsically photosensitive retinal ganglion cells that are most sensitive to blue light of 480 nm [42] project from the retina to the SCN and play an essential role in melatonin release. These novel types of photoreceptors were first discovered by Foster, Provencio et al. [5] in 1991 in the eyes of mice where they were shown to mediate circadian rhythms. However, it took a decade before Provencio et al. [4] showed that most retinal ganglion cells that project to the SCN express the photopigment melanopsin. In the following years, Gooley, Berson, Hattar et al. [6, 7, 43, 44], verified that melanopsin is most probably the visual pigment of the ipRGCs that sets the circadian clock and initiates other non-image-forming visual functions.

However, melatonin has the potential to be involved in alertness at nighttime, but not at daytime, when melatonin levels are low. Therefore the mechanisms behind light-induced daytime alertness must be something else. Plitnick, Figueiro et al. [45], who recently studied the impact of light on brain activity, alertness, sleepiness, and mood, also reported that more than one mechanism, not just the melatonin pathway, must be involved in

light-induced alertness. The answers have been sought from other efferent projections of the ipRGCs, including several hypothalamic, thalamic, striatal, brainstem, and limbic structures [46].

In 2006 Vandewalle et al. [47] used functional magnetic resonance imaging to characterise the neural correlates of the alerting effects. They assessed the responses to an auditory oddball task, devoid of any visual processing, before and after a short exposure to bright white light and compared it to subjective alertness. Light-induced improvements in subjective alertness were shown to be linearly related to the responses in the posterior thalamus. Their findings suggested that light can dynamically modulate the activity of subcortical brain structures involved in alertness in the daytime too.

A year later Vandewalle et al. [9] further reported specific pathways which relay light information from the retina to different brain areas and suggested that light can indirectly enhance cortical responses by recruiting brain structures in the brainstem and thalamus. Because blue light (473 nm) had a greater effect on brain activity than violet light (430 nm), they suggested that melanopsin-expressing retinal ganglion cells make the most important contribution to the changes. The functional significance of most of these projections reviewed above has, however, not yet been clarified [12].

Besides the projections from ipRGCs, much emphasis has been put on the monoaminergic and cholinergic neurotransmitters located in the nuclei in the hypothalamus and brainstem regions. They regulate the daily cycles of sleep and wakefulness [48] by activating the thalamus and cerebral cortex. These neurotransmitters will be further discussed in Chapter 3, “Alertness and its physiology”.

In 2001 Aston-Jones et al. [49] examined mechanisms for the regulation of circadian and sleep-waking functions by injecting a pseudo-rabies virus followed by a tracer to reveal the indirect projections from the SCN to the monoaminergic neurotransmitter locus coeruleus (LC). On the basis of the investigations they proposed a signalling pathway from the SCN to the dorsomedial hypothalamic nucleus (DMH) and further to the LC and the thalamus and the cortex. Many years of consistent studies performed by Aston-Jones have verified that LC, which contains noradrenalin (also known as norepinephrine), plays an important role in the circadian regulation of alertness [50].

Today hypothalamic neuropeptides called hypocretins (also known as orexins) are also considered important regulators of sleep and wakefulness and of the maintenance of arousal because they innervate with the monoaminergic and cholinergic nuclei that take part in the activation between the autonomic nervous system and the cerebral cortex [51]. Among others, Winsky-Sommerer et al. [52] and España et al. [53] have used tracing to study the hypocretin system efferents to the LC and other arousal-related structures. Sakurai has suggested that the input from the limbic system [54] regulates the activity of orexin neurons upon emotional stimuli and evokes emotional arousal [51, 55]. This provides the basis for a new theory presented in Chapter 5, “Brain mechanisms behind light-induced daytime alertness”.

Despite the recent series of neuroimaging and tracing studies that have aimed to identify the brain areas activated by the light exposure, the mechanisms behind light-induced alertness, especially in the daytime, are still largely unknown today. The possible missing links in the neurological mechanisms will be discussed in Chapter 5.

3 ALERTNESS AND ITS PHYSIOLOGY

3.1 Physiology of alertness

The theory of the activation system, also known as the “ascending reticular activating system”, was first presented in 1949 by Moruzzi and Magoun [56]. It suggests that stimuli travelling from the brainstem through the thalamus, hypothalamus, and basal forebrain (BF) to the cerebral cortex give rise to the level of alertness [56, 57]. Therefore external stimuli increase alertness but a lack of them reduces it.

The ascending reticular activating system is located in the reticular formation, a broad and netlike formation in the core of the brainstem near the junction of the pons and the midbrain, as presented in Figure 1. There are many neurons in the reticular formation that play an essential role in the regulation of alertness. The most important of them are noradrenergic, histaminergic, dopaminergic, serotonergic, and cholinergic neurons located in the locus coeruleus (LC), tuberomammillary nucleus (TMN), ventral tegmental area (VTA), dorsal raphe nucleus (DR), and laterodorsal and pedunculopontine tegmental area (LDT/PPT), respectively [48]. These nuclei have many afferents and efferents and they are also connected to each other. Their involvement in alertness is briefly described here.

The LC is a nucleus that reacts easily to stimuli and improves alertness by increasing its noradrenalin secretion to the cortex [58]. This enables the body to perform well in stressful situations. The LC is considered to be the most important nucleus when alertness is being considered because a single noradrenergic neuron can innervate the entire cerebral cortex via its branches, mediating arousal and priming the brain’s neurons to be activated by stimuli [49, 50]. Noradrenalin normally produces effects such as increased heart rate, blood pressure, and sweat gland activity, and the dilation of the pupils and of the air passages in the lungs. Hence, the LC is in

direct connection to the autonomic nervous system (ANS). In fact, the activation of the ANS is often used as the conceptual definition of alertness.

The TMN is a nucleus in the hypothalamus that contains histamine, a neurotransmitter required for arousal [59]. It interacts with the cholinergic mechanism, constituting a crucial mechanism within the ascending neuronal network responsible for the maintenance of cortical activation and wakefulness.

The VTA secretes dopamine when activated by stress. This results in increased vigilance and motion activity. The secretion of dopamine inhibits the secretion of many other hormones. Therefore dopamine can both increase and reduce sleepiness, depending on which dopaminergic neurons are activated. The VTA has projections to the cortical area and the limbic system. [60]

The DR is the largest serotonergic nucleus and provides a substantial proportion of the serotonin innervations to the forebrain. It is known that serotonin can have both a calming and an arousing effect, depending on where in the brain is it secreted. Among other things, the dorsal raphe projects serotonin to the LC. [61]

The LDT and the PPT are cholinergic nuclei situated in the brainstem. They take part in modulating sustained attention and in mediating alerting responses and are considered to be one of the main components of the reticular activating system. The LDT and the PPT send acetylcholine projections to many subcortical and cortical structures, including the cerebral cortex, thalamus, hypothalamus, and the VTA. Noradrenergic (LC) and serotonergic (DR) mechanisms inhibit these cholinergic mechanisms. [62]

As shown in Figure 1, the ascending reticular activating system contains two branches [63]. The first branch innervates the thalamus by projections originating in the two cholinergic structures – the LDT/PPT nuclei. The second branch projects into the lateral hypothalamus, basal forebrain, and the cerebral cortex from the monoaminergic LC, DR, VTA, and TMN. These projections promote arousal, the state of increased physiological activity [64].

During sleep the neurons of the ventrolateral preoptic nucleus (VLPO) block the activation system by efferents containing gamma-aminobutyric acid (GABA) and galanin [65]. The interaction between the VLPO branches is mutually inhibiting, and it has been said to work like an “on-off” switch [63]. For a more detailed review of the ascending reticular activating system and its branches, see e.g. [57].

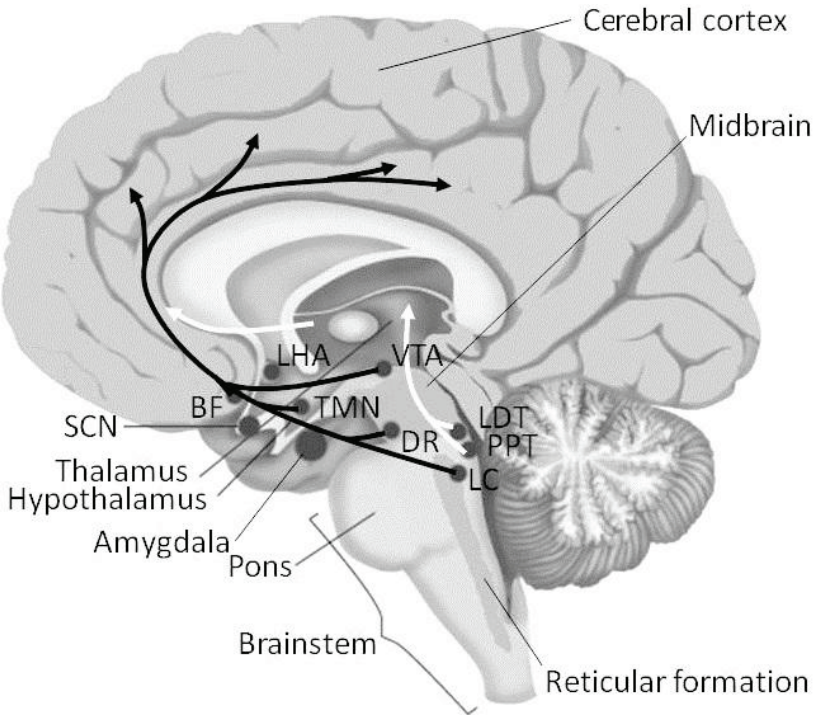

Figure 1. *A schematic drawing showing the most important components of the ascending reticular activating system and their projections. The cerebral cortex receives messages via thalamus but also directly from a number of nuclei in the brainstem. Adapted from Rautkylä et al. [24].*

3.2 Definition of alertness

Alertness has been widely studied but poorly defined. In general, the precise meaning of the term "alertness" differs between languages and situations. It seems that the English word originates from sleep research, where it has been used to mean a state that can occur in the daytime. The word is formed from "alert", which comes from the Italian "all'erta", meaning "on the watch". According to the Merriam-Webster Online Dictionary, it was first used in 1618 [66].

According to The New Penguin English Dictionary, "alert" is a synonym for "watchful, aware" [67]. This definition is, however, restricted, because it relates alertness to sensitivity to external stimuli but does not indicate that alertness would result in any kind of physical or cognitive function. The Merriam-Webster Online Dictionary [66] and Cambridge Online Dictionary [68], on the other hand, expand the picture and suggest that an alert person perceives and acts quickly. This definition indicates that alertness is not a

passive state but instead it drives active processes. It links alertness to performance, the ability to perform [69]. Seeing alertness as readiness to respond to stimuli explains why reaction tests are so often used for attempts to measure alertness.

In neuroanatomy alertness is seen as consisting of two parts. Intrinsic alertness represents the state of general wakefulness and arousal, while phasic alertness represents the ability to increase response readiness to external cues [70]. However, inconsistency can be seen in the use of the term "arousal" as in some of the literature arousal is used as a synonym for alertness to refer to the level of brain activity [41], whereas some researchers see arousal as a change in behaviour associated with transitions from slow-wave sleep to waking and by alertness they refer to the waking end of this continuum [71].

In practice alertness is often approached through its presumed antonym, "sleepiness". The Merriam-Webster Online Dictionary defines sleepiness as "readiness to fall asleep" and proposes "drowsiness" and "somnolence" as its synonyms. "Fatigue" and "tiredness" are also commonly equated with "sleepiness" [72]. The Swedish sleep researcher Torbjörn Åkersted from the Karolinska Institute considers sleepiness to be an effort to resist sleep, implying that someone who does not fight back against sleep does not experience any sleepiness [73]. Assuming that alertness was straightforwardly opposite to sleepiness, it would mean that a person who does not fight back against sleep is alert. However, the Canadian sleep researchers Shen, Barbera and Shapiro state that no clear consensus on the definition of the term "sleepiness" has been reached [21]. Shen and Shapiro, together with Moller and Davins, have also investigated the correlation of sleepiness and alertness scales and state that sleepiness is not the inverse of alertness [22]. Therefore caution should be taken if alertness is assessed through sleepiness.

The neuropsychological approach is that alertness[i] is connected to the activation system of the brain. It suggests that alertness is a state of sustained attention where the brain is excited and ready to operate. This kind of readiness to operate appears as an ability to perform cognitive functions and complex tasks [20]. The opposite to that is the state where consciousness is fading and attentiveness and brain functions are disturbed. This leads to tiredness or fatigue, which can thus be considered as signs of re-

[i] In neurophysiology the term "vigilance" is often used instead of "alertness"[20].

duced alertness. As can be seen, explaining alertness through activation gives a broader insight into alertness compared to the performance-based definitions because it takes into consideration the involvement of alertness in logical functioning. After all, alertness involves cognitive processing [20] and helps to store information for long-term memory retrieval [74].

On the basis of the preceding discussion of the different terms related to alertness, as well as the physiology of alertness presented in Section 3.1., the following definition of alertness is formed:

Alertness is an activation state of the brain. It enables target-oriented cognitive and physical functioning to take place. Stimuli induce alertness and a lack of them reduces it.

The thesis follows this definition.

4 METHODOLOGY IN DAYTIME ALERTNESS RESEARCH

4.1 Aspects for choosing and designing proper methods

As stated by Rautkylä et al. [26], the current weakness of lighting research is that the methods used for evaluating light-induced daytime alertness are not always suitable for such research.

When the effects of light on daytime alertness are assessed it is essential to use methods that are based on the physiology of alertness. In practice, however, it is difficult to measure the state of activation. Therefore the assessment is often performed by observing the effects of activation instead of the activation itself. This is the case in e.g. performance evaluations that measure how well the person is functioning but do not indicate the physiological activity.

Naturally, the method is not the only thing that makes a successful alertness study. Because alertness is negatively affected by factors such as sleep deprivation [75] and sleep inertia [76], it is important to consider at which time of the circadian day the study is performed and what kind of a sleep schedule the subject has kept during the preceding days. The chronotype is an attribute of human beings that reflects whether they are alert and prefer to have their activities early or late in the day [77]. Therefore the chronotypes of the subjects should also be considered when choosing the timing and subjects for the study.

When the test bed for a study of light and alertness is being designed, it should be kept in mind that light is a delicate stimulus. Therefore there is a risk that the effects of other stimuli such as caffeinated beverages [78], indoor climate [79], or auditory stimuli [80] will mask the effect of light. Other stimuli should either be eliminated from the test set-up or separated out in the analysis. The light exposure should be equated to photon densities instead of lux levels or luminance or contrast, because photoreceptors

behave like photon catchers and therefore they are better units of measurement in a non-image-forming system [81].

Other important things to consider are the duration of the light exposure and when and for how long the effects are measured. One can use short light pulses or longer exposure times, and measure the effect during the exposure, shortly after it, or after a longer time period, depending on whether the short-term or long-term effects are being investigated. Another option is to run a continuous recording that outlasts the light exposure. This can have an impact on the chosen method, because not all methods are capable of long and continuous recording.

It is essential to note that in addition to direct effects, light can also have indirect effects. This is the case in e.g. auditory tests where light is used to modulate the response to auditory stimuli [47]. The evaluation of the methods in the following sections will be limited to how suitable the method is for studying light-induced alertness when light is the only stimulus and the alerting effects of light are direct.

4.2 Evaluation of subjective methods

Subjective evaluation is a commonly used research method because it is easy to conduct both in laboratory and field conditions. It can be conducted with a Likert-type discrete scale [82] or a continuous visual analogue scale (VAS) anchored by word descriptors at each end [83]. Alertness is typically derived from the results of sleepiness. Perhaps the most popular subjective measure of sleepiness is the Karolinska sleepiness scale [84], which uses a discrete Likert scale from 1 to 9, where 1 = “very alert” and 9 = “very sleepy, great effort to stay awake” or “fighting sleep”. The KSS has been validated to correlate significantly with electroencephalographic and behavioural variables [85] and is therefore considered a reliable measure of sleepiness. As discussed in Chapter 3, alertness is not, however, always the inverse of sleepiness [22].

The main criticism of any type of subjective assessment arises from the fact that it relies on self-reporting, leaving it open to misinterpretation, unintended bias, and falsification for any number of reasons (e.g. the act of verbal rating itself can affect sleepiness [86]). It is possible that the subjects may evaluate their alertness differently in light than in darkness, even though there was no real difference in their level of alertness. In fact, there is no real placebo control for light, but it can only be hoped that the subject assesses his alertness time after time following the same logic. Another

weakness of subjective assessment in a study of light-induced alertness is that it can only be used to point out the changes in the subject's way of responding to light, but it does not show anything about the reasons or the mechanism behind the changes. Therefore it can never give as much input to the study as objective measures that are linked to physiology.

It is also hard to be sure that the effect is caused by light and not something else. Using subjective assessments thus requires a very strictly controlled test environment where there are no other factors that could affect the person's way of answering. Finally, one major disadvantage of using subjective assessment in lighting studies is that the data recording is not continuous. Because self-reports are produced after certain time periods, the information about the state of alertness between the measuring points is automatically lost. One could say that the data expire as soon as they are recorded. This is a big problem because it hinders one in detecting whether it is a question of a fast or a slow response to light.

4.3 Evaluation of objective methods

4.3.1 Reaction tests

Reaction tests are often used to evaluate how alert a person is [87, 88]. This is based on the assumption that alertness involves increased reactivity to internal or external stimuli; thus an alert person reacts fast to stimuli. However, using reaction tests to evaluate alertness is not as problem-free and easy as it might at first seem. For example, the test itself can act as an activating stimulus and hence affect alertness [87].

The reaction tests need to be well designed in terms of the complexity of the test because the subject should be able to perform the test without too great an effort. Another important factor is how the subject manages to retain his motivation throughout the whole test. That depends on whether the subject is being rewarded after a successful test, but also on the duration of the test. For a long time it was thought that a reaction test should last no less than 10 minutes because studies indicated that shortening a performance task resulted in reduced sensitivity to changes in performance [89]. However, recently the study of Roach et al. [90] showed that a 5-minute test correlates well with a 10-minute test. They tested the psychomotor vigilance test [91], which has been shown to be a reliable indicator of decreased alertness [62] and is commonly used for assessing neurobehavioural performance.

The advantage of the PVT is that it reflects the tiredness-related reduction in performance without being confounded by the learning effect, a factor that often causes bias in the experimental data. In the traditional study protocol a visual stimulus appears on the display and the subject is instructed to press the response button as fast as possible after detecting the stimulus.

Another and more modern option is to use auditory stimuli in a psychomotor vigilance test. In the auditory PVT the subject presses a button after hearing the stimuli in the same way as in the visual PVT. By using two buttons and two different stimuli instead of one it is also possible to add complexity to the test. Today there are portable, palm-held devices that make it possible to conduct experiments in real environments such as workplaces, instead of only laboratories [91]. The Walter Reed Army Institute of Research, Maryland, offers test and analysis software for this kind of field-portable reaction time tester for free [92]. However, their PalmPVT does not allow auditory stimuli to be used.

In theory, these kinds of reaction tests can be used in lighting research in two ways. First of all, if light with the specific characteristics under study acts as the stimulus, the reaction time will show how easy it is to detect that stimulus. In practice, however, this only shows that the person reacts to light but not whether the light induces any alerting effects. Another option is to use an exogenous stimulus in the PVT to assess vigilance after being exposed to light for a certain amount of time. Following e.g. Lockley's example [10], in this kind of protocol it is better to use an auditory stimulus instead of a visual one to prevent the PVT stimulus from masking the light-induced effect under study. This has potential for revealing how the exposure to light affects the reaction times.

The biggest disadvantage of using a PVT in studies of light-induced alertness is that it measures sustained attention rather than alertness and therefore it is not a suitable method for evaluating the activation system in detail. Furthermore, it does not measure the functioning of the LC or other body parts that take part in light-induced alertness but instead it exhibits the circadian and homeostatic processes that take care of the natural sleep/awake rhythm. Therefore a PVT is better suitable for chronobiology research [93].

4.3.2 Pupillometry

Research has shown that there is a close relationship between alertness, pupil size, and pupil stability [94]. A well-rested individual can maintain

constant pupil size in darkness but as he becomes sleepier the pupil size will become less stable and it exhibits spontaneous fluctuations called “hippus” or “pupillary noise” [95]. The hippus is characterised by a random noise in the frequency range of 0.05 to 0.3 Hz [96]. The measurement, called pupillometry, is often used to objectively identify sleepiness, alertness, and fatigue [94, 97, 98]. It consists of measuring the size of the pupil and analysing how the pupil changes.

Typically, the human pupillary light reflex (PLR) exhibits roughly three phases, rapid phasic constriction in response to the onset of light, which is followed by a steady-state pupil, and finally, depending on the light stimulus, there can be the post-stimulus persistence of a constricted pupil even after light offset [99].

The pupil provides control over the retinal illumination and the depth of focus [100]. In addition to constricting as a response to increased light flux and vice versa, the pupil also responds e.g. to accommodative changes [101] and to anticipating effects for an instructed task [102], illustrating the wide range of confounding factors involved in pupil recordings.

Given that pupil size modulates the retinal illuminance, precautions are needed to control the exact retinal illuminance. These precautions include monitoring the pupil size via a video-based infrared pupillometer [103] with or without dilating the pupil to a constant size during the recording. Additionally, one can use a Maxwellian view [104], as opposed to a free view in which the stimulus sizes are smaller than the smallest physiological pupil diameter; hence pupil size has no modulating effect on retinal illuminance.

The pupil size can be measured using a direct approach with binocular light stimulation or by a consensual approach, where only one eye is stimulated and the response of the unstimulated eye is recorded. To avoid contamination of pupillary measurements by spontaneous fluctuations of the pupil, a continuous monitoring of the pupil is preferred.

The pupillometric hardware is similar to that used in the eye tracking literature [105]. Typical temporal resolutions range from 30 Hz in low-cost setups [106] to 6-12 kHz in more customised setups [107], with spatial resolutions going down to 0.008 mm [108] depending on the sensor resolution, quality of the optics, and the signal-to-noise ratio of the video signal. The temporal resolution can be increased by using complementary metal oxide semiconductor (CMOS) sensors instead of charge-coupled device (CCD) sensors [109].

Pupillary fluctuations have been widely exploited as an easy and non-invasive measure to track changes in autonomic nervous system activity. One example of such an approach is the pupillary unrest index (PUI), which measures the cumulative changes in pupil size, typically during periods ranging from 25 seconds to 15 minutes [97] in darkness or under light. The PUI was used, for example, by Szabó et al. [110] to measure the changes in the vigilance levels of subjects during bright light exposure. Among others, Nikolau et al. [111] found pupillary assessment to be a promising objective tool to detect pharmacologically induced changes in alertness. However, it should be noted that the majority of studies on pupillary fluctuations have been carried out in darkness and the relationship between fatigue and oscillations in daylight requires further validation, adding some restraints to real-life lighting studies with pupillometric alertness assessment.

Considering that the pupillometer is comfortable for the subject and the protocol does not include any tasks to be performed, it might work as a good objective indicator for light-induced alertness. The method operates with a fairly delicate apparatus and requires the subject to sit still without extra blinking and head movements. There are, however, some indications that it could be used in field studies too [112]. Recent studies suggest that pupil size measurements could offer a simpler way to estimate autonomic nervous system activity than the commonly used heart rate [113].Therefore it is reasonable to suggest that the reactivity of the pupil could well be used in lighting-related psychophysical experiments.

4.3.3 Heart Rate

The heart responds to psychological stress via the autonomic nervous system [114]. Over the years a correlation between the heart rate and arousal/alertness caused by light exposure has been found both in rats and humans [115, 116]. Heart rate variability (HRV) has become the conventionally accepted term to describe the variations of interbeat intervals that represent autonomic nervous activity [117].

Heart rate variability is normally recorded by placing 10 electrodes on the skin on the subject's arms, legs, and chest. They measure the activity of different parts of the heart muscle and transmit it to an electrocardiogram (ECG) machine. The machine produces an ECG tracing of these cardiac electrical impulses. In clinical studies the heart rates or cycle intervals are recorded over long time periods, traditionally 24 hours, allowing more reliable calculations of the measures. Because the analysis of HRV data is more

complex than is generally appreciated, there is a potential for incorrect conclusions and unfounded generalisations [118]. The experimental procedures and analysis of the results should be carried out in accordance with the recommendations of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [119]. In fact, Peña et al. [120] state that caution should be exercised concerning the use of short recording segments, a circumstance not fully considered in several studies. Therefore, although heart rate is easily measured in the presence of a light stimulus, the method does not meet the needs of detecting the effects of short-term light exposure.

From the subject's point of view, studying light-induced alertness by observing the heart rate is an easy research method because there is no task to be performed. However, real clinical equipment contains detectors and wires that can hinder the subject from doing other things, as is often required in field studies. Fortunately, there are commercial and cost-effective heart rate monitors that can be used in studies where it is possible to reduce accuracy in order to gain mobility. There is evidence that motion does not contaminate the signal too much [121]. It should, however, be considered that in field studies heart rate data are even more sensitive to distractions than in laboratory studies. Hence, the effects of the light stimulus are easily masked by other unintended stimuli.

4.3.4 Skin conductance

Because of the connection between the autonomic nervous system and locus coeruleus, alertness has long been assessed through the skin's ability to conduct electricity [122]. In fact, activation theorists long considered skin conductance to be the most appropriate measure of a generalised arousal response [123]. Skin conductance, galvanic skin response, and electrodermal response are different terms for the same physiological measure. It is known that as a person becomes more or less stressed, the skin's conductance increases or decreases proportionally [124].

The easiest way to measure electrodermal activity (EDA) is by strapping two electrodes to two fingers, namely the little finger and index finger of the non-dominant hand. The skin acts as a resistor whose conductance (inverse of resistance) changes with time according to the changes in hydration in the sweat glands [125]. Changes in EDA occur with even a slight rise or decrease in the amount of sweat within the glands [126]. Therefore a typical

signal recorded from a skin conductor sensor shows relatively rapid increases and slower decreases.

From the lighting research point of view measuring the skin's ability to conduct electricity can be considered a good research method for light-induced alertness because it can be used within and between light exposures with both continuous and short-term light stimuli. The recording apparatus is small and the experimental protocol does not involve any kind of task performance by the subject. However, it has not been used often in lighting studies. One major disadvantage is that the wiring hinders its use in real-life settings.

The analysis is rather easy as long as the recordings are time-locked to specific events to allow the analyser to select the right blocks of data from the general data [127]. The analysis has the potential to show the intensity of the alerting effect of light on a human being. However, it is important to note that changes in the signal may be caused by external stimuli or internal events [128]. Hence, it might become hard to distinguish the effects of different stimuli from one another. Therefore, to make electrodermal activity a proper indicator of the intensity of light-induced alertness, all other emotional cues that might mask the effect of light have to be eliminated.

4.3.5 Electro-oculogram

Eye movements react to a decrease in alertness. The attenuation of blinking is often a marker of the fact that the person is losing interest. At the same time the duration of a blink becomes longer and the eyelids become lazier. When the eyelid closes, the eyeball makes slow roll-like horizontal movements that are called slow eye movements [129]. From these visible neurophysiological factors it can be seen when the person is transiting from being awake to asleep. Therefore eye blink rate and SEMs are considered reliable correlates of human alertness [130].

Clinical alertness evaluation takes advantage of the knowledge that a person who is not alert finds it hard to follow targets. In the electrophysiological test called an electro-oculogram (EOG) two skin electrodes are placed as close as possible to both eyes. Moving the eyes induces a voltage between them. The voltage varies from one to several millivolts, depending on the ambient retinal illumination. The subject is instructed to look back and forth at a steady fixation rate between two fixation targets to generate consistent saccades. These saccades are amplified and registered to be considered for analysis [131]. Normally, EOG amplitude increases significantly if

the eye is kept first in darkness and then in light [132]. However, it has been shown that in electro-oculogram analysis it is better to use the light peak-to-dark trough amplitude ratio instead of the actual amplitude values because the amplitude varies widely among individuals [133].

The method is well suited to use in lighting research, both during and between light exposures. However, when designing the light stimulus, it is important to make sure that the entire visual field is evenly illuminated and that there is no direct glare present that could hinder the subject from focusing on the targets [131]. As the eyes alternate direction every 1 to 2.5 seconds, the test soon becomes uncomfortable and tiresome for the subject. Therefore it is advisable to record the movements in sets and let the eyes rest between the sets. According to the international standard approved by the International Society for Clinical Electrophysiology of Vision, one set of 10 saccades per minute is enough to recognise the relevant peaks and troughs in the EOG data. The standard for EOG technology and protocol also offers other valuable recommendations for the recording technique, facilitating the comparability of EOG data throughout the world.

A drawback in using an EOG to study light-induced alertness is that it does not allow the subject to concentrate on other tasks at the same time. That, and the presence of skin detectors and recording apparatus, makes the method unsuitable for real-life settings. Despite its minor impracticalities, the EOG technique is quite commonly used to assess alertness objectively [134], either alone or together with brain activity measures.

4.3.6 Electroencephalogram

A number of observations suggest that there is a possible causal link between the activity of the locus coeruleus and electroencephalogram (EEG) activation [135]. Because the activation of the LC has been shown to induce EEG signs of cortical and hippocampal activation [136], it is reasonable to claim that by observing the EEG activity of the forebrain it might be possible to monitor the alerting process.

Electroencephalographic activation is a direct measure of the general cortical activation level. A set of electrodes is placed on the subject's skull to detect and amplify the small electrical voltages that are generated by brain neurons when they fire. Similarly to muscle fibres, neurons in different locations can fire at different rates. The EEG is typically described in terms of rhythmic activity and transients. The rhythmic activity is divided into bands by frequency.

Jung and Makeig state that it is possible to use the EEG power spectrum to estimate alertness [137]. The spectrum Beta band (15-20 Hz) is generally regarded as a normal rhythm, which explains why changes in Beta activity are often used to reflect different levels of alertness [138]. A decrease in Alpha activity (8-13 Hz) has also been reported to be associated with a drop in alertness and cognitive performance across the waking day [139]. This means that high levels of EEG Alpha activity could indicate a high level of alertness during an eyes-open condition, similarly to Beta. Theta (4-8 Hz) and Delta (2-4 Hz) activity are linked to increased drowsiness and reductions in performance [140]. However, Theta and Delta activity are rarer in awake adults.

An EEG has both advantages and limitations in alertness research. One of the advantages as a correlate to human alertness is that it measures the brain's electrical activity directly, while other methods record the responses of the autonomic system. Another advantage is that an EEG is capable of detecting changes in electrical activity in the brain on a millisecond time scale. Compared to techniques such as functional magnetic resonance imaging that have a time resolution between seconds and minutes, an EEG has a much higher temporal resolution. However, the spatial resolution of an EEG is poor and therefore it is not able to indicate the location of the activity of the brain. One possibility is to use an EEG simultaneously with fMRI, so that data with a high temporal resolution can be recorded at the same time as data with a high spatial resolution. However, there are technical difficulties associated with analysing the activity of the brain in exactly the same time frame. Furthermore, currents can be induced in moving EEG electrode wires as a result of the magnetic field of the MRI scanner.

As a research method an EEG is fairly comfortable for the subject, because it records spontaneous brain activity in the absence of tasks. Therefore light can easily act as a short-term or continuous stimulus. Despite the easiness of the study protocol, using it in real-life settings is complex because of the wiring and its interference-prone nature.

4.3.7 Brain imaging

Brain imaging provides an opportunity to study what is really happening in the human brain as a result of light exposure. There are two techniques, namely functional magnetic resonance imaging and positron emission tomography (PET), which provide an anatomical and a functional view of the brain and are commonly used for brain imaging [70].

fMRI measures changes in the blood flow to particular areas of the brain. Through a process called the hemodynamic response, blood releases oxygen to neurons, creating magnetic signal variation. This variation can be detected using an MRI scanner. PET, for one, detects radioactive material that is injected or inhaled. The material collects in the area of the brain being examined, where it gives off energy in the form of gamma rays [141]. The procedure and analysis of both techniques is complex and requires knowledge of fields such as physics, psychology, neuroanatomy, statistics, and electrophysiology.

With brain imaging it is rather easy to identify the precise areas that are activated in the brainstem as a result of the light. A conventional 1.5-Tesla fMRI scanner has a spatial resolution of 3 mm, but the higher-strength 3-T and 4-T magnets may reduce the spatial resolution to as low as 0.4 mm [142]. A standard PET is not as accurate; the effective spatial resolution of a PET remains at 4-6 mm [143]. However, the development of high-resolution PET scanners for imaging small animals has led to significantly higher spatial resolutions of 0.5-1.0 mm [144, 145].

Temporal resolution is also superior with fMRI. However, compared to an EEG, which has a time resolution of only a single millisecond, PET and fMRI are slow, because they can detect a new stimulus only some seconds after the first stimulus. As a matter of fact, with PET it is not at all possible to pick out neural activation patterns associated with individual stimuli measures, so event-related phenomena, such as the effect of a short exposure to light, can only be detected with fMRI. From the lighting research point of view this hinders the use of subsequent light pulses as stimuli.

The strong magnetic field around the functional magnetic resonance imaging scanner also causes other limitations on using light as a stimulus. The light source cannot be installed in the study room because the electricity will interfere with the magnetic field. Instead, the light stimulus has to be transmitted by an optic fibre, as was done recently by Vandewalle et al. [9]. The same problem arises when trying to measure other physiological measures during the scans to help in the interpretation of the brain imaging data. Generally speaking, it is possible to measure EEG, EOG, electromyogram (EMG), ECG, or skin conductance only during the scans to prevent the magnetic field from inducing a current in the electrode wires. However, several techniques are under development to deal with these issues and there are already good experiences of recording fMRI and EEG simultane-

ously [146]. Positron emission tomography, for one, is free of physical limitations of this kind.

If the problems mentioned above are to be overcome, there are still many practical issues that impede the use of brain imaging in a typical lighting study. First of all, there are only 100-200 MRI centres and 20-30 PET centres worldwide where the studies can be conducted. They cannot be used in field studies, but in laboratory studies too their use is limited as a result of their huge expense, which is around $500 per session with fMRI and $1500-2000 with PET [141]. In a lighting study it is often necessary to have many subjects and run various sessions with each one, which makes the costs enormous. These two requirements can also be hard to realise for safety reasons. With fMRI the suitability of the subject for the test is very restricted (e.g. no pregnancy, tattoos, pacemaker, or claustrophobia) and with PET the repeated studies are limited by the annual permissible radiation exposure. The number or duration of fMRI tests is not limited but since the scanner is very sensitive to motion, the subject can only be expected to hold still for some hours.

4.4 Summary of the evaluation

Table 1. *Summary of the pros and cons of the research methods in terms of their suitability for studying light-induced alertness. ANS = autonomic nervous system, CNS = central nervous system.*

METHOD	PROS	CONS
Subjective evaluation	Easy to conduct, Karolinska sleepiness scale is validated to correlate with EEG and behavioural indicators of sleepiness	No real placebo control for light, not continuous, no real physical link to activation system
Reaction tests	Possible to use auditory or visual stimulus, variety of equipment available	May mask the actual stimulus, measures rather sustained attention/performance, no real physical link to activation system
Pupillometry	High temporal resolutions possible, continuous, measures ANS activity	Burdensome, not for long-term effects, fatigue and oscillations in light not validated, sensitive to movement and blinking
Skin conductance	Suitable for both short-term and long-term reaction assessment, affordable, measures ANS activity	Sensors very sensitive to emotional cues, wiring disables use in field, strong age factor
Heart rate	Cost-effective monitors available, continuous, measures ANS activity	Sensitive to emotional cues, data analysis is complex, not for short-term effects
Electro-oculogram (EOG)	Standardised, suitable for short-term and long-term reaction assessment, measures ANS activity	Tiresome, long and continuous recordings are not possible, not suitable for field studies
Electroencephalogram (EEG)	High temporal resolution, suitable for short-term and long-term reaction assessment, measures the brain's electrical activity directly (CNS)	Low spatial resolution, data analysis is complex, not suitable for field studies
Functional Magnetic Resonance Imaging (fMRI)	High spatial resolution, measures brain activity through blood flow (CNS)	Interference-prone nature, data analysis is complex, expensive, restrictions with subjects, not suitable for field studies
Positron Emission Tomography (PET)	High spatial resolution, no physical restrictions with electricity, measures brain activity through the energy of radioactive material (CNS)	Not possible to detect individual stimuli, expensive, limited availability, limited dose, not suitable for field studies

5 BRAIN MECHANISMS BEHIND LIGHT-INDUCED DAYTIME ALERTNESS

5.1 Connections from the retina to the activation nuclei

Figure 2 shows the most essential connections from the retina to the nuclei that promote alertness and were introduced in Section 3.1. These connections explain how the light entering the retina can transform into a stimulus activating different brain regions and delivering messages to the hypothalamus, thalamus, and the cerebral cortex.

Orexin (hypocretin) is a neuropeptide produced in the lateral hypothalamus (LHA) [147]. It has been suggested that neurons containing orexin increase arousal by innervating with the nuclei that take part in the activation between the autonomic nervous system and the cerebral cortex [148]. Orexin-1 receptors (OX1R) are found in the LC [53, 149, 150] orexin-2 receptors (OX2R) in the TMN [151], and both types of receptors in the DR [152] and LDT [153]. Serotonin and noradrenaline neurons in the DR and LC, respectively, also send inhibitory feedback to the orexin neurons in the LHA [154]. Histamine in the TMN does not seem to have any effect on orexin neurons.

As shown in Figure 2, cholinergic and monoaminergic nuclei also project to each other. Noradrenergic LC and serotonergic neurons of the DR have reciprocal connections [155]. Dopamine in the VTA appears to have an excitatory action on the LC, increasing alertness [156]. The cholinergic neurons PPT and LDT are both excited and inhibited by noradrenaline from the LC, and PPT and LDT [157] in turn project to the LC, increasing the firing of LC neurons and thus increasing arousal [158]. The histaminergic neurons of the TMN also project to the LC, however, by inhibiting noradrenaline release [159]. In contrast to other hypothalamic nuclei, the LC does not project reciprocally to the TMN [160].

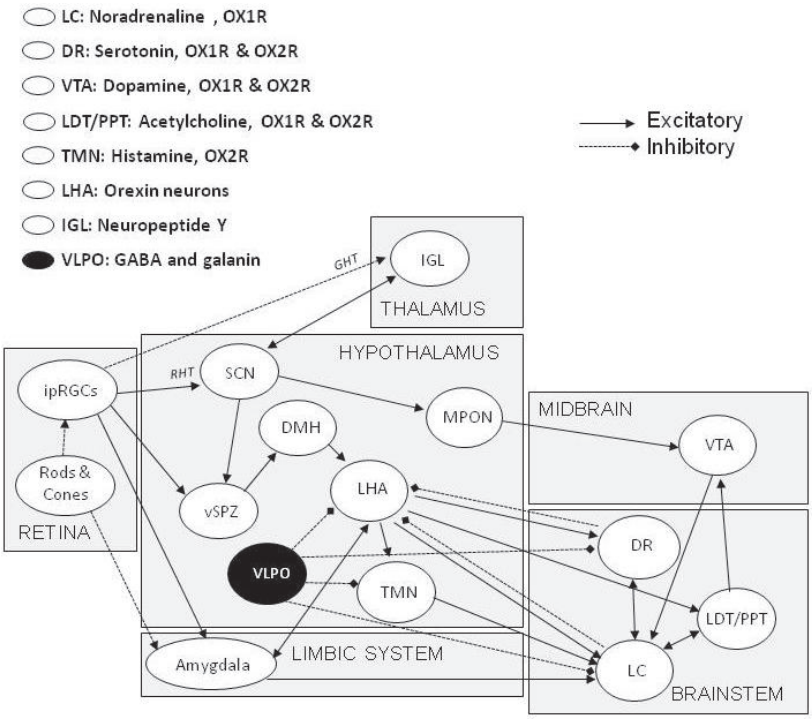

Figure 2. *A schematic diagram showing the projections between the retina and the nuclei that take part in the activation between the autonomic nervous system and the cerebral cortex. VLPO promotes sleep and LHA maintains wakefulness. Adapted from Rautkylä et al. [24]. Note that the majority of the connections were found while testing rodents or monkeys.*

The suprachiasmatic nucleus is the brain's master clock [161] that coordinates the circadian rhythms on the basis of the light input from the outside world during the daytime and by melatonin secretion during the nighttime [162]. It is located in the hypothalamus.

The input and the output signalling pathways to and from the SCN have been widely studied. Photic information is transmitted to the SCN directly along the retinohypothalamic tract (RHT) from the melanopsin-containing intrinsically photosensitive retinal ganglion cells located in the retina [6]. Although ipRGCs are sufficient for photoentrainment, recent findings have shown that rods and cones also contribute to the photic entrainment of circadian rhythms [163]. In humans, the SCN also seems to receive indirect input from the retinorecipient intergeniculate leaflet (IGL) in the thalamus via the geniculohypothalamic tract (GHT) [164, 165].

The SCN projects indirectly to the LC using the ventral subparaventrical zone (vSPZ), DMH, and LHA as relays [49, 166]. vSPZ also gets direct pro-

jection from ipRGCs [46]. Recent studies show that there is an indirect projection from the SCN to VTA and that the medial preoptic nucleus (MPON) is a major intermediary in that circuit [167].

In addition to the SCN and zSPV, ipRGCs also project directly to the amygdala [46] located in the limbic system. As shown in Figure 2, the amygdala sends limbic inputs to the orexin neurons in LHA [54]. These inputs include the corticotrophin-releasing factor (CRF) neurons that originate in the amygdala [52]. Neurones containing CRF in the amygdala also project to the LC [168], indicating that CRF acts as a neurotransmitter to activate the LC during stress [169].

5.2 Limbic and circadian pathways

On the basis of the neurological connections illustrated in Figure 2, a model of two separate major paths from the retina to the activation system and then on to the cerebral cortex is proposed. The model is presented in Figure 3.

The first path is formed by the retinohypothalamic tract in the non-image-forming visual system. When this path is used, the light stimulus enters the ipRGCs in the retina and travels via the RHT or GHT, giving input to the SCN and further to the circadian system. The involvement of rods and cones in the circadian pattern is also possible [163]. From now on this path is referred to as the circadian pathway.

The second path starts from the retina, but instead of continuing directly or indirectly to the SCN, it continues to the amygdala, a limbic structure involved in many brain functions, including emotion. The fact that light with a shorter wavelength has been found to have a stronger effect on emotional responses than longer wavelengths [170] indicates that the photoreceptors involved in this pathway are ipRGCs and not rods and cones. It also means that the visual system in question is non-image-forming. However, the involvement of the classical photoreceptors cannot be ruled out [170]. It is possible that part of the emotional response is related to the image-forming visual system and that light stimulates the classical photoreceptors in the same way as other visual stimuli [171]. From now on this path is referred to as the limbic pathway.

As shown in Figure 2, the amygdala and the SCN both use orexin neurons in the LHA to deliver messages to the LC, the core of the activation system. Therefore it is suggested that the different paths are parallel to each other

and that they unite in orexin neurons continuing on the same path to the activation system, as illustrated in Figure 3.

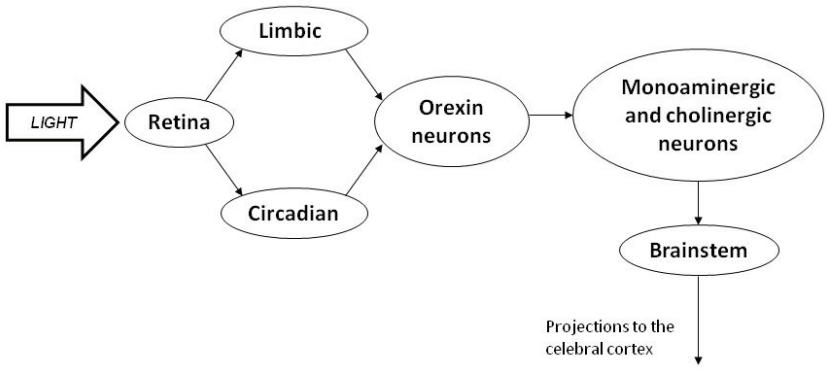

Figure 3. *Two parallel pathways from the retina to the activation system. The light stimulus can travel via the retinohypothalamic tract in the circadian system or use the limbic system to create an emotional response to the light cue. Both pathways project to orexin neurons in the lateral hypothalamus and promote cortical arousal through the neurons of the activation system. The retinal photoreceptors involved in both pathways are ipRGCs. In addition, it is possible that rods and cones take part in the photoreception of the pathways. Adapted from Rautkylä et al. [24].*

The ability of light to affect alertness via melatonin suppression is well established [172] and it has been used to explain the changes in alertness during night-time light exposure. Therefore the circadian pathway can be considered a known pathway for light-induced alertness. The limbic pathway, on the other hand, has never before been considered as the mechanism behind the alerting effects of light, although the theory is in accordance with the findings of Vandewalle et al. [9], who report that light can modulate emotional processing by the amygdala. The theory is also consistent with Figueiro et al. [45, 173], who recently conducted a series of studies with long-wavelength red light and short-wavelength blue light and reported that more than one mechanism, not just the melatonin pathway, must be involved in light-induced alertness.

There is also recent evidence that these two proposed pathways work at the same time and influence one another. In mice, disturbances of the limbic system have been found to affect the circadian system [174] and vice versa [175]. It should be noted that some neural connections presented in Figure 2 have been characterised in only a few mammalian species, primarily nocturnal rodents and not diurnal mammals [176]. Therefore in future studies it should be ensured that the circadian and limbic pathways as described in Figure 2 are present in humans. If they were, they could explain

why it is so hard to reach consensus on the parameters of light, in terms of the timing and duration of exposure, light spectrum, colour temperature, and light level that produce the greatest responses in alertness [9, 10, 15-19, 25, 31].

5.3 Light, emotions, mood, and alertness

If the limbic system, and, more precisely, the amygdala, is involved in light-induced alertness, it means that alertness can result from an emotional stimulus caused or modulated by the light. Hence, the alerting response depends heavily on what kind of emotions the light induces.

The hypothetical model opens up two questions: first, how it can be verified, and second, what the relationship of light, emotions, and alertness is. Section 5.3 will discuss what is currently known about these relationships. In Section 5.4 a suggestion as to how to test the model will be presented.

First, however, it is essential to discuss the terms “emotion” and “mood”. Vandewalle et al. [170] state that emotional reactions are transient phenomena that are triggered by external cues. Mood, on the other hand, is a sustained emotional state that does not require a triggering stimulus. Emotional reactions can have a great impact on mood. Respectively, alterations in mood, such as in mood disorders, can modify the emotional responses of the brain, resulting in different reactions to those that a person without the mood disorder would have. Because emotions and mood are closely linked and affect one another, mood state is used as an indicator of emotion [177].

Brain imaging studies show that emotions and arousal are connected and that functional brain differences are associated with stimulus arousal [178]. Activation of the visual cortex is greater when people are exposed to emotional stimuli, as compared to neutral ones [178]. In skin conductance measurements, unpleasant stimuli have been shown to increase electrodermal activity more than pleasant stimuli. Interestingly, women show a bias towards more activation for unpleasant stimuli than for pleasant ones and men show a tendency in the opposite direction [179]. On the assumption that the alerting response depends on the pleasantness of the stimulus, it is important to consider what makes a light stimulus pleasant or unpleasant.

The psychology of colour has been widely studied [180] and it is well known that colour elicits positive or negative feelings and emotions [181, 182]. For instance, the colour red has been associated with excitement, yellow with cheerfulness, and blue with comfort and security [183]. In a study

of college students, a blue colour was found to elicit both negative and positive emotions [184]; positive, because blue was associated with the ocean and relaxing, calming effects, and negative, because blue was also associated with night and depression. This means that colours can provoke either type of emotions and that the alerting response depends on the emotions that it provokes. However, it also means that caution should be taken when asserting relationships between specific colours and emotional states because it is subject to large individual and even cultural differences [45] in response.

Because colour is clearly connected to emotions, the same can be expected to apply to the colour of light. In fact, in psychophysiological tests the colour of light has been shown to relate to the pleasantness and activating effects of light [185]. In a workplace study conducted in 2008 blue-enriched white light was found to improve subjective measurements of alertness and positive mood [32] compared to normal white light. In a laboratory study conducted in 2010 [45] both red and blue lights reduced sleepiness and improved momentary mood. These results indicate that light can directly affect mood and alertness and that the spectral composition of the light plays a role in these effects.

The parameters of light in the investigations of the relationship of light, emotions, and alertness are highly interesting to lighting researchers. So far the studies have concentrated on the impact of colour or the combination of colour and intensity of light on emotions, and the impact of the duration and timing of the light exposure on emotions still remains largely unknown. To be able to develop a broad understanding of the physiological mechanisms behind the relationship Plitnick et al. [45] suggest that the light stimulus should be defined independently of its apparent colour.

It is important to distinguish between the direct or indirect effects of light on emotions and hence on alertness, because that allows light to be used in different applications. A direct effect is when the light itself is able to induce emotion, such as a sunny sky that makes a person happy. An indirect effect is caused by light or lighting that modulates the response to another stimulus and therefore indirectly affects the mood and alertness. This is the case in theatre lighting.

Recently Vandewalle et al. [170] investigated the indirect effects of the light spectrum in the presence of vocal stimuli and demonstrated the acute influence of light on emotional brain processing. The next step would be to study whether light has direct effects on emotions by excluding all other

stimuli in laboratory conditions. Knowledge of the direct effects could be used in different light treatment applications to acutely enhance alertness by light. Indirect effects of ambient light could be applied to workplaces and other environments where there is a need to modulate the mood to retain a good level of alertness.

5.4 Proposal for how to test the model

As reported by Phan et al. 2001 [186], the amygdala has a specialised role in processing visual emotional stimuli compared to auditory or recall stimuli. Passive viewing, hence emotional visual stimuli without any cognitive task, activates the amygdala. However, to be able to create a conscious emotion the visual stimulus has to be strong [187]. If the emotional stimulus is too brief or too weak the amygdala might not direct it to the conscious thinking [188]. This has been shown to be the case with blinking light [189]. Therefore a wide range of irradiance values with a long enough exposure time should be used to achieve a broad understanding of the relationship of light and emotions.

To test the suggested model and to see whether light can evoke emotions that induce alertness, the following three-step study protocol is proposed. The protocol is published in Rautkylä et al. [24].

In the first step the subjects are exposed to different light stimuli, as well as darkness, and they are asked to rate their mood on the Visual Analogue Mood Scale (VAMS) [190] with the absence of any other stimuli or tasks. The purpose of the first step is to simply investigate how the light stimuli affect the emotional state. Using the same light stimuli as in the second step allows the results to be compared.

The second step consists of four subtests with darkness as the baseline, as illustrated in Figure 4. The first two subtests are done at scotopic lighting levels with blue and red light as the stimuli, and the following two at photopic lighting levels with blue and red light respectively. The lighting levels are chosen to be such that different retinal ganglion cells would be activated. Lall et al. [191] have suggested that at low scotopic lighting levels (irradiance of 10^7 photons/cm^2/s at 500 nm [192]) rods play a dominant role, probably signalling solely via the visual pathways. At moderate lighting levels (irradiance of 10^{12} photons/cm^2/s at 500 nm [192]) both rods and cones give input to non-image forming vision; however, light adaptation seems to limit the influence of cones. According to Lall et al. [191], melanopsin en-

codes high irradiances (irradiance of 10^{15} photons/cm^2/s at 500 nm [192]) and drives responses throughout most daylight.

In the third step the study protocol is advanced by four more subtests to investigate the gradient change from photopic to scotopic lighting level during a 4-minute light exposure and vice versa with both blue and red light. This simulates the change in lighting conditions that takes place naturally at dusk and dawn, respectively, and is needed to test whether such changes intensify the emotional and alerting effects of light stimuli.

Each subtest in steps 2 and 3 is recorded by using fMRI scanning sessions over the baselines and the light exposure. Self-ratings of sleepiness and emotion are measured verbally throughout the recording at 1-minute intervals. Sleepiness is measured with KSS [85] and emotion with a shortened version of the Profile of Mood States (POMS) [193]. Mood state is used as an indicator of emotion [177] because measuring emotional reaction is complex.

From the fMRI scans the activation and the deactivation of the amygdala, the SCN, and the LC are analysed as a function of time. The activation patterns have the potential to reveal three things: first, whether there is any order of activation and therefore a causal relationship between the light induced activation of the amygdala or the LC and the increase in experienced levels of emotions or alertness; second, whether the amygdala and the SCN are activated simultaneously or in turn depending on the light stimulus, and third, whether different light stimuli induce non-image-forming responses that outlast the exposure and decline slowly, or classical image-forming responses that cease very shortly after the stimulation [47].

In addition, if low and high irradiances of light activate different retinal cells, as suggested by Lall et al. [191], by looking at the responses to different irradiances it is possible to learn more about projections from the three photoreceptors to the brain areas in question.

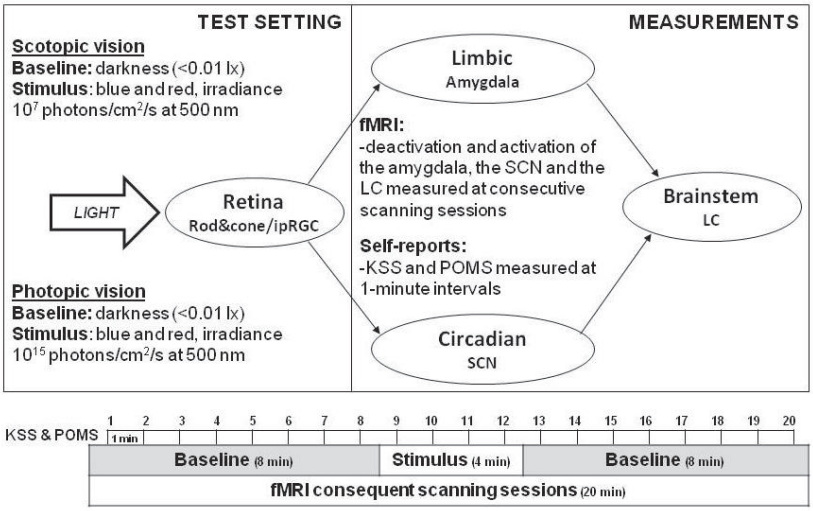

Figure 4. *The second step in the experimental design on how to test the effects of light on alertness via the amygdala. It consists of four 20-minute subtests, each subtest containing a 4-minute exposure to a selected light stimulus in between two 8-minute baseline lighting conditions (darkness). The selected light stimuli are blue and red light from the scotopic and photopic range. Each subtest is recorded with fMRI. The activation and the deactivation of the amygdala, the SCN, and the LC by function of time are compared to the self-rated sleepiness and mood. They are measured at 1-minute intervals by the KSS and POMS. In the third step the study protocol is advanced by four more subtests to investigate the gradient change from photopic to scotopic lighting level. Adapted from Rautkylä et al. [24].*

6 PRACTICAL STUDIES

6.1 Study I: Experiment on the effect of the correlated colour temperature, illuminance, and timing of the light exposure on daytime alertness

6.1.1 Experimental setup

The primary aim of Study I was to examine the effect of the correlated colour temperature (T_{cp}) of artificial light on students' alertness in a natural lecture environment when other possible external factors were taken into account. On the basis of previous field studies on the relationship of the T_{cp} of light and the daytime alertness [31, 32] it was hypothesised that high-T_{cp} light induces a greater effect on alertness during daytime working hours than low-T_{cp} light. The secondary aim was to investigate whether the subjects' reaction to light of a certain T_{cp} is dependent on the time of year or day. Because in addition to the overall light exposure, the spectral composition of daylight exposure has been found to vary during the day and with the season [194], it was hypothesised that the T_{cp} of the artificial light would have a different meaning and effect on human beings at different times of the year and day.

The study and its results have been previously published in Rautkylä et al. [25]. The discussion here will be based on that research paper.

The study took place at Helsinki University of Technology, Finland, in two stages; the first stage in late spring, in May, and the second in late autumn, in November. This was to observe the seasonal effects on the study results. From now on the two stages will be referred as the spring study and the autumn study. The number of daylight hours was approximately 12 hours in the spring study and 9 hours in the autumn one.

All experiments were conducted in lecture environments with university students as subjects. They were carried out while the subjects were attending university courses to make the test setting as natural as possible for

them. Both studies lasted 6 weeks, during which 10 lectures took place. Lecturers, course content, and lecture session topics varied between the different sessions studied. The subjects were not informed that this was a study of lighting. They were told that the study was about environmental factors in a learning situation. The lecturer was aware of the study but did not take part in it.

In the spring a total of 16 university students participated in the study (all male; age range 22-27 years; mean 24 years). On the basis of the Morningness-Eveningness questionnaire (MEQ) [195], 6 subjects of the 16 were categorised as “morning type” and 2 subjects as “evening type” by their chronotype. Eight subjects were neither evening nor morning type and were thus classified as “neither type”. In the autumn a total of 138 students participated in the study (17 female, 121 male; age range 19-30 years; mean 22 years). By chronotype grouping, 33 were “morning type”, 22 “evening type” and 83 “neither type”. The subjects were different in the spring and autumn studies and no student could take part in both studies.

One answer sheet was provided per subject per lecture attended. Because attending university lectures is voluntary, the number of participants decreased in each study as the course progressed. On average, each subject took part in 46% of the lectures in the spring (73 returned answer sheets) and 22% of the lectures in the autumn (309 answer sheets).

The experiment room was a 620-m² amphitheatre-shaped lecture hall equipped with 69 OfficeNova 240TCS luminaires with D6 optics by Philips. In each luminaire there were two different 49-W light sources: a T5 lamp with T_{cp} of 4,000 K ($R_a > 80$) and a Philips ActiViva lamp with T_{cp} of 17,000 K ($R_a > 80$). Both types of lamps were dimmable. The Helvar DIGIDIM lighting control system used a digital addressable lighting interface protocol (DALI). Because of the dark surfaces the T_{cp} provided by the 4,000-K fluorescent light source was actually 3,870 K and the T_{cp} provided by the 17,000-K light source was 12,370 K. The spectral power distributions of the two lighting environments, measured with an Ocean Optics HR400 High-resolution Spectrometer, are presented in Figure 5. As in [25], the lighting environments will be referred here as the 4,000-K and 17,000-K environments according to the light sources. The environments are shown in Figure 6.

The two light sources were used randomly in turn so that in half of the 10 lectures of each experiment the lighting was provided by the 4,000-K fluorescent lamps and in half of them by the 17,000-K fluorescent lamps.

The lighting conditions were alike except for the light spectrum. No daylight was allowed in the lecture hall.

The illumination levels and illumination distribution were set to be suitable for visual tasks, such as reading the lecture slides and taking notes. On the basis of a pilot study the horizontal illuminance in the hall was set to 800 lx (measured at 0.8 m in all studies) in the first study. However, feedback from the subjects indicated the need to increase the illumination level. Hence, in the second study the illuminance was set to 1,000 lx.

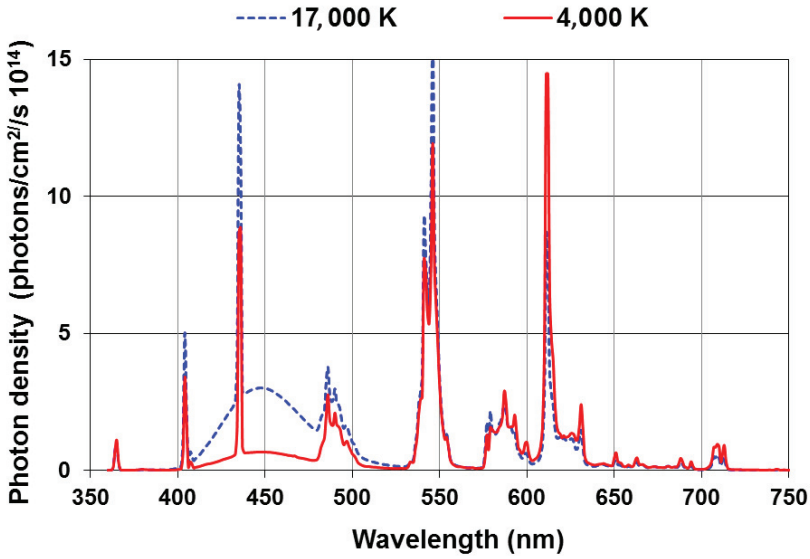

Figure 5. *The spectral power distribution of the light sources. The light spectra of the two lighting conditions was measured in the middle of the hall with the maximum luminous output of the lamps (measured at 0.8 m, i.e. table height). The T_{cp} provided by the 4,000-K fluorescent light source was 3,870 K and the T_{cp} provided by the 17,000-K light source was 12,370 K. Dimming the lights did not change the T_{cp} significantly.*

Figure 6. *A view of the lecture hall in the 4,000-K lighting environment (left) and in the 17,000-K lighting environment (right) in the autumn study. In the spring study the view was similar but the illuminances were 200 lx lower.*

The luminance distribution was measured using a Nikon Coolpix 8400 digital camera equipped with a Nikon FC-E9 fisheye lens. The images that were acquired were analysed using the PHOTOLUX 2.1 software [196], which has a calibration profile for the camera used. Luminance distributions are presented in Figure 7.

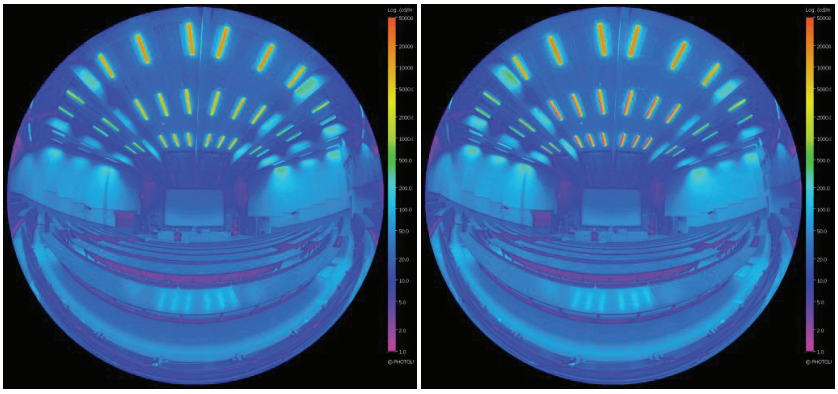

Figure 7. *Luminance distributions of the light sources in the 4,000-K lighting environment (left) and in the 17,000-K lighting environment (right) in the autumn study. The maximum value was 50,000 cd/m² (orange colour) on the logarithmic scale. In the spring study the luminance distributions were similar but the maximum value was 20,000 cd/m².*

Both experiments included tests at two different times of the day, morning and afternoon. In the first stage in the spring, the lectures took place between 9:15 and 10:45 and 12:15 and 13:45. For the second stage the lectures were chosen so that there would be a longer time period between them. Therefore the lectures in autumn were held between 8:15 and 9:45 and 14:15 and 15:45. The morning and afternoon lectures were held on different weekdays to avoid order effect with different light sources. Each lecture was 90 minutes, with no breaks. The test conditions in the spring and autumn studies are presented in Table 2.

Table 2. *The test conditions in the spring and autumn studies. The lighting conditions were improved after the feedback given by the subjects in the spring study. In both studies 10 experiment lectures were held during 6 weeks. Five of them were held in the morning and five of them in the afternoon.*

	Spring study	Autumn study
Number of lectures	10	10
Number of subjects	16	138
Time of experiment	9:15-10:45 or 12:15-13:45	8:15-9:45 or 14:15-15:45
T_{cp} of the light source	4,000 K or 17,000 K	4,000 K or 17,000 K
Illuminance	800 lx	1 000 lx
General uniformity	0.7	0.8

6.1.2 Methods

At the beginning of both studies the subjects were assigned a personal identifier and they completed a pre-questionnaire which linked the age, sex, and the identifier that the subjects used throughout the entire study. One essential part of the pre-questionnaire was a Morningness-Eveningness questionnaire [195]. This questionnaire was used to determine the chronotype of the person. Because of the nature of the study (a random sample of students as subjects, a real-life test setting) the subjects were not asked to follow a certain sleep-wake routine throughout the study.

The room temperature and the carbon dioxide concentration (CO_2) in the lecture hall were measured at the beginning and at the end of each lecture in both studies. The actual study was carried out with a two-part questionnaire that was completed before and after each lecture. During the lecture no questionnaires were completed.

The first part consisted of subjective self-ratings for sleepiness and questions about the use of stimulants, such as coffee, energy drinks etc, and eating before the lecture. The sleepiness was evaluated on the Karolinska sleepiness scale [84]. In the second study the subjects were also asked about their movements within the past hour prior to the lecture to collect data about the lighting conditions the subjects had been exposed to immediately preceding the lecture. For the same reason the illuminance in the corridor and outside the building were measured before the lecture in the second study.

The second part of the questionnaire was completed immediately after the lecture. The subjects self-rated their sleepiness again, as well as giving their rating on how the lecture had felt in terms of their interest in the lecture. This was done to study the effect of the lecturer, course content, and lecture session topic on alertness. In the second questionnaire there were also questions about environmental factors, such as air draughts and heat and noise levels.

After both studies in autumn the subjects were asked to give free, voluntary feedback on the lighting conditions. A part of the spring feedback was used to improve the lighting conditions in the autumn study.

6.1.3 Results

To investigate the effect of lighting conditions on students' alertness throughout the entire course, all observations were used in the analysis in-

stead of choosing, for example, the lecture with the greatest amount of participants, i.e. the largest sample.

The individuals were in different states of alertness when they arrived at the lecture. To be able to compare the effect of the T_{cp} between subjects and lectures, the effect was evaluated in terms of the changes in alertness instead of the absolute values of alertness at the beginning and at the end of the lecture. Therefore the change from 1 to 4 was considered the same as the change from 5 to 8; hence in both cases the alertness decreased by three steps, regardless of whether it remained on the "alert" or the "sleepy side" of the Karolinska sleepiness scale.

The change in self-rated alertness was measured by comparing the first evaluation at the beginning and the second evaluation at the end of the lecture. The significance of the change was determined by using a two-tailed paired Student's *t*-test for means and its probability value P_t. This *t*-test is a special case of analysis of variance between groups that assesses whether the means of two groups are statistically different.

The individual changes in alertness in the spring and in the autumn, in morning or afternoon lectures, and in 4,000-K or 17,000-K lighting environments, are presented in Table 3. The individual changes were averaged into mean values, which are also shown in Table 3. As can be seen from the probability values in the column "P_t", the change did not prove to be significant in any of the four lighting conditions ($P_t > 0.05$) in the spring. As for the autumn, the change proved to be significant ($P_t < 0.05$).

Table 3. *The change in self-rated alertness during the lectures in different lighting conditions. The headers [-8, 4] indicate how much the alertness changed. If the change < 0, the alertness decreased, if the change > 0, the alertness increased, if the change = 0, the alertness did not change. The numbers in the columns [-8, 4] stand for the number of responses. T_{cp} = correlated colour temperature, N = number of subjects, SD = standard deviation, P_t = two-tailed probability value; if $P_t < 0.05$, the change in alertness is significant.*

Timing	T_{cp} (K)	N	-8	-7	-6	-5	-4	-3	-2	-1	0	1	2	3	4	Mean	SD	P_t
Spring – morning	**4,000**	28					1		6	2	11	5	3			-0.25	1.46	0.372
	17,000	10							3	2		4	1			-0.20	1.55	0.693
Spring – afternoon	**4,000**	15				1			3		5	4	2			-0.20	1.86	0.683
	17,000	20					1	2	3	4	3	3	3	1		-0.40	1.93	0.366
Autumn – morning	**4,000**	139		2	1	3	13	14	33	25	29	6	10	2	1	-1.32	1.97	0.000
	17,000	34				1	4	4	10	5	5	3	1		1	-1.44	1.93	0.000
Autumn – afternoon	**4,000**	50	1		1	6	9	5	10	6	9	1	1		1	-2.28	2.24	0.000
	17,000	86			2	2	2	5	21	20	24	3	5	1	1	-1.01	1.76	0.000

In the spring the alertness of the students decreased by only 0.2–0.4 point on average. In autumn in the morning lecture the alertness decreased on average by 1.3 points with T_{cp} = 4,000 K, and 1.4 points with T_{cp} = 17,000 K. In the afternoon the decreases were 2.3 points and 1.0 point respectively. The change in alertness with each lighting condition is presented in Figures 8 and 9.

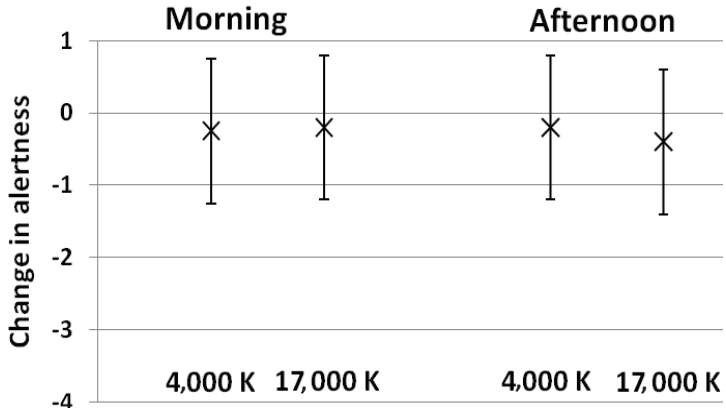

Figure 8. *The mean change in alertness in the spring. The starting value at the beginning of the lecture is 0 and "x" marks the final value after the change. Vertical bars indicate standard deviation.*

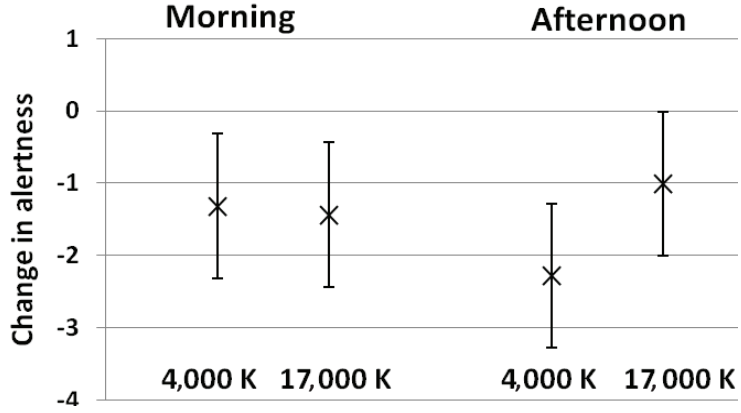

Figure 9. *The mean change in alertness in the autumn. The starting value at the beginning of the lecture is 0 and "x" marks the final value after the change. Vertical bars indicate standard deviation.*

The relationship between the T_{cp} and the change in alertness was measured with Pearson's chi-square test, which is appropriate for assessing associations of categorical variables. This was done for each lighting condition separately.

In the spring no difference was detected in the change in alertness that could be explained by the light source used. That applied to both the morning and the afternoon lectures, as can be seen in Table 4. Table 4 is based on the alertness data presented in Table 3. As for the autumn study, a significant difference was detected in the change in alertness, depending on whether light of low T_{cp} or high T_{cp} was used ($P_{cs} = 0.019 < 0.05$). Compared to low-T_{cp}, exposure to light of high T_{cp} helped the students to retain their alertness better in the afternoon hours. In the morning lectures in the autumn the T_{cp} of the light had no effect on the changes in alertness ($P_{cs} = 0.899 > 0.05$).

Table 4. *The effect of the T_{cp} on the changes in alertness in different lighting conditions. N = number of subjects, P_{cs} = Pearson's chi-square probability value; if $P_{cs} < 0.05$, T_{cp} correlates significantly with the changes in alertness.*

Timing	T_{cp} (K)	N	P_{cs}
Spring - morning	**4,000**	28	0.206
	17,000	10	
Spring - afternoon	**4,000**	15	0.316
	17,000	20	
Autumn - morning	**4,000**	139	0.899
	17,000	34	
Autumn - afternoon	**4,000**	50	0.019
	17,000	86	

To verify the results of the effects of the T_{cp} on afternoon alertness, the factoring of the lecture content, prior lighting conditions, use of stimulants, consumption of food, chronotype of the subject, and environmental factors in the results was analysed. This was done by creating a contingency table (also known as cross-tabulation) from the T_{cp} and the change in alertness and adding layers to it. Fisher's exact test was used in the analysis of contingency tables, because the sample sizes were too small to be able to run a reliable Pearson's chi-square test. (Note that in reference [25] Pearson's chi-square test was used. Both tests give similar results. However, Fisher's test is exact and can therefore be used regardless of the sample characteristics, while Pearson's chi-square test provides an approximation and is only reliable with large samples.)

In order for the correlation of the T_{cp} and the change in alertness to apply despite the factors mentioned, the Fisher's P_f values had to be within the

significance level of 0.05 with each added layer. These subject-related variables, which possibly influence the relationship of the T_{cp} and change in alertness, are presented in the contingency tables in Table 5.

Table 5. *Subject-related variables factored in the correlation of the T_{cp} and the change in alertness in the autumn afternoons. The headers [-8, 4] indicate how much the alertness changed. If the change < 0, the alertness decreased, if the change > 0, the alertness increased, if the change = 0, the alertness did not change. The numbers in the columns [-8, 4] stand for the number of responses. P_f = Fisher's exact test probability value; if P_f < 0.05, the variable did not influence the correlation. In "Lecture" 1 = "not interesting at all", 5 = "very interesting".*

Variable	Rating	T_{cp} (K)	N	-8	-6	-5	-4	-3	-2	-1	0	1	2	3	4	P_f
Lecture	**1**	**4,000**	8			1		2	1		3	1				0.293
		17,000	13			1		3	2	5	1	1				
	2	**4,000**	11	1			3	1	1	2	1		1		1	0.016
		17,000	29		1	1		1	8	3	11	1	3			
	3	**4,000**	14			2	1	1	6	2	2					0.390
		17,000	25		1		1		8	7	6	1		1		
	4	**4,000**	10		1	3	2	1	1	2						0.014
		17,000	15					1	3	2	6		2		1	
	5	**4,000**	7				3		1		3					0.044
		17,000	4				1			3						
Chronotype	**Morning**	**4,000**	19	1		4	3	1	5	2	1	1	1			0.013
		17,000	18		1		1	1	2	5	8					
	Neither	**4,000**	19		1	1	5	3	4		5					0.006
		17,000	53		1	1	1	4	17	13	8	3	3	1	1	
	Evening	**4,000**	12			1	1	1	1	4	3				1	0.335
		17,000	15			1			2	2	8		2			
Prior exposure	**Outdoor**	**4,000**	31		1	3	6	3	9	2	6	1				0.017
		17,000	39			1	1	1	8	10	10	3	4		1	
	Indoor	**4,000**	19	1		3	3	2	1	4	3		1		1	0.017
		17,000	47		2	1	1	4	13	10	14		1	1		
Stimulants	**NO**	**4,000**	24		1	3	5	2	5	5	1	1			1	0.009
		17,000	50		2	1	1	4	14	10	15	1	2			
	YES	**4,000**	26	1		3	4	3	5	1	8		1			0.050
		17,000	36			1	1	1	7	10	9	2	3	1	1	
Food	**NO**	**4,000**	16		1	3	4		3	2	3					0.172
		17,000	25			1	1	1	5	6	9	1	1			
	YES	**4,000**	34	1		3	5	5	7	4	6	1	1		1	0.094
		17,000	61		2	1	1	4	16	14	15	2	4	1	1	

On average the amount of interest the subjects had in the lecture was 2.74 ± 1.17 standard deviation (SD), which referred to a fairly neutral feeling on a scale from 1 “not interesting at all” to 5 “very interesting”. The statistical analysis showed that it did not affect the correlation between the T_{cp} and the change in alertness but the correlation applied independently of the lecture (P_f = (0.014, 0.016 and 0.044) < 0.05). In addition, Fisher’s exact test showed that the relationship between the T_{cp} and the change in alertness did not depend on the subject’s chronotype. Instead, the reaction to the colour temperature appeared to be similar in the majority of the chronotype categories (P_f = (0.013 and 0.006) < 0.05).

P_f values for prior exposure to light were found to be below 0.05 (P_f = 0.017 < 0.05), indicating that the correlation between the T_{cp} and the change in alertness was independent of the lighting conditions that the subjects were exposed to prior to the lecture. However, how long each subject had spent in the previous lighting conditions was not recorded. Therefore, to be able to fully exclude the effect of prior exposure on the changes in alertness during the test, the lighting conditions should have been investigated more thoroughly.

Using stimulants, such as coffee or energy drinks, did not prove to have any effect on the results (P_f = (0.006 and 0.013) < 0.05). In contrast, eating before the lecture was found to influence the correlation, so that those subjects who had eaten before the lecture were not found to react to the high T_{cp} (P_f = (0.172 and 0.094) > 0.05).

The room temperature and the CO_2 concentration were lower at the beginning and increased towards the end of the afternoon lectures in the autumn. The lowest and the highest value, as well as the mean value during each lecture, are presented in Figure 10.

The increase in the CO_2 concentration had a strong, positive Pearson’s correlation with the number of subjects attending the lecture (r = 0.975, P_r = 0.009 < 0.05), meaning that the increase in the CO_2 concentration was probably caused by the students. The concentration was the highest in the lecture with the highest number of subjects; however, it never rose above 800 ppm, a value often considered to be one at which the air starts to feel stuffy [197]. The room temperature remained between 20 °C and 22 °C throughout the test period and its variation was hardly influenced by the number of subjects (r = 0.271, P_r = 0.402 > 0.05). The variation in room temperature was justified by the use of heat-creating electronic devices.

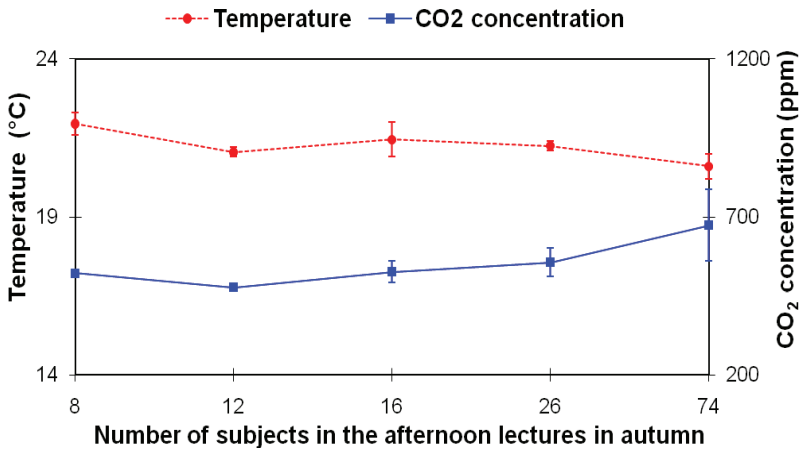

Figure 10. *Mean room temperature (left y-axis) and mean CO_2 concentration (right y-axis) for each afternoon lecture in the autumn presented in the order from the lowest number of subjects to the highest (x-axis). The values were recorded twice during each lecture: at the beginning and at the end. The values were lower at the beginning and increased towards the end of the lecture. The lowest and the highest values during each lecture are marked with vertical bars.*

In subjective assessment of the environmental factors the majority gave the noisiness, the heat, the draughtiness, the dryness of the air, the dustiness, the smelliness, and the air quality a rating of 3, which referred to a neutral feeling on a scale from 1 “too hot” to 5 “too cold”. As presented in Tables 6 and 7, the statistical analysis performed with Fisher’s exact test showed that the environmental factors in question affected the correlation between the T_{cp} and the change in alertness ($P_f > 0.05$) so that when the environmental factors were rated neutral, the correlation was likely to exist.

In the free feedback given at the end of the studies, the 4,000-K lighting environment did not provoke comments. As for the 17,000-K environment, the light was found strange and too bright. One person felt as if they were in a hospital in the 17,000-K lighting environment.

Table 6. *Environmental variables (noisiness, heat, draughtiness, dryness) factored in the correlation of the T_{cp} and the change in alertness in the autumn afternoons. The headers [-8, 4] indicate how much the alertness changed. If the change < 0, the alertness decreased, if the change > 0, the alertness increased, if the change = 0, the alertness did not change. The numbers below the headers [-8, 4] stand for the number of responses. N.A = correlation cannot be calculated. P_f = Fisher's exact test probability value; if P_f < 0.05, the variable did not influence the correlation.*

Variable	Rating	T_{cp} (K)	N	-8	-6	-5	-4	-3	-2	-1	0	1	2	3	4	P_f
Noisiness	**1**	**4,000**	1					1								1.000
Mean 3.02±0.58 SD		**17,000**	1								1					
1=too noisy	**2**	**4,000**	4			1	1		1	1						0.748
5=too quiet		**17,000**	10				1	1	2	1	3		1	1		
	3	**4,000**	34	1		5	6	2	6	4	8	1			1	0.008
		17,000	66		2	1	1	4	16	17	18	3	3		1	
	4	**4,000**	10		1		1	2	3	1	1		1			0.834
		17,000	9			1			3	2	2		1			
	5	**4,000**	1				1									*N.A*
		17,000	0													
Heat	**1**	**4,000**	0													*N.A*
Mean 3.23±0.61 SD		**17,000**	0													
1=too hot	**2**	**4,000**	1						1							1.000
5=too cold		**17,000**	7		1	1			1	1	1		2			
	3	**4,000**	30	1		1	4	3	8	5	6	1	1			0.377
		17,000	62		1		1	5	18	13	18	2	3	1		
	4	**4,000**	14		1	5	3	1		1	3					0.071
		17,000	15			1	1		2	5	5	1				
	5	**4,000**	4				2	1	1							0.600
		17,000	1							1						
Draughtiness	**1**	**4,000**	8			2	3	1	1		1					*N. A*
Mean 3.36±1.16 SD		**17,000**	0													
1=too draughty	**2**	**4,000**	8		1	2	1	2			2					0.128
5=too stuffy		**17,000**	16			2		1	3	5	4	1				
	3	**4,000**	14	1		2	2	1	3	3	1		1			0.062
		17,000	28					1	8	7	9	1	2			
	4	**4,000**	11				2	1	4		2	1			1	0.590
		17,000	24		2		2	1	5	3	6	1	3	1		
	5	**4,000**	9				1		2	3	3					0.802
		17,000	18					2	5	5	5				1	
Dryness	**1**	**4,000**	1							1						*N.A*
Mean 2.76±0.55 SD		**17,000**	0													
1=too dry	**2**	**4,000**	15		1	2	5	2	2	1	1		1			0.016
2=too humid		**17,000**	20			1		1	6	4	7		1			
	3	**4,000**	32	1		4	4	3	7	4	7	1			1	0.150
		17,000	65		2	1	2	4	15	16	17	3	3	1	1	
	4	**4,000**	0													*N.A*
		17,000	1										1			
	5	**4,000**	2						1		1					*N.A*
		17,000	0													

Table 7. *Environmental variables (dustiness, smelliness, air quality) factored in the correlation of the T_{cp} and the change in alertness in the autumn afternoons. The headers [-8, 4] indicate how much the alertness changed. If the change < 0, the alertness decreased, if the change > 0, the alertness increased, if the change = 0, the alertness did not change. The numbers in the columns [-8, 4] stand for the number of responses. N.A = correlation cannot be calculated. P_f = Fisher's exact test probability value; if $P_f < 0.05$, the variable did not influence the correlation.*

Variable	Rating	T_{cp} (K)	N	-8	-6	-5	-4	-3	-2	-1	0	1	2	3	4	P_f
Dustiness	**1**	**4,000**	0													*N.A*
Mean 3.34±0.69 SD		**17,000**	0													
1=too dusty	**2**	**4,000**	4			1			1	1	1					0.891
5=too clean		**17,000**	7					1	2	1	3					
	3	**4,000**	30	1		4	4	3	6	4	5	1	1		1	0.173
		17,000	44		2	1	1	2	9	9	13	2	4	1		
	4	**4,000**	14		1	1	4	2	2	1	3					0.055
		17,000	31			1	1	2	8	10	8	1				
	5	**4,000**	2				1		1							1.000
		17,000	4						2				1		1	
Smelliness	**1**	**4,000**	8			2	3	1	1		1					*N. A*
Mean 3.33±0.69 SD		**17,000**	0													
1=too smelly	**2**	**4,000**	1					1								0.556
5=too neutral		**17,000**	8			1	1		2	1	2			1		
	3	**4,000**	31	1	1	4	5	3	6	4	5	1	1			0.017
		17,000	50		2	1		2	11	13	16	2	3			
	4	**4,000**	15			2	4	1	4		3				1	0.051
		17,000	23				1	2	6	6	5	1	2			
	5	**4,000**	3							2	1					0.429
		17,000	5					1	2		1				1	
Air quality	**1**	**4,000**	2								2					*N.A*
Mean 3.27±0.78 SD		**17,000**	0													
1=too stuffy	**2**	**4,000**	4			1	2		1							0.110
5=too fresh		**17,000**	14		1			1	7	2	2		1			
	3	**4,000**	22	1		3	3	3	6	2	3				1	0.086
		17,000	39		1	2	1	2	5	12	11	2	1	1	1	
	4	**4,000**	21		1	2	2	2	3	3	6	1	1			0.547
		17,000	30				1	2	9	6	8	1	3			
	5	**4,000**	3				2			1						0.500
		17,000	1								1					

6.1.4 Discussion

Prior to the study it was hypothesised that high-T_{cp} light would have a greater effect on alertness during daytime working hours than low-T_{cp} light. This was partly shown to be true. In the spring the T_{cp} of the light exposure did not have an effect on the alertness, but in the autumn, and only in the afternoon hours, it did. The fact that it applied only in the autumn and only in the afternoon lectures indicates that the second hypothesis was true. Hence, the T_{cp} of the artificial light had a different effect on humans at dif-

ferent times of the year and day. The reasons behind the seasonal differences, as well as the differences between the morning and the afternoon lectures, are discussed below.

It has been shown that the overall light exposure is significantly higher in summer months (April–August) than in winter (November–February) ones [194]. This was verified by the measurements, which showed that in the spring study in April the outdoor illuminance was approximately 4000 lx prior to the morning lecture (9:15-10:45) and 30,000 lx prior to the afternoon lecture (12:15-13:45) measured vertically at 1.6 m, i.e. eye level in open space. In the autumn study in November, the outdoor illuminance prior to the morning lecture (8:15-9:45) was below 100 lx as a result of the earlier timing of the lecture and later sunrise. The afternoon lecture was held later than in spring (14:15-15:45) and the outdoor illuminance was approximately 2,000 lx. Therefore the intensity of the daylight that the subject was exposed to prior to the test period depended on the season and was higher in the spring study compared to the study in the autumn.

The fact that in autumn alertness decreased significantly during the lectures, which was not seen in the spring, indicated that the lack of daylight related to the season might have affected the coping during the lecture as a result of decreasing alertness. Because the indoor light conditions were different in terms of their illuminance in the two stages, it is unfortunately not possible to compare the results from the spring and autumn and verify the role of daylight in the changes in alertness in the study. The small sample size in spring also causes a lack of statistical power in the spring cohort. However, there is evidence that the whole light history plays a role in the determination of the level of alertness, not only the momentary artificial lighting during the lecture [198].

The differences between the morning and afternoon lectures in the autumn can be explained by the hormonal activity of humans, which varies at different times of the day from the morning to the afternoon. According to the previous studies, cortisol levels are high and body temperature low in the morning. In the afternoon the levels are other way round [199] and work performance decreases between 1 pm and 4 pm [200]. This dip in performance during the midafternoon hours is often referred to as the post-lunch dip effect.

Because of the post-lunch dip, the alertness decreased more in the late afternoon lectures than in the morning ones in the autumn. However, that only applied to the lectures with the 4,000-K lighting environment. When a

17,000-K light source was used the dip did not occur. Instead, using 17,000 as the colour temperature of the light source helped the students to retain their alertness better in the afternoon lectures.

Why the post-lunch dip did not occur in the spring can be explained by the timing of the lectures. In the autumn the afternoon lecture was held late in the afternoon, at 14:15-15:45, when the post-lunch dip appears to be strong. In the spring the lecture was held at 12:15-13:45, hence close to noon and before the actual dip time. The earlier timing of the afternoon lecture in the spring can well explain why no effect of the T_{cp} on the changes in alertness was seen in the afternoon lectures in the spring; T_{cp} played a role only during the actual post-lunch dip time.

Part of the explanation of why such an effect was not seen in the spring study can also relate to the seasonal light history. Because during winter evenings the relative contribution of blue light to the daylight spectrum has been found to be significantly lower than in summer evenings [194], it is possible that in the spring study the subjects did not need a blue light boost but in the autumn study the blue-enriched 17,000-K light helped to supplement the lack of natural blue light.

These results are in line with the claim that cool light stimulates and activates the body [201]. They indicate that it might be possible to control the alertness by altering the light parameters during the day. With that they support the suggestion of Van Bommel to use dynamic lighting that allows the colour of the light, as well as its intensity, to be changed at different moments during the day [202].

It has been suggested that the post-lunch dip phenomenon can occur even when the individual has not had lunch [203]. However, in this study a significant correlation was found between those who had had lunch prior to the lecture and the way the T_{cp} affected their level of alertness. In fact, eating was found to promote tiredness in the afternoon hours, reducing the alerting effect of the light.

It has been proven that e.g. caffeine reduces physical fatigue and restores mental alertness [203]. Therefore it was expected that stimulants would mask the effect of the T_{cp}. However, stimulants were not shown to affect the correlation between the T_{cp} and the changes in alertness. In further studies the questionnaire should be improved to provide information about the normal caffeine consumption of the subject. In this study it was not known whether the subject was e.g. deeply addicted to caffeine and needed a

certain amount to gain the stimulating effects, or whether he had perhaps missed his daily portion and was affected by its absence.

6.2 Study II: Experiment on the suitability of research methods for light-induced alertness research

6.2.1 Experimental setup

The aim of Study II was to examine in practice how well the methods used for measuring alertness are able to represent the light-induced changes in alertness. The methods were chosen for the practical testing on the basis of their potential value for alertness research and on the available resources. Together with the theoretical evaluation in Chapter 4, the study was meant to provide help in choosing suitable methods for assessing light-induced daytime alertness. One should note that the purpose of the study was not to investigate the effects of different light exposures on alertness, although the presence of the effects was analysed in order to gain a better understanding of the possible correlations.

In the study pupil size, heart rate, and the skin's electro-conductivity were measured. These objective measurements were compared to the KSS, a validated subjective method for sleepiness research [85]. On the basis of the previous studies discussed in Chapter 4, all the above-mentioned methods have been considered to be objective measurements of vigilance [110], sleepiness, or alertness [111]. Therefore it was hypothesised that they would correlate with the KSS ratings.

The study and its results have been previously reported in a peer-reviewed conference paper [26] presented at Experiencing Light 2009, an International Conference on the Effects of Light on Wellbeing held in Eindhoven, the Netherlands.

The study consisted of laboratory tests that took place in the spring in the Lighting Unit of Helsinki University of Technology, Finland. Each test session took 2 hours between 15:00 and 17:00. In the study the subjects were exposed to conditions of darkness and light, as illustrated in Figure 11.

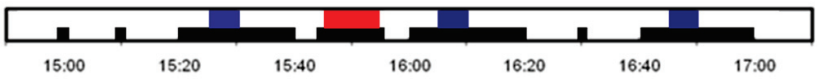

Figure 11. *One 2-hour test session between 15:00 and 17:00. Black = recording period of the pupil, white = time in darkness, blue = exposure time to quasimonochromatic blue light, red = exposure time to broadband orange-red light.*

Between the recording periods the subjects were free to stretch their legs by moving around in the experimental room, which was light-proofed with dark curtains. The quasimonochromatic "standard 5-mm" blue light-emitting diodes (LEDs) used in the study had a peak wavelength of λ_{max} = 454 nm and a half-bandwidth of hbw = 26 nm and they provided corneal illuminance of 40 lx. The broadband orange-red light that was used between the blue light pulses was a mixture of two types of Luxeon Star III LEDs: red (λ_{max} = 633 nm, hbw = 20 nm) and amber (λ_{max} = 602 nm, hbw = 14 nm). The corneal illuminance provided by this broadband red-orange light was 83 lx. The spectral power distributions of the light sources are presented in Figure 12.

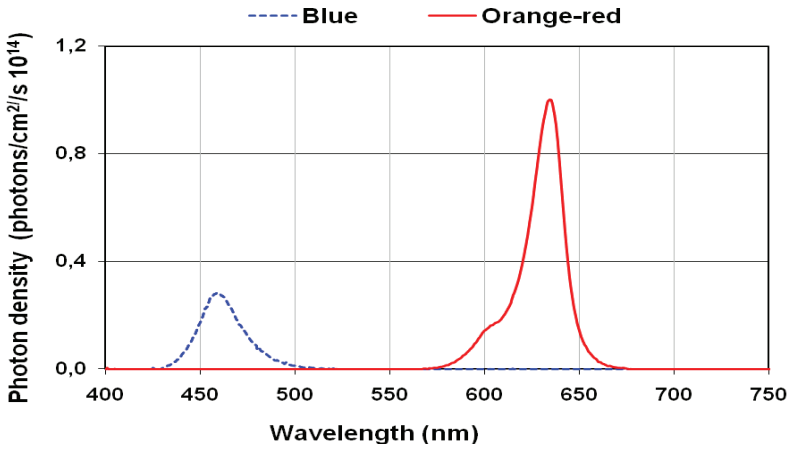

Figure 12. *The spectral power distribution of the LED light sources.*

All the LEDs were mounted on a Goldman perimeter, a piece of equipment commonly used for visual field examinations. They provided a uniform light distribution, as presented in Figure 13. The luminance distribution was measured and analysed using the same Nikon Coolpix 8400 digital camera and PHOTOLUX 2.1 software as in Study I. Luminance distributions are presented in Figure 14.

Twelve healthy young volunteers (5 women and 7 men; age range 20-28; mean age 24.4 years) and nine healthy older volunteers (5 women and 4 men; age range 50-62; mean age 56.6 years) participated in the study. Before the study the subjects' chronotypes were assessed using the MEQ [195]. Extreme chronotypes that scored below 31 ("definitely evening type") or above 69 ("definitely morning type") were excluded from the study. The chronotypes were lower in the younger group than in the older one (score

range, mean score ± SD: 32-56, 47.3 ± 7.6 points vs. 53-63, 57.1 ± 3.3 points; *t*-test: P_t = 0.001). The duration of sleep before the study did not differ significantly between the groups (duration range, mean duration ± SD young: 6:30-9:30, 7:56 ± 0:59 hours vs. older: 5:35-9:30, 7:36 ± 1:05 hours; *t*-test: P_t = 0.240). The subjects were instructed to avoid alcohol, coffee, tea, and other drinks containing caffeine for 3 hours prior to the study.

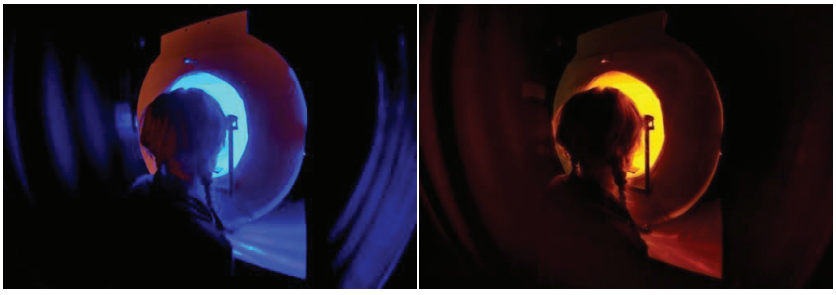

Figure 13. *The test setting. The light exposure was provided by a Goldman perimeter (diameter 60 cm) equipped with a chin rest. Each session included three periods with quasimonochromatic blue light (left) and one period with broadband orange-red light (right).*

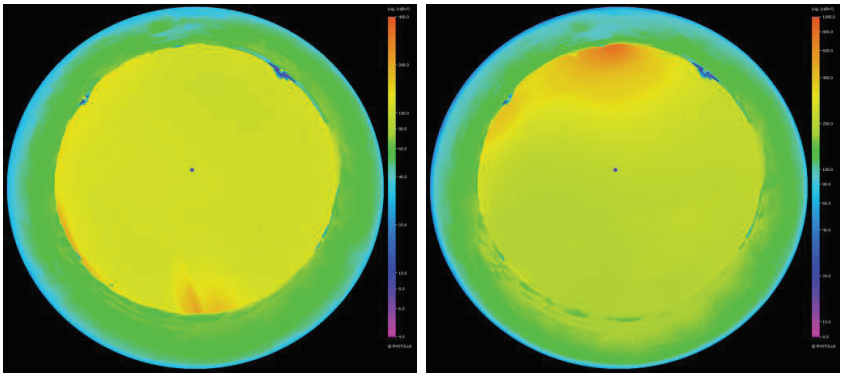

Figure 14. *Luminance distribution of the Goldman sphere with the blue LEDs (left) and with the red-orange LEDs (right). The dark spot at the centre of the sphere had the pupil camera mounted on it.*

6.2.2 Methods

The pupil size of the subject was recorded during the periods illustrated in Figure 11. The idea was to investigate whether the pupil size remains stable or changes rapidly. Those changes are called “hippus” or “fatigue waves” and they are used as an indicator of whether the person is alert. The pupil size was recorded using a Unibrain Fire-I OEM (Unibrain Inc., San Ramon, California, USA) digital monochrome board camera with a resolution of 320 x 240 and a sample rate of 30 Hz. The camera was mounted at the back

of the Goldman perimeter at a distance of 30 cm from the subject's eye. The camera was equipped with a telephoto lens and an infra-red bandpass. The minimum focusing distance was reduced with home-made extension tubes that also made the depth of the field narrower.

The pupil was illuminated with infrared LEDs (Everlight HIR204/H0, λ_{max} = 850 nm, hbw = 45 nm, beam angle = 60°) positioned off-axis close to the eye. The pupil size was to be determined from a recorded uncompressed video file using an edge-based segmentation program under Matlab (Mathworks, USA). The corneal irradiance of the infrared LEDs was below the safety levels of 10 mW/cm² for chronic infrared exposure at λ = 720-1 400 nm as defined by the International Commission on Non-Ionising Radiation Protection (ICNIRP) [204].

Figure 15. *Polar Rs800sd heart rate monitor (left) and belt (middle), Unibrain Fire-I OEM pupil camera (right).*

Figure 16. *ProComp Infiniti Encoder (left) and detectors (right).*

Heart rate (HR) was monitored and recorded continuously during the whole experiment using a Polar Rs800sd heart rate monitor (Polar Electro, Vantaa, Finland). Heart rate was analysed with Kubios HRV Analysis Software [205] by dividing the raw heart rate data into 5-minute bins. The mean of each bin was calculated for heart rate, low-frequency power (LF), high-frequency power (HF), and the LF/HF ratio, which is considered to be a good index of cardiac activity [206].

Skin conductance was measured continuously using a ProComp Infiniti Encoder (ThoughtTechnology, Montreal, Canada). 256 samples were recorded per second with BioGraph Infiniti software. Mean skin conductance was determined for the same 5-minute bins as with heart rate.

Subjective sleepiness was self-rated using the Karolinska sleepiness scale [84] every 20 minutes during the experiment. The mean subjective sleepiness was calculated every five minutes by extrapolating the data.

The test equipment is illustrated in Figures 15 and 16.

6.2.3 Results

The changes in values by the function of time provided by the different measuring methods were analysed with the two-tailed paired Student's *t*-test for means and its probability value P_t.

The subjective sleepiness increased significantly by time with both the young ($P_t = 0.000 < 0.05$) and the older ($P_t = 0.000 < 0.05$) test groups. The LF/HF ratio decreased somewhat (young: $P_t = 0.113 > 0.05$; older: $P_t = 0.112 > 0.05$; not significant) and normalised heart rate values decreased significantly (young: $P_t = 0.002$; older: $P_t = 0.046$), corresponding to reduced alertness. In contrast, the skin conductance values supported an increase in alertness with time, but only with the young subjects (young $P_t = 0.010$; older: $P_t = 0.379$).

The mean values of the normalised skin conductance, the normalised heart rate, the LF/HF ratio, and the subjective sleepiness every 5 minutes for the young and the older test groups during the 2-hour test period are illustrated in Figure 17.

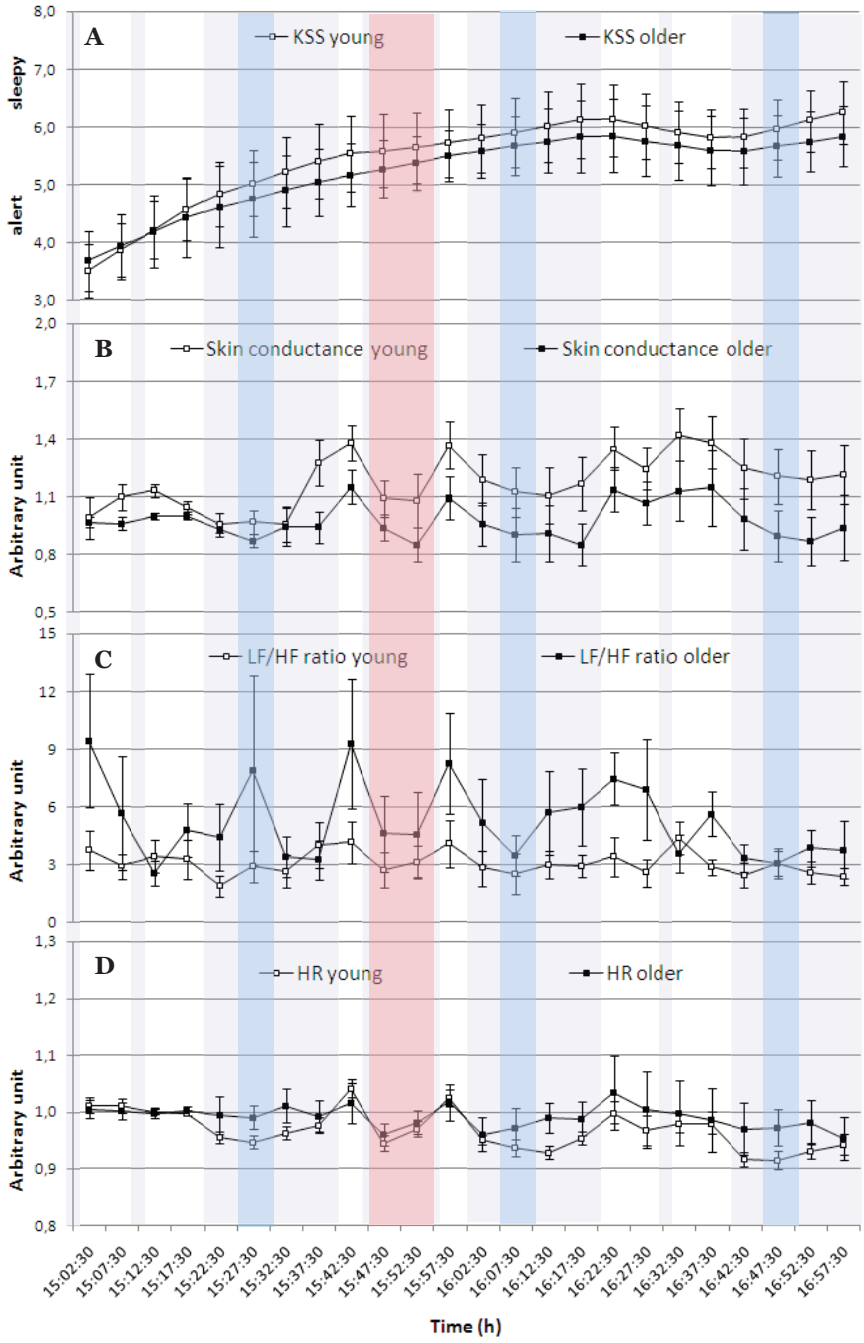

Figure 17. *The time course of subjective sleepiness (A), normalised skin conductance (B) LF/HF ratio (C), and normalised heart rate (D). Mean values at 5-min intervals ± standard error of mean. Grey = recording period of the pupil, white = time of darkness, blue = exposure time to quasimonochromatic blue light, red = exposure time to broadband orange-red light.*

Unfortunately, there were not enough applicable recordings to be able to complete the analysis for the pupil size. The intention was to take frames from the video recordings and calculate the hippus every 10 minutes by using segmentation as illustrated in Figure 18. Part of the problem was due to low image quality caused by an unfocused lens, camera vibration, and the absence of a fixation point of the eye. Another part was that when the person got sleepier, the eyelid started to drop and it moved on top of the pupil. Because of that the pupil could not be seen in the video any more. The subject could not be reminded to keep their eyes open, because that would have been a stimulus that could have affected their alertness.

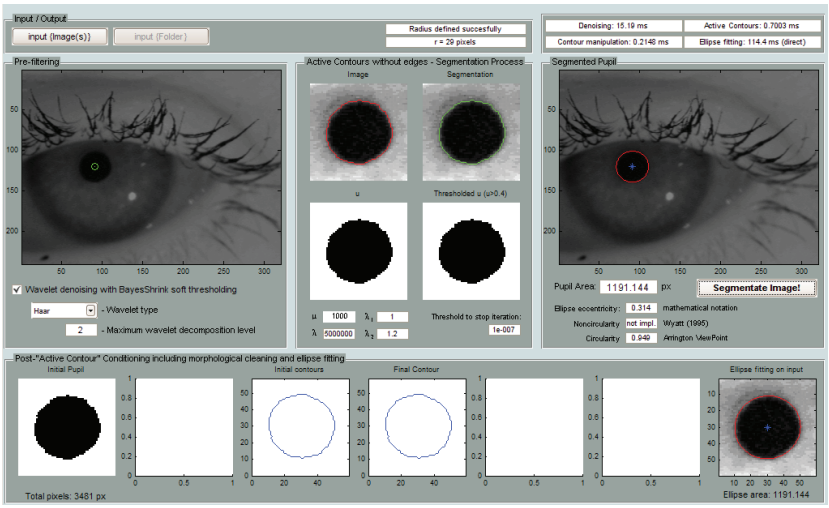

Figure 18. *Edge-based segmentation tool to calculate the hippus from the pupil recordings. The analysis failed as a result of a lack of data.*

The changes in values provided by different measuring methods during the light exposures and recording periods were analysed with the two-tailed paired Student's *t*-test for means and its probability value P_t. This was done to see whether the changing conditions affected the values.

Exposure to light (either quasimonochromatic blue or broadband orange-red) did not cause any significant effect on the values in the young group ($P_t > 0.05$ with all methods). In the older group there were differences in the heart rate and skin conductance values during the light period compared to darkness (heart rate: $P_t = 0.045$; skin conductance: $P_t = 0.021$). However, the effect of the recording period appeared much stronger in the values. In both age groups the heart rate, LF/HF ratio, and skin conductance were significantly higher during the periods when the subject could move freely in the dark experimental room compared to the periods when

he or she was attached to the Goldman perimeter (young: P_t = 0.000, 0.007, 0.050; older: P_t = 0.000, 0.022, 0.000; P_t = [heart rate, LH/HF ratio, skin conductance]). Within the recording periods there was no difference in the responses to light exposure compared to darkness in any of the methods in either of the age groups, meaning that recording was a more dominative state than the light (P_t > 0.05 with all methods in both age groups). Sleepiness acted independently and did not follow the recording or the lighting conditions.

The correlations of different methods within the age group and of the same methods between the age groups were determined with Pearson's correlation coefficient r and its probability value P_r (r = 0.00 = no correlation and $|r|$ = 1.00 = perfect correlation, range [-1, 1]). Pearson's correlation was also used to investigate the time correlation of the measures.

The behaviour of the skin conductance correlated negatively with the behaviour of the LF/HF ratio in both age groups (young: r = -0.50, P_r = 0.006; older: r = -0.27, P_r = 0.043). With the young subjects the KSS correlated positively with the skin conductance (r = 0.54, P_r = 0.003), giving conflicting information about the changes in alertness. However, the negative correlation of the KSS and HR (r = -0.50, P_r = 0.006) implied that their alertness did indeed decrease with time. These inter-method correlations were not found significant in the older test group. However, all the measures showed corresponding behaviour in both age groups (heart rate: r = 0.73, P_t = 0.000; LF/HF ratio: r = 0.35, P_r = 0.049; skin conductance: r = 0.70, P_r = 0.000; KSS: r = 0.99, P_r = 0.000).

6.2.4 Discussion

Subjective sleepiness ratings and heart rate measures showed that the subjects became sleepier during the test. That is in conflict with the skin conductance responses, which suggest that the subjects became more aroused. It is possible that the KSS ratings reflected reduced motivation rather than alertness. However, a more likely explanation for the inconsistency is that while becoming sleepier the subjects were trying harder to fight against the desire to sleep. That appeared in the skin conductance data as arousal.

The effect of light exposure was shown in the older test group as a change in skin conductance and heart rate. However, the variations in the functions of the autonomic nervous system were mainly detected when the subject was able to move freely in the experimental room without having his or her head attached to the Goldman perimeter. This indicates that the presence of

the pupil camera affected the ANS responses, thus masking the effect of the light stimulus. This is a practical illustration of the sensitivity of the ANS methods to external stimuli. It shows that more effort has to be put into the study protocol to either exclude everything that could appear as external, unwanted stimuli, or choose methods that can be used in the presence of such stimuli.

Apparently, sitting still in front of the Goldman perimeter eye facing towards the camera was a task that did not go together with skin conductance and heart rate measurements. Hence, in this type of study setting the measurement of pupil size cannot be used at the same time as other methods recording the activation of the autonomic nervous system. Furthermore, the recording protocol has to be designed in such a way as to be so comfortable for the subject that no difference between the recording period and the rest of the experiment can be detected. The KSS was not sensitive enough to detect changes in the conditions and therefore the lighting or recording conditions were not shown in the KSS ratings.

The biggest drawback of the study was the unsuccessful recording of the pupil size, which happened despite the fact that the protocol had been tested in a pilot study. It was not possible to adjust the focus of the camera, so the focusing had to be done by manually adjusting the distance to the eye. In future studies one could try to adjust the distance by attaching the camera to a microrail on which the camera can move back and forth. To reduce the noise in the image, more infrared light should be applied. That is challenging because the light should be kept invisible to the subject. In this study difficulties were encountered in keeping the camera still. During some of the experimental sessions the heavy camera could not be held in a steady position, causing the eye to change its position in the image. Therefore not all the data could be read and processed with the Matlab program. This could be corrected by using a separate stand for the camera instead of attaching the camera directly to the Goldman perimeter.

All the methods that were tested have been considered to be objective measurements of vigilance, sleepiness, or alertness. Therefore it was hypothesised that they would correlate with the KSS ratings. This hypothesis was shown to be partly true. The heart rate and the LF/HF ratio correlated negatively with the KSS, and the skin conductance correlated positively with the KSS. The correlation between the pupil fluctuation measurements and the KSS ratings could not be calculated.

6.3 Study III: Experiment on the relationship of mood and alertness

6.3.1 Experimental setup

The aim of Study III was to investigate the relationship of light, emotional reaction, and alertness in changing lighting conditions that correspond to a normal lecture environment. Because measuring the emotional reaction is complex, changes in mood were used to indicate emotions, as suggested in Rautkylä et al. [24].

On the basis of the model of two pathways presented in Chapter 5, two things were hypothesised. First, if light creates an emotional reaction, different parameters of light will change the mood and the alertness differently. Second, if emotions and alertness are associated, changes in mood and alertness will correlate.

The study and its results have not been previously reported and are discussed here for the first time.

The study consisted of four lectures that took place in April and May in four different locations in Finland: Oulu (65°01′N, 25°28′E), Lahti (60°58'N, 25°40'E), Tampere (61° 30'N, 23°45'E), and Turku (60°27'N, 22°17'E), one lecture in each city in this order. From now on, the lectures will be referred as lectures 1, 2, 3, and 4, according to the order in which the lectures were held. Each lecture lasted 90 minutes and took place in the late afternoon, with no breaks.

The lecture was about lighting products, and it was the same in each city. The subjects were of working age. No subject could take part in any more than one of the lectures. 33 subjects participated in lecture 1 (28 male/5 female), 16 in lecture 2 (16 male/0 female), 39 in lecture 3 (38 male/1 female), and 31 in lecture 4 (30 male/1 female). The subjects were mainly contractors, electrical wholesalers, and designers who had basic knowledge about lighting.

The lighting was done with fluorescent light in each location, as presented in an example photo in Figure 19. In three locations the correlated colour temperature of the light was 3,000 K and in one it was 4,000 K (lecture 4). The lighting conditions were altered in the rooms so that during the lecture the lights were dimmed (lighting condition 1) and after the lecture the illuminance was increased (lighting condition 2). In one lecture (lecture 3) no change was applied, but during and after it the conditions were the same. The lighting parameters are presented in Table 8.

Figure 19. *View of the lecture room in Lahti (lecture 2).*

Table 8. *The lighting parameters in the four locations. In lectures 1 (3,000 K) and 4 (4,000 K) the lighting altered from 50 lx to 600 lx. In lecture 2 the lighting altered from 50 lx to 1,200 lx. In lecture 3 the lighting remained constant.*

Location	Lecture	Lighting condition 1 (lx)	Lighting condition 2 (lx)	T_{cp} (K)
Oulu	**1**	600	50	3,000
Lahti	**2**	1,200	50	3,000
Tampere	**3**	300	300	3,000
Turku	**4**	600	50	4,000

Different lighting parameters allowed us to investigate the effect of the correlated colour temperature, as well as how the magnitude of the alteration in illuminance between the lighting conditions 1 and 2 affects the results.

6.3.2 Methods

The study was carried out with a two-part questionnaire. Before the lecture (light condition 1) the subjects completed the first part, which consisted of subjective self-ratings for sleepiness and mood. Sleepiness was evaluated on the 9-step Likert-type Karolinska sleepiness scale [84] (1 referring to “very alert” and 9 to “very sleepy, an effort to keep awake”), and mood on a tailor-made 9-step Likert-type mood scale (1 referring to “very happy” and 9 to “very sad”), similarly to the sleepiness in order to allow comparisons. During the lecture (lighting condition 1) no questionnaires were completed. After the lecture, immediately after the light level had been increased (lighting condition 2), the second part of the questionnaire was completed. The subjects self-rated their sleepiness and mood again, and gave their

opinion on whether the light level in condition 2 was “too low”, “good”, or “too high”. At the end they gave an overall rating to the lecture on a 5-step Likert scale (1 referring to “very bad” and 5 to “very good”).

6.3.3 Results

The effect of light exposure on mood and alertness was investigated by measuring how the self-ratings of mood and alertness changed during the lecture. This was done by comparing the first evaluation at the beginning of the lecture and the second evaluation at its end. The significance of the change was determined by using a two-tailed paired Student’s *t*-test for means and its probability value P_t.

The mood and the alertness remained unchanged in the majority of the individuals. This can be seen in Tables 9 and 10 in column “0”, referring to “no change in mood/alertness”. The individual changes were averaged into mean values also shown in Tables 9 and 10. There was no significant change in the average mood or the alertness during the lectures ($P_t > 0.05$).

Table 9. *The change in mood during the four lectures. The headers [-4, 4] indicate how much the mood changed. If the change < 0, the mood worsened, if the change > 0, the mood improved, if the change = 0, the mood did not change. The numbers below the headers [-4, 4] stand for the number of responses. N = number of subjects, SD = standard deviation, P_t = two-tailed probability value; if $P_t < 0.05$, the mood changed significantly during the lecture.*

Lecture	N	-4	-3	-2	-1	0	1	2	3	4	Mean	SD	P_t
1	33	0	0	1	5	19	6	2	0	0	0.09	0.84	0.540
2	16	0	0	0	3	7	6	0	0	0	0.19	0.75	0.333
3	39	1	0	1	3	23	8	3	0	0	0.13	1.06	0.453
4	31	0	1	2	2	15	8	0	2	1	0.29	1.40	0.256

Table 10. *The change in alertness during the four lectures. The headers [-5, 3] indicate how much the alertness changed. If the change < 0, the alertness decreased, if the change > 0, the alertness increased, if the change = 0, the alertness did not change. The numbers below the headers [-5, 3] stand for the number of responses. N = number of subjects, SD = standard deviation, P_t = two-tailed probability value; if $P_t < 0.05$, the alertness changed significantly during the lecture.*

Lecture	N	-5	-4	-3	-2	-1	0	1	2	3	Mean	SD	P_t
1	33	0	0	0	1	8	17	4	2	1	0.03	1.02	0.865
2	16	0	0	0	0	2	7	6	0	1	0.44	0.96	0.089
3	39	1	0	1	4	7	20	4	2	0	-0.38	1.29	0.070
4	31	0	0	0	0	2	18	7	4	0	0.42	0.81	0.107

To highlight the direction over the magnitude, the individual values of Tables 9 and 10 were grouped into three categories, as presented in Figures 20 and 21. The figures show whether the average was positive (increased alertness/improved mood), negative (decreased alertness/worsened mood), or whether there was no self-reported change during the lecture.

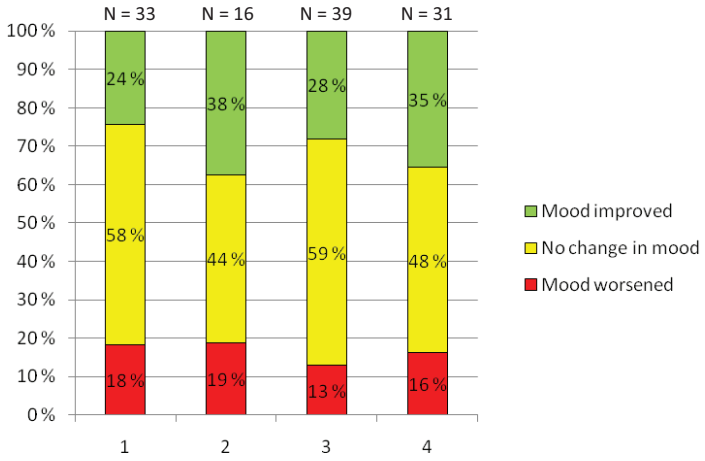

Figure 20. *The individual changes in mood grouped into three categories: "mood improved", "no change in mood", and "mood worsened". N= number of participants. The numbers on the x-axis stand for the lecture. The y-axis indicates the number of subjects as a percentage, when 100% is the total number of subjects at each lecture.*

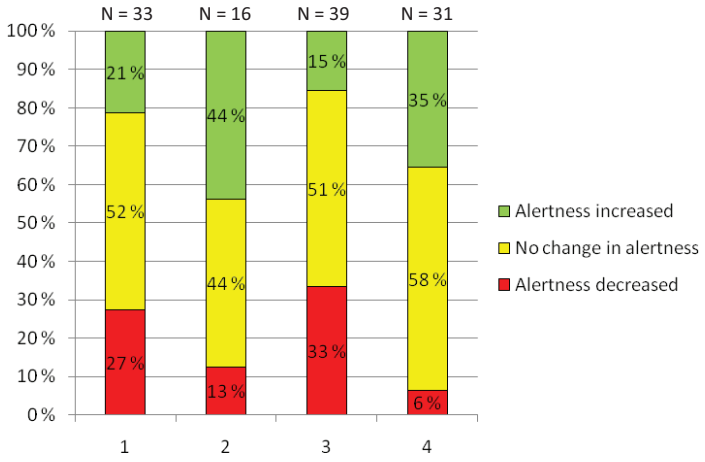

Figure 21. *The individual changes in alertness grouped into three categories: "alertness increased", "no change in alertness", and "alertness decreased". N= number of participants. The numbers on the x-axis stand for the lecture. The y-axis indicates the number of subjects as a percentage when 100 % is the total number of subjects at each lecture.*

To investigate the effect of different lighting parameters on mood, comparisons between the lectures with different lighting conditions were made. The significance was determined by a two-tailed two-sample Student's *t*-test with unequal variances and its probability value P_t.

First, the effect of the T_{cp} was investigated. This was done by comparing the change in mood in lectures 1 and 4, as apart from the T_{cp}, the other lighting parameters in the two lectures were the same. After that the effect of the magnitude of the alteration in illuminance between the lighting conditions 1 and 2 was investigated. This was done by first comparing lectures 1 and 2 to one another, and then comparing both lectures to lecture 3, as in lecture 3 there was no alteration in illuminance.

As presented in Table 11, the mood changed similarly in different lighting conditions ($P_t > 0.05$), unlike what had been hypothesised. The alertness, however, changed differently in lectures 1 and 4, 1 and 2, and 2 and 3 ($P_t < 0.05$). Between lectures 1 and 3 no difference was detected ($P_t > 0.05$).

Table 11. *The effect of the lighting parameters on the change in mood/alertness. In each row the cells with the vertical lines indicate the two lectures used in the comparison. ΔM = change in mood, ΔA = change in alertness, P_t = two-tailed probability value; if $P_t < 0.05$, the change in mood/alertness was significantly different in the two lighting conditions compared to one another.*

Lecture 1: 50 lx → 600 lx 3,000 K	Lecture 2: 50 lx → 1,200 lx 3,000 K	Lecture 3: 300 lx 3,000 K	Lecture 4: 50 lx → 600 lx 4,000 K	ΔM P_t	ΔA P_t
▮			▮	0.438	0.034
▮	▮			0.355	0.032
▮		▮		0.658	0.376
	▮	▮		0.522	0.004

The correlation between the change in mood and in alertness was measured by Pearson's correlation (short for Pearson's product moment correlation) and its probability value P_r. Pearson's correlation coefficient r indicated the strength of a linear relationship between the variables in the range [-1, 1].

The correlation was moderately positive and statistically significant in lectures 1, 3, and 4, as presented in Table 12 ($0.50 < r$ (ΔM, ΔA) < 0.75, $P_r < 0.05$). In lecture 2 the positive correlation was strong

(r (ΔM, ΔA) = 0.90, P_r < 0.05), indicating that the change in mood and alertness were strongly associated with the lighting condition.

Table 12. *The correlation between the change in mood and the change in alertness. N = number of subjects, r = Pearson's correlation coefficient [-1, 1], ΔM = change in mood, ΔA = change in alertness, P_r = two-tailed probability value; if P_r < 0.05, the correlation ρ between the change in mood and the change in alertness was significant.*

Lecture	N	r (ΔM, ΔA)	P_r
1	33	0.547	0.001
2	16	0.892	0.000
3	39	0.494	0.001
4	31	0.585	0.001

The subjects evaluated the lighting level at the end of the lecture, as presented in Figure 22. The majority rated the lighting level as "good" in all the lectures. Except for lecture 2, the ratings did not differ significantly from each other. The significance was determined by a two-tailed two-sample Student's t-test with unequal variances and its probability value P_t. At lecture 2 19% of the subjects rated the lighting level as "too high" and no-one gave a rating of "too low". Therefore the overall evaluation differated significantly from the other lectures, as presented in Table 13 (P_t < 0.05).

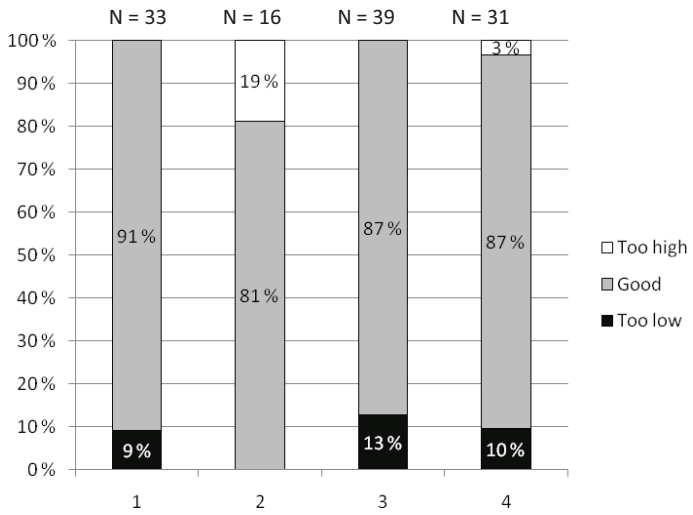

Figure 22. *The self-ratings of the lighting level at the end of the lecture. N = number of participants. The numbers on the x-axis stand for the lecture. The y-axis indicates the number of subjects as a percentage when 100% is the total number of subjects at each lecture.*

Table 13. *The comparisons between the lighting level self-ratings at different lectures. The percentages under the lecture headers stand for the ratings "too low", "good", and "too high" as presented in Figure 22. In each row the cells with the vertical lines indicate the two lectures used in the comparison. P_t = two-tailed probability value; if $P_t < 0.05$, the lighting levels in the two lighting conditions compared to one another were rated as significantly different.*

Lecture 1: 9%, 91%, 0%	Lecture 2: 0%, 81%, 19%	Lecture 3: 13%, 87%, 0%	Lecture 4: 0%, 87%, 3%	P_t
▮	▮			0.022
▮		▮		0.617
▮			▮	0.749
	▮	▮		0.011
	▮		▮	0.044
		▮	▮	0.453

In lecture 2 the self-rated lighting level correlated significantly with the change in mood but not with the change in alertness (mood: $r = 0.537$, $P_r = 0.032 < 0.05$; alertness: $r = 0.484$, $P_r = 0.057 > 0.05$). There was no correlation between the self-rated lighting level and the measured parameter in any of the other lectures. The correlation was measured by Pearson's correlation and its probability value P_r, as presented in Table 14.

Table 14. *The correlation between the lighting level self-ratings and the change in mood/alertness. N = number of subjects, r = Pearson's correlation coefficient [-1,1], E_s = self-rated lighting level, ΔM = change in mood, ΔA = change in alertness, P_r = two-tailed probability value; if $P_r < 0.05$, the self-rated lighting level correlated significantly with the change in mood/alertness.*

Lecture	N	r (E_s, ΔM)	P_r	r (E_s, ΔA)	P_r
1	33	0.300	0.879	-0.028	0.879
2	16	0.537	0.032	0.484	0.057
3	39	-0.028	0.863	0.012	0.944
4	31	0.051	0.785	0.092	0.624

The self-rated lighting level also had an effect on the correlation between the change in mood and the change in alertness. The effect was evaluated by adding the rating as a layer in the cross-tabulation of the variables, as presented in Table 15. The association was determined by Fisher's exact test and its probability value P_f.

The analysis showed that when the lighting was rated "good", it had a significant effect on the positive correlation between the change in mood and alertness ($P_f < 0.05$). When the lighting level was "too low" it did not affect the correlation ($P_f > 0.05$). The lighting was not rated "too high" enough times for it to be possible to calculate the effect (P_f not available). Individual values showed that under the "too high" lighting, the mood worsened or remained unchanged and the alertness increased.

Table 15. *The effect of the lighting level self-rating on the correlation between the change in mood and the change in alertness. The numbers below the header "Change in alertness" stand for the number of responses. E = lighting level, P_f = Fisher's exact test probablity value; if $P_f < 0.05$, the self-rating of the lighting level affected the correlation significantly. N.A. = the effect could not be calculated because of the small sample size.*

		Change in Alertness			Self-rating E	P_f
		decreased	no change	increased		
Change in Mood	worsened	1	1	0	Too low	0.424
	no change	0	4	2		
	improved	1	2	0		
	worsened	11	5	1	Good	0.000
	no change	12	41	4		
	improved	1	9	20		
	worsened	0	0	1	Too high	N.A.
	no change	0	0	3		
	improved	0	0	0		

The subjects rated the lecture on a Likert scale from 1 to 5 (1 referring to "very bad" and 5 to "very good"), as presented in Figure 23. The differences between the ratings of the different lectures were determined with a two-tailed two-sample Student's *t*-test for means with unequal variances and its probability value P_t. Each lecture was rated between 4.2 and 4.4 on average. No difference was found between the ratings of the lectures, as presented in Table 16 ($P_t > 0.05$). It means that the lecture itself affected the mood and alertness in the same way during each lecture and was therefore not a cause of difference between the changes in mood and alertness during the lectures.

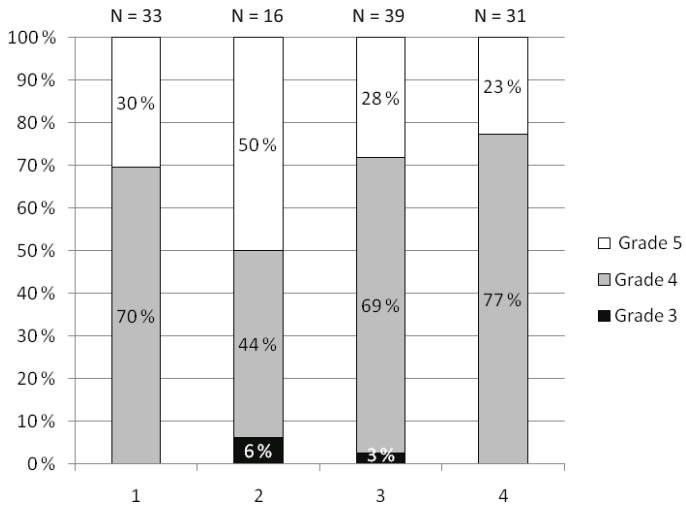

Figure 23. *The self-ratings of the lectures on a Likert scale from 1 to 5. The numbers on the x-axis stand for the lecture. The y-axis indicates the number of subjects as a percentage when 100% is the total number of subjects at each lecture.*

Table 16. *The overall ratings of the four lectures on a Likert scale from 1 to 5. The numbers below the lecture headers stand for the mean values of the ratings at each lecture. In each row the cells with the vertical lines indicate the two lectures used in the comparison. P_t = Pearson's probablity value; if $P_t < 0.05$, the evaluation of the different lectures differed significantly.*

Lecture 1: 4.3	Lecture 2: 4.4	Lecture 3: 4.3	Lecture 4: 4.2	P_t
‖	‖			0.455
‖		‖		0.684
‖			‖	0.491
	‖	‖		0.315
	‖		‖	0.239
		‖	‖	0.783

6.3.4 Discussion

When the averages for the change in mood and alertness during each lecture were calculated, neither the mood nor the alertness was found to have changed significantly. Instead, the mood and the alertness of the majority remained unchanged.

However, after the individual changes had been grouped into three categories (decrease, no change, increase), significant differences were detected in the alertness under the different lighting conditions. The alteration from 50 lx to 1,200 lx in lecture 2 induced a more positive effect on alertness

than the alteration from 50 lx to 600 lx in lecture 1. So did the alteration from 50 lx to 1,200 lx compared to no alteration at all in lecture 3. No significant difference was detected between the alteration from 50 lx to 600 lx compared to no alteration at all. This indicated that the illuminance has to increase to a level that is above the normal office lighting level (500 lx) to have a positive effect on alertness. Furthermore, it implies that changes in the light exposure are more likely to induce alerting effects than constant light exposure.

The correlated colour temperature of the light also played a role in the alerting response. Exposure to 4,000-K light increased the alertness more than that to 3,000-K light, when the illuminances were the same in both conditions. In both conditions the lighting levels were rated as "good" on average. One subject rated the lighting level in the 4,000-K condition as "too high". Although one rating is not enough for statistical significance, it implies that light with a higher T_{cp} might have created a stronger lighting experience than light with a lower T_{cp}. If this was true, it would indicate the involvement of melanopsin-containing retinal ganglion cells in the alerting procedure, since the classical rods and cones would be more sensitive to longer wavelengths than the short wavelengths present in the spectrum of the 4,000-K light source.

Mood was less sensitive to different lighting parameters and did not change differently under different lighting conditions. However, the possible link between the light stimulus and the limbic system cannot be ruled out on the basis of these results. It is possible that the lighting conditions were not different enough to provoke different emotional reactions and therefore no difference was detected between the lectures in terms of a change in mood.

It has been shown that the visual stimulus has to be strong to create a conscious emotion [187]. If the emotional stimulus is too brief or too weak the amygdala might not process it and direct it to the conscious thinking [188]. Because of that it is possible that the subjective evaluation method was not sensitive enough to detect the emotional response.

The change in mood and alertness were found to correlate in all lighting conditions and the correlation was strongest in lecture 2 when the lighting conditions altered the most. Some of the subjects even rated the latter conditions as "too high", indicating that the light created a negative feeling. The changes in mood and alertness were, however, towards the positive. Not enough subjects rated the lighting level as "too high" for it to be possible to

calculate its effect on the correlation of mood and alertness. The correlation proved to be the most positive under the lighting level rated “good”.

Apart from the lighting conditions, the lectures were the same each time. The lectures were rated as good each time and the effect of the lecture on the differences in the mood and alertness was ruled out statistically. Therefore one could be sure that the effects seen in the results were caused by the light stimulus and not something else. It is, however, possible that the methodology used in the study caused some bias to the correlation. Because both the mood and the alertness were evaluated on the same Likert scale from 1 to 9, the ratings might have affected one another. Therefore, in further studies, it might be better to use evaluation methods with different scales and anchor the ratings only for the analysis.

Prior to the study two things were hypothesised. First, if light creates an emotional reaction, different parameters of light will change the mood and the alertness differently. Second, if emotions and alertness are associated, changes in mood and alertness will correlate. These two hypotheses were shown to be partly true. The emotional reaction caused by the light exposure could not be verified, because unlike the alertness, the mood did not change differently in different lighting conditions. However, the change in mood correlated positively with the change in alertness in each lecture and lighting was shown to affect the strength of the correlation. One should note that the confirmed association between mood and alertness does not indicate causality. The causality can only be proven by scanning the brain structures involved and detecting the activation and deactivation patterns caused by the light stimulus, as suggested in Section 5.4.

7 DISCUSSION

Alertness is not only part of the circadian sleep-wake pattern but also an activation state that can be induced by external or internal stimuli. The thesis suggests that a lack of stimuli reduces alertness. This is supported by the results of Study I. In the autumn the alertness decreased during the lecture in the 4,000-K lighting environment but the 17,000-K lighting environment helped the students to retain their alertness. Hence blue-enriched white light acted as a stronger stimulus and induced greater alerting effects than normal white light. This was also hypothesised on the basis of the previous field studies of others [31, 32].

The results of Study III implied that changes in the light exposure are more likely to induce alerting effects than constant light exposure. The results of Study II also support the claim of the change being more determinative than the length of the exposure because the person adapts to the light. This is in accordance with the physiological model and the definition of alertness presented in Chapter 3, which states that an internal or external stimulus is needed to activate the brain and to induce alertness. It is also in line with the recent studies of Lall et al. [191], who suggest that light adaptation limits the influence of cones in non-image-forming vision and therefore their involvement can mainly be seen after abrupt changes in irradiance.

It is interesting to consider whether the effects of the light in Study I were direct or indirect. According to the feedback from the subjects, blue-enriched white light evoked emotional reactions, whereas the normal white light did not. Such feedback indicates that 17,000-K light might have affected emotions which led to increased alertness. As presented in Chapter 5, the retina, the amygdala, which is responsible for emotional processing, and the brain areas involved in activation and arousal are connected physiologically. Therefore, there is reason to believe that in addition to the circadian alertness pathway, the light can also have an effect on alertness via the lim-

bic pathway through the amygdala. Study III reported in Section 6.3 supports the involvement of emotions in alertness by showing the correlation between mood and alertness in altering lighting conditions. Previous studies too have shown alertness and mood reacting similarly to light [17, 32].

For two decades scientists have tried to define and quantify the optimal parameters for light exposure to maximise its alerting properties in clinical and non-clinical applications. The debate has covered the light intensity, the spectral distribution, the duration of the light exposure, and the circadian phase in which the light is administered. However, not enough attention has been paid to the fact that the seasonal variation of daylight is likely to influence how a human reacts to artificial light. As could be seen in Study I, the alerting effects of light were different in April and in November, suggesting that artificial light was needed to give the boost in the autumn, when the dose of daylight (duration and intensity) is smaller and the relative contribution of blue light to the daylight spectrum in significantly lower compared to the spring [194]. This indicates that special attention should be paid to the characteristics of general lighting in the winter months.

If the optimal parameters for light have previously been considered from the alertness point of view only, the possible involvement of emotions in alerting effects expands the discussion to what kind of light has the strongest effect on mood. In Study III alertness was found to change differently, depending on the illuminance and the correlated colour temperature of light. With mood such dependency on the lighting level and T_{cp} of light were not seen. It raises the question of whether mood is also sensitive to short wavelengths in the same way as alertness, or whether some other wavelengths are more likely to cause an emotional effect.

Bright light has typically been used to treat mood disorders [207], and it has also been shown to improve the vitality of healthy people [208]. However, a specific spectrum for the exposure has not been established. The fact that light does not necessarily have only positive effects on mood adds complexity to determining the optimal parameters for light. There is no evidence that emotion could not be negative in inducing alertness. However, in practical applications it is more reasonable to try to provoke positive emotions than negative ones. Another factor adding complexity is darkness. Fear of the dark can increase the responsiveness of the mind and body to a sudden unexpected stimulus (also called the startle effect) [209]. Sudden darkness has been found to increase activity and diminish anxiety in rats [210], suggesting that darkness can have an effect on the emotions.

In Study II in Section 6.2, it was shown that with both the young and the older subjects the sleepiness increased in darkness when no activating stimulus was present. This indicates alertness and mood having opposite reactions to darkness.

All in all, the theory of the two pathways, the circadian and the limbic, could explain why it has been so hard to define the optimal parameters for light to maximise its alerting effects. As discussed previously in this chapter, light, or its absence, can have different effects, depending on which pathway it is signalling. An essential question is whether these two proposed pathways work in turns or at the same time, and whether they influence one another, as discussed in Section 5.3.

Practical experiments are needed to verify the existence of the limbic pathway for light-induced alertness. As suggested by Rautkylä et al. [24], different wavelengths and a broad range of scotopic and photopic lighting levels should be tested when eliciting emotional responses to light. The time course of activation patterns should be measured with fMRI scannings from the amygdala (representing the limbic system), the SCN (representing the circadian system), and the LC (representing the activation system). This type of investigation has the ability to reveal possible causality between light, emotions, and alertness.

In general, the best method for each study on the alerting effects of light depends on the objectives and nature of the research. Subjective evaluation is a good behavioural indicator and an easy method to conduct. However, it should be kept in mind that ratings on scales such as the Karolinska sleepiness scale do not necessarily indicate changes in alertness but sustained attention or sleepiness. Furthermore, there is no real placebo for light, but the subject can feel more alert under certain lighting conditions compared to others. Alternatively, the subject might not become aware of the alerting effect of light, and hence the subjective evaluation method might not be sensitive enough to detect the change. After all, a human reacts unconsciously to various things in his environment, but these reactions can only be detected by electrophysiological measurements. Therefore subjective evaluation should always be used together with objective tests.

If objective tests are required, but it is enough to detect the effects of light, one can observe the activation of the autonomic nervous system connected to the LC, one of the key components of the ascending reticular activating system. Because the activation of the autonomic nervous system increases as the level of alertness increases, it is possible to see how the

stimulus activates the body by observing the changes in the ANS. For measuring ANS activity through skin conductance and heart rate, there is relative cheap, low-tech equipment available. However, the practical testing in Study II showed that the equipment is very sensitive to external stimuli, which can limit its use in lighting studies. The test encountered some difficulties in the recording of the pupil data. However, it is foreseen that with more careful study design pupillometry could be a suitable method for use in light-induced alertness research.

Previous studies show that as a result of their high temporal resolution, EEGs and EOGs are reliable correlates of human alertness. In Study II it was unfortunately not possible to test CNS variables. In general electrophysiological recordings are validated methods used in clinical applications to detect whether a person is awake, tired, or asleep. The thesis claims, however, that out of all the methods discussed in Chapter 4, the greatest potential lies in brain imaging. Brain scanning can reveal the mechanisms behind the (hypothetical) light-induced daytime alertness and emotions by spotting the neural correlates. Unfortunately the protocol is expensive and hard to design because of the numerous restrictions discussed in Section 4.3.7.

8 CONCLUSIONS AND CONTRIBUTION

The two-stage lecture hall study reported as Study I confirmed the benefits of using blue-enriched white light to help people to retain alertness during the natural dip time in the afternoon. The test settings in the spring and in the autumn differed from one another in terms of sample size and lighting conditions and therefore their results could not be compared. However, the study was unique because it presented investigations in two seasons when the dose and spectral composition of daylight are different. Another clear richness of the study was in the real-life test setting. It showed that in field studies where only a few parameters can be controlled, it is important to consider all the variables that might have a masking effect on the relationship between light and alertness.

In general Study I showed that consistent work is needed to find out the optimal parameters for light and to reveal the mechanisms responsible for the alerting effects of light in the daytime. To find them alertness should be defined and proper methods that are based on the physiology of light should be applied. That is what set the objectives for the thesis.

The thesis was the first one in this extent to review the term “alertness” and to qualify its special characteristics in relation to the terms closely linked to it, such as “arousal”, “vigilance”, and “sleepiness”. It defined alertness as an activation state of the brain that is induced by stimuli and reduced by the lack of them. The definition was followed uniformly throughout the thesis.

After studying the physiology behind alertness, the thesis evaluated the suitability of the methods currently used in alertness research to study the relationship between light and alertness. The theoretical evaluation was performed according to two criteria: how well the method represents physiological alertness and how well the method deals with the special de-

mands that using light as a stimulus imposes on the method and the study design.

In the practical evaluation reported as Study II, the results of the heart rate, the skin conductance, and the pupil size measurements were compared to the self-ratings on the KSS, a scale validated to correlate with EEG recordings. Unfortunately, the analysis of the pupil recordings failed as a result of the lack of suitable pupil data. There is, however, reason to believe that the spontaneous fluctuations called hippus could be used as an indicator of alertness. Heart rate and skin conductance proved to correlate well with the KSS, indicating that autonomic nervous system activity represents the alerting effects well. However, the recordings were prone to external disturbances, such as the action required for the pupil recordings. The practical testing contributed to lighting research not only by evaluating the methodology but also by reporting the practical problems present in the study setting. If the problems were reported more often, research groups could avoid making the same mistakes in their study designs.

Together, the theoretical and practical evaluation show that the methods based on the autonomic nervous system activity are good tools for detecting the alerting responses, but that electrophysiological methods monitoring the central nervous system are needed to find out about the causes behind the effects. Brain imaging was proven to be the most valuable method in the search for the mechanisms. Because of its spatial resolution it was able to reveal the activity patterns in different parts of the activation system. In field studies one is unfortunately forced to lean on subjective evaluation and reaction tests that are indirect indicators of alertness and prone to subject- and protocol-related bias.

Studying the physiological connections between the retina and the ascending activation system responsible for the regulation of alertness, led to a proposal of a novel theory of two pathways, the circadian and the limbic pathways. The theory suggests that in addition to the circadian entrainment light can evoke emotions that further induce alertness. It means that the amygdala, the key structure in the regulation of emotional responses, is involved in light-induced alertness.

The link between light exposure, emotions, and alertness was supported by the subject feedback of Study I, but also by the results of Study III showing that mood and alertness correlate under changing lighting conditions. Such studies can, however, only be considered preliminary to the actual studies, because they only provide information about the correlation, not

about the causality between light exposure, emotions, and alertness. Therefore, a test protocol was suggested to investigate the causal relationship of the light exposure and the response of the amygdala (representing the limbic system), the LC (representing the activation system), and the SCN (representing the circadian system) to light cues. By comparing the activation and deactivation patterns shown in the fMRI scans to self-ratings of mood and alertness one could see whether the limbic and the circadian structures are activated simultaneously or in turn. It would also be possible to gain knowledge about the photoreceptor projections to these brain areas, as well as the image-forming/non-image-forming nature of the stimuli.

Recently, various research groups have suggested that there needs to be a pathway separate from the melatonin pathway responsible for the alerting effects of light during the daytime. So far, however, no such pathway has been established. The novel theory is substantial because it could reveal the missing pathway and explain why study results on the optimal parameters of light have been partly controversial: it is possible that emotions and alertness are sensitive to different lighting parameters.

9 REFERENCES

[1] A. J. Lewy, T. A. Wehr, F. K. Goodwin, D. A. Newsome, and S. P. Markey, "Light suppresses melatonin secretion in humans," *Science (New York, NY)*, vol. 210, no. 4475, pp. 1267-1269, 1980.

[2] S. S. Campbell, D. J. Dijk, Z. Boulos, C. I. Eastman, A. J. Lewy, and M. Terman, "Light treatment for sleep disorders: consensus report. III. Alerting and activating effects.," *Journal of biological rhythms*, vol. 10, no. 2, p. 129, 1995.

[3] C. Cajochen, "Alerting effects of light," *Sleep Medicine Reviews*, vol. 11, no. 6, pp. 453–464, 2007.

[4] I. Provencio, I. R. Rodriguez, G. Jiang, W. P. Hayes, E. F. Moreira, and M. D. Rollag, "A novel human opsin in the inner retina," *Journal of Neuroscience*, vol. 20, no. 2, p. 600, 2000.

[5] R. G. Foster, I. Provencio, D. Hudson, S. Fiske, W. Grip, and M. Menaker, "Circadian photoreception in the retinally degenerate mouse (rd/rd)," *Journal of Comparative Physiology A: Neuroethology, Sensory, Neural, and Behavioral Physiology*, vol. 169, no. 1, pp. 39-50, 1991.

[6] D. M. Berson, F. A. Dunn, and M. Takao, "Phototransduction by retinal ganglion cells that set the circadian clock," *Science*, vol. 295, no. 5557, p. 1070, 2002.

[7] J. J. Gooley, J. Lu, T. C. Chou, T. E. Scammell, and C. B. Saper, "Melanopsin in cells of origin of the retinohypothalamic tract," *Nature Neuroscience*, vol. 4, no. 12, p. 1165, 2001.

[8] F. H. Zaidi et al., "Short-wavelength light sensitivity of circadian, pupillary, and visual awareness in humans lacking an outer retina," *Current Biology*, vol. 17, no. 24, pp. 2122-2128, 2007.

[9] G. Vandewalle et al., "Brain responses to violet, blue, and green monochromatic light exposures in humans: prominent role of blue light and the brainstem," *PloS one*, vol. 2, no. 11, p. 1247, 2007.

[10] S. W. Lockley, E. E. Evans, F. A. Scheer, G. C. Brainard, C. A. Czeisler, and D. Aeschbach, "Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans," *Sleep*, vol. 29, no. 2, pp. 161–168, 2006.

[11] S. Hattar, H. W. Liao, M. Takao, D. M. Berson, and K. W. Yau, "Melanopsin-containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity," *Science*, vol. 295, no. 5557, p. 1065, 2002.

[12] G. Vandewalle, P. Maquet, and D.-J. Dijk, "Light as a modulator of cognitive brain function," *Trends in Cognitive Sciences*, vol. 13, no. 10, pp. 429-438, Oct. 2009.

[13] M. Terman and J. S. Terman, "Light therapy for seasonal and non-seasonal depression: efficacy, protocol, safety and side effects," *CNS spectrums*, vol. 10, no. 8, p. 647, 2005.

[14] T. S. Horowitz and T. Tanigawa, “Circadian-based new technologies for night workers,” *Industrial health*, vol. 40, no. 3, pp. 223–236, 2002.

[15] J. Phipps-Nelson, J. Redman, D. Dijk, and S. Rajaratnam, “Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance,” *Sleep*, vol. 26, no. 6, pp. 695-700, 2003.

[16] C. Cajochen et al., “High sensitivity of human melatonin, alertness, thermoregulation, and heart rate to short wavelength light,” *Journal of Clinical Endocrinology & Metabolism*, vol. 90, no. 3, p. 1311, 2005.

[17] V. L. Revell, J. Arendt, L. F. Fogg, and D. J. Skene, “Alerting effects of light are sensitive to very short wavelengths,” *Neuroscience letters*, vol. 399, no. 1-2, pp. 96–100, 2006.

[18] M. Rüger, M. Gordijn, D. G. M. Beersma, B. de Vries, and S. Daan, “Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure,” *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, vol. 290, no. 5, p. R1413, 2006.

[19] V. C. Thessing, A. M. Anch, M. J. Muehlbach, and P. K. Schweitzer, “Two-and 4-hour bright light exposures differentially effect sleepiness and performance the subsequent night.,” *Sleep: Journal of Sleep Research & Sleep Medicine*, 1994.

[20] B. S. Oken, M. C. Salinsky, and S. M. Elsas, “Vigilance, alertness, or sustained attention: physiological basis and measurement,” *Clinical neurophysiology: official journal of the International Federation of Clinical Neurophysiology*, vol. 117, no. 9, p. 1885, 2006.

[21] J. Shen, J. Barbera, and C. M. Shapiro, “Distinguishing sleepiness and fatigue: focus on definition and measurement.,” *Sleep medicine reviews*, vol. 10, no. 1, p. 63, 2006.

[22] H. J. Moller, G. M. Devins, J. Shen, and C. M. Shapiro, “Sleepiness is not the inverse of alertness: evidence from four sleep disorder patient groups,” *Experimental Brain Research*, vol. 173, no. 2, pp. 258-266, Apr. 2006.

[23] K. Archibald, *Effects of noise, temperature, humidity, motion and light on the sleep patterns of the Crew of HSV-2 SWIFT*. Monterey CA: Naval postgraduate school, 2005.

[24] E. Rautkylä, M. Puolakka, and L. Halonen, “Alerting effects of daytime light exposure – proposed link between light exposure and brain mechanisms,” *Lighting Research and Technology*, in press.

[25] E. Rautkylä, M. Puolakka, E. Tetri, and L. Halonen, “Effects of correlated colour temperature and timing of light exposure on daytime alertness in lecture environments,” *Journal of Light & Visual Environment*, vol. 34, no. 2, pp. 59-68, 2010.

[26] E. Rautkylä, P. Teikari, M. Puolakka, and L. Halonen, “Evaluation of today’s research methods for assessing light-induced alertness,” presented at the Experiencing Light - International Conference on the Effects of Light on Wellbeing, Eindhoven, 2009, pp. 162-173.

[27] “Valkee brain stimulation headset.” [Online]. Available: http://www.valkee.com/uk/.

[28] S. S. Campbell and P. J. Murphy, “Extraocular circadian phototransduction in humans,” *Science*, vol. 279, no. 5349, p. 396, 1998.

[29] P. Badia, B. Myers, M. Boecker, J. Culpepper, and J. R. Harsh, “Bright light effects on body temperature, alertness, EEG and behavior,” *Physiology & behavior*, vol. 50, no. 3, pp. 583–588, 1991.

[30] C. Cajochen, J. M. Zeitzer, C. A. Czeisler, and D. J. Dijk, “Dose-response relationship for light intensity and ocular and electroence-

phalographic correlates of human alertness," *Behavioural Brain Research*, vol. 115, no. 1, pp. 75–83, 2000.

[31] P. R. Mills, S. C. Tomkins, and L. J. M. Schlangen, "The effect of high correlated colour temperature office lighting on employee wellbeing and work performance," *Journal of Circadian Rhythms*, vol. 5, no. 1, p. 2, 2007.

[32] A. Viola, L. James, L. Schlangen, and D. Dijk, "Blue-enriched white light in the workplace improves self-reported alertness, performance and sleep quality," *Scandinavian journal of work, environment & health*, vol. 34, no. 4, pp. 297-306, 2008.

[33] A. A. Borbély, "A two process model of sleep regulation," *Human neurobiology*, 1982.

[34] D. Dawson, Y. Ian Noy, M. Harma, T. Åkerstedt, and G. Belenky, "Modelling fatigue and the use of fatigue models in work settings," *Accident Analysis & Prevention*, vol. 43, no. 2, pp. 549–564, 2011.

[35] T. Åkerstedt, S. Folkard, and C. Portin, "Predictions from the three-process model of alertness," *Aviation, space, and environmental medicine*, vol. 75, no. 1, p. A75-A83, 2004.

[36] C. B. Saper, G. Cano, and T. E. Scammell, "Homeostatic, circadian, and emotional regulation of sleep," *The Journal of Comparative Neurology*, vol. 493, no. 1, pp. 92-98, 2005.

[37] C. A. Czeisler et al., "Stability, precision, and near-24-hour period of the human circadian pacemaker," *Science*, vol. 284, no. 5423, p. 2177, 1999.

[38] J. Aschoff and H. Pohl, "Phase relations between a circadian rhythm and its zeitgeber within the range of entrainment," *Naturwissenschaften*, vol. 65, no. 2, pp. 80–84, 1978.

[39] M. Menaker, "Circadian photoreception," *Science*, vol. 299, no. 5604, p. 213, 2003.

[40] C. A. Czeisler et al., "Suppression of melatonin secretion in some blind patients by exposure to bright light," *New England Journal of Medicine*, vol. 332, no. 1, p. 6, 1995.

[41] T. Partonen, O. Vakkuri, and C. Lamberg Allardt, "Effects of exposure to morning bright light in the blind and sighted controls," *Clinical physiology*, vol. 15, no. 6, pp. 637-646, 1995.

[42] M. W. Hankins, S. N. Peirson, and R. G. Foster, "Melanopsin: an exciting photopigment," *Trends in neurosciences*, vol. 31, no. 1, pp. 27–36, 2008.

[43] S. Hattar et al., "Melanopsin and rod–cone photoreceptive systems account for all major accessory visual functions in mice," *Nature*, vol. 424, no. 6944, pp. 75-81, 2003.

[44] J. J. Gooley, J. Lu, D. Fischer, and C. B. Saper, "A broad role for melanopsin in nonvisual photoreception," *Journal of Neuroscience*, vol. 23, no. 18, p. 7093, 2003.

[45] B. Plitnick, M. G. Figueiro, B. Wood, and M. S. Rea, "The effects of red and blue light on alertness and mood at night," *Lighting Research and Technology*, vol. 42, no. 4, pp. 449-458, 2010.

[46] S. Hattar et al., "Central projections of melanopsin-expressing retinal ganglion cells in the mouse," *The Journal of comparative neurology*, vol. 497, no. 3, pp. 326–349, 2006.

[47] G. Vandewalle et al., "Daytime light exposure dynamically enhances brain responses," *Current Biology*, vol. 16, no. 16, pp. 1616–1621, 2006.

[48] C. B. Saper, T. E. Scammell, and J. Lu, "Hypothalamic regulation of sleep and circadian rhythms," *Nature*, vol. 437, no. 7063, pp. 1257–1263, 2005.

[49] G. Aston-Jones, S. Chen, Y. Zhu, and M. L. Oshinsky, "A neural circuit for circadian regulation of arousal," *Nature Neuroscience*, vol. 4, no. 7, pp. 732–738, 2001.

[50] G. Aston-Jones, "Brain structures and receptors involved in alertness.," *Sleep medicine*, vol. 6, p. S3-S7, 2005.

[51] T. Sakurai, "The neural circuit of orexin (hypocretin): maintaining sleep and wakefulness," *Nature Reviews Neuroscience*, vol. 8, no. 3, pp. 171–181, 2007.

[52] R. Winsky-Sommerer et al., "Interaction between the corticotropin-releasing factor system and hypocretins (orexins): a novel circuit mediating stress response," *Journal of Neuroscience*, vol. 24, no. 50, p. 11439, 2004.

[53] R. A. España, K. M. Reis, R. J. Valentino, and C. W. Berridge, "Organization of hypocretin/orexin efferents to locus coeruleus and basal forebrain arousal-related structures," *The Journal of Comparative Neurology*, vol. 481, no. 2, pp. 160–178, 2005.

[54] K. Yoshida, S. McCormack, R. A. España, A. Crocker, and T. E. Scammell, "Afferents to the orexin neurons of the rat brain," *The Journal of comparative neurology*, vol. 494, no. 5, pp. 845–861, 2006.

[55] K. Ohno and T. Sakurai, "Orexin neuronal circuitry: role in the regulation of sleep and wakefulness," *Frontiers in neuroendocrinology*, vol. 29, no. 1, pp. 70-87, 2008.

[56] G. Moruzzi and H. W. Magoun, "Brain stem reticular formation and activation of the EEG," *Electroencephalography and clinical Neurophysiology*, vol. 1, no. 1-4, pp. 455-473, 1949.

[57] J. R. L. Schwartz and T. Roth, "Neurophysiology of sleep and wakefulness: basic science and clinical implications," *Current Neuropharmacology*, vol. 6, no. 4, p. 367, 2008.

[58] E. R. Samuels and E. Szabadi, "Functional neuroanatomy of the noradrenergic locus coeruleus: its roles in the regulation of arousal and autonomic function part II: physiological and pharmacological manipulations and pathological alterations of locus coeruleus activity in humans," *Current Neuropharmacology*, vol. 6, no. 3, p. 254, 2008.

[59] R. Parmentier, H. Ohtsu, Z. Djebbara-Hannas, J. L. Valatx, T. Watanabe, and J. S. Lin, "Anatomical, physiological, and pharmacological characteristics of histidine decarboxylase knock-out mice: evidence for the role of brain histamine in behavioral and sleep-wake control," *Journal of Neuroscience*, vol. 22, no. 17, p. 7695, 2002.

[60] R. D. Oades and G. M. Halliday, "Ventral tegmental (A10) system: neurobiology. 1. anatomy and connectivity," *Brain Research Reviews*, vol. 12, pp. 117-165, 1987.

[61] B. L. Jacobs and E. C. Azmitia, "Structure and function of the brain serotonin system," *Physiological Reviews*, vol. 72, no. 1, pp. 165-229, 1992.

[62] D. A. McCormick and T. Bal, "Sleep and arousal: thalamocortical mechanisms," *Neuroscience*, vol. 20, 1997.

[63] C. B. Saper, T. C. Chou, and T. E. Scammell, "The sleep switch: hypothalamic control of sleep and wakefulness," *TRENDS in Neurosciences*, vol. 24, no. 12, pp. 726–731, 2001.

[64] "Arousal - definition of arousal by the Free Online Dictionary, Thesaurus and Encyclopedia." [Online]. Available: http://www.thefreedictionary.com/arousal. [Accessed: 02-Feb-2011].

[65] S. E. Gaus, R. E. Strecker, B. A. Tate, R. A. Parker, and C. B. Saper, "Ventrolateral preoptic nucleus contains sleep-active, galaninergic

neurons in multiple mammalian species," *Neuroscience*, vol. 115, no. 1, pp. 285–294, 2002.

[66] "Alert - Definition and More from the Free Merriam-Webster Dictionary." [Online]. Available: http://www.merriam-webster.com/dictionary/alert. [Accessed: 02-Feb-2011].

[67] R. Allen, "Alert," *The New Penguin English Dictionary*. Penguin Group, 2000.

[68] "Definition of alert adjective from Cambridge Dictionary Online: Free English Dictionary and Thesaurus." [Online]. Available: http://dictionary.cambridge.org/dictionary/british/alert_1. [Accessed: 02-Feb-2011].

[69] "Performance - Definition and More from the Free Merriam-Webster Dictionary." [Online]. Available: http://www.merriam-webster.com/dictionary/performance. [Accessed: 02-Feb-2011].

[70] W. Sturm and K. Willmes, "On the functional neuroanatomy of intrinsic and phasic alertness," *Neuroimage*, vol. 14, no. 1, p. S76–S84, 2001.

[71] S. Makeig and T. P. Jung, "Changes in alertness are a principal component of variance in the EEG spectrum," *NeuroReport*, vol. 7, no. 1, pp. 213-217, 1995.

[72] R. D. Chervin, "Sleepiness, Fatigue, Tiredness, and Lack of Energy in Obstructive Sleep Apnea," *Chest*, vol. 118, no. 2, p. 372, 2000.

[73] T. Åkerstedt, "Sleepiness," *Sleep Medicine Reviews*, vol. 2, no. 1, pp. 1-2, 1998.

[74] W. Revelle and D. A. Loftus, "The implications of arousal effects for the study of affect and memory," in *The handbook of emotion and memory: Research and theory*, New Jersey: Lawrence Erlbaum Associates, Inc., 1992, pp. 113–149.

[75] M. Thomas et al., "Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity," *Journal of Sleep Research*, vol. 9, no. 4, pp. 335-352, 2000.

[76] M. E. Jewett, J. K. Wyatt, C. Ritz De, S. B. Khalsa, D. J. Dijk, and C. A. Czeisler, "Time course of sleep inertia dissipation in human performance and alertness," *Journal of sleep research*, vol. 8, no. 1, pp. 1-8, 1999.

[77] S.-J. Paine, "The Epidemiology of Morningness/Eveningness: Influence of Age, Gender, Ethnicity, and Socioeconomic Factors in Adults (30-49 Years)," *Journal of Biological Rhythms*, vol. 21, no. 1, pp. 68-76, Feb. 2006.

[78] I. Hindmarch, U. Rigney, N. Stanley, P. Quinlan, J. Rycroft, and J. Lane, "A naturalistic investigation of the effects of day-long consumption of tea, coffee and water on alertness, sleep onset and sleep quality," *Psychopharmacology*, vol. 149, no. 3, pp. 203–216, 2000.

[79] N. T. Cable, B. Drust, and W. A. Gregson, "The impact of altered climatic conditions and altitude on circadian physiology," *Physiology & Behavior*, vol. 90, no. 2-3, pp. 267-273, 2007.

[80] N. Goel and G. R. Etwaroo, "Bright light, negative air ions and auditory stimuli produce rapid mood changes in a student population: a placebo-controlled study," *Psychological medicine*, vol. 36, no. 9, pp. 1253-1263, 2006.

[81] R. G. Foster and R. J. Lucas, "Photobiology for the Chronobiologist: Part I - Units of Light Measurement," *Biological Rhythms Bulletin*, no. 1, pp. 6-9, 1999.

[82] E. Hoddes, V. Zarcone, H. Smythe, R. Phillips, and W. C. Dement, "Quantification of sleepiness: a new approach," *Psychophysiology*, vol. 10, no. 4, pp. 431-436, 1973.

[83] C. McCabe and K. Stevens, *Visual Analogue Scales: do they have a role in the measurement of preferences for health states?* The University of Sheffield, 2004.
[84] T. Åkerstedt and M. Gillberg, "Subjective and objective sleepiness in the active individual," *International Journal of Neuroscience*, vol. 52, no. 1, pp. 29-37, 1990.
[85] K. Kaida et al., "Validation of the Karolinska sleepiness scale against performance and EEG variables," *Clinical Neurophysiology*, vol. 117, no. 7, pp. 1574-1581, 2006.
[86] K. Kaida, T. Åkerstedt, G. Kecklund, J. P. Nilsson, and J. Axelsson, "The effects of asking for verbal ratings of sleepiness on sleepiness and its masking effects on performance," *Clinical Neurophysiology*, vol. 118, no. 6, pp. 1324-1331, 2007.
[87] R. Conradt, U. Brandenburg, T. Penzel, J. Hasan, A. Värri, and J. H. Peter, "Vigilance transitions in reaction time test: a method of describing the state of alertness more objectively.," *Clinical neurophysiology: official journal of the International Federation of Clinical Neurophysiology*, vol. 110, no. 9, p. 1499, 1999.
[88] M. Sallinen, M. Härmä, T. Åkerstedt, R. Rosa, and O. Lillqvist, "Promoting alertness with a short nap during a night shift," *Journal of Sleep Research*, vol. 7, no. 4, pp. 240–247, 1998.
[89] M. H. Bonnet, "Performance during sleep," *Biological rhythms, sleep, and performance*, pp. 205-237, 1982.
[90] G. D. Roach, D. Dawson, and N. Lamond, "Can a shorter psychomotor vigilance task be used as a reasonable substitute for the ten-minute psychomotor vigilance Task?," *Chronobiology International*, vol. 23, no. 6, pp. 1379-1387, Jan. 2006.
[91] R. T. Wilkinson and D. Houghton, "Field test of arousal: a portable reaction timer with data storage," *Human Factors: The Journal of the Human Factors and Ergonomics Society*, vol. 24, no. 4, pp. 487-493, 1982.
[92] D. R. Thorne, D. E. Johnson, D. P. Redmond, H. C. Sing, G. Belenky, and J. M. Shapiro, "The Walter Reed palm-held psychomotor vigilance test," *Behavior Research Methods*, vol. 37, no. 1, p. 111, 2005.
[93] K. Blatter and C. Cajochen, "Circadian rhythms in cognitive performance: Methodological constraints, protocols, theoretical underpinnings," *Physiology & Behavior*, vol. 90, no. 2-3, pp. 196-208, Feb. 2007.
[94] R. E. Yoss, N. J. Moyer, and R. W. Hollenhorst, "Pupil size and spontaneous pupillary waves associated with alertness, drowsiness, and sleep.," *Neurology*, vol. 20, no. 6, p. 545, 1970.
[95] I. E. Loewenfeld, *The pupil: Anatomy, physiology, and clinical applications*. Ames: Iowa State University Press, 1993.
[96] L. Stark, "Stability, oscillations, and noise in the human pupil servomechanism," *Proceedings of the IRE*, vol. 47, no. 11, pp. 1925-1939, 1959.
[97] J. W. McLaren, P. J. Hauri, S. C. Lin, and C. D. Harris, "Pupillometry in clinically sleepy patients," *Sleep Medicine*, vol. 3, no. 4, pp. 347-352, 2002.
[98] Y. Morad, H. Lemberg, N. Yofe, and Y. Dagan, "Pupillography as an objective indicator of fatigue," *Current Eye Research*, vol. 21, no. 1, pp. 535-542, 2000.
[99] P. D. R. Gamlin, D. H. McDougal, J. Pokorny, V. C. Smith, K. W. Yau, and D. M. Dacey, "Human and macaque pupil responses driven by melanopsin-containing retinal ganglion cells," *Vision research*, vol. 47, no. 7, pp. 946–954, 2007.

[100] S. Marcos, E. Moreno, and R. Navarro, “The depth-of-field of the human eye from objective and subjective measurements,” *Vision Research*, vol. 39, no. 12, pp. 2039–2049, 1999.
[101] S. Kasthurirangan and A. Glasser, “Characteristics of pupil responses during far-to-near and near-to-far accommodation,” *Ophthalmic and Physiological Optics*, vol. 25, no. 4, pp. 328-339, 2005.
[102] R. S. L. Young and E. Kimura, “Pupillary correlates of light-evoked melanopsin activity in humans,” *Vision research*, vol. 48, no. 7, pp. 862-871, 2008.
[103] W. Szczepanowska-Nowak, A. Hachol, and H. Kasprzak, “System for measurement of the consensual pupil light reflex,” *Optica Applicata*, vol. 34, no. 4, pp. 619-634, 2004.
[104] G. Westheimer, “The maxwellian view,” *Vision Research*, vol. 6, no. 11-12, pp. 669-682, 1966.
[105] A. T. Duchowski, *Eye tracking methodology: Theory and practice*. Springer-Verlag New York Inc, 2007.
[106] D. Li, J. Babcock, and D. J. Parkhurst, “openEyes: a low-cost head-mounted eye-tracking solution,” in *Proceedings of the 2006 symposium on Eye tracking research & applications*, 2006, pp. 95–100.
[107] A. Talukder, J. M. Morookian, S. Monacos, R. Lam, C. LeBaw, and J. L. Lambert, “Eye-tracking architecture for biometrics and remote monitoring,” *Applied optics*, vol. 44, no. 5, pp. 693-700, 2005.
[108] A. Hachol et al., “Measurement of pupil reactivity using fast pupillometry,” *Physiological Measurement*, vol. 28, p. 61, 2007.
[109] P. Magnan, “Detection of visible photons in CCD and CMOS: A comparative view,” *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*, vol. 504, no. 1-3, pp. 199–212, 2003.
[110] Z. Szabó, Z. Tokaji, J. Kálmán, L. Oroszi, A. Pestenácz, and Z. Janka, “The effect of bright light exposure on pupillary fluctuations in healthy subjects,” *Journal of affective disorders*, vol. 78, no. 2, pp. 153-156, 2004.
[111] A. Nikolaou, S. E. Schiza, S. G. Giakoumaki, P. Roussos, N. Siafakas, and P. Bitsios, “The 5-min pupillary alertness test is sensitive to modafinil: a placebo controlled study in patients with sleep apnea,” *Psychopharmacology*, vol. 196, no. 2, pp. 167-175, 2008.
[112] K. Ukai, K. Tsuchiya, and S. Ishikawa, “Induced pupillary hippus following near vision: increased occurrence in visual display unit workers,” *Ergonomics*, vol. 40, no. 11, pp. 1201-1211, 1997.
[113] J. McNames and M. Aboy, “Reliability and accuracy of heart rate variability metrics versus ECG segment duration,” *Medical & Biological Engineering & Computing*, vol. 44, no. 9, pp. 747-756, Aug. 2006.
[114] Y. Masaoka, K. Hirasawa, F. Yamane, T. Hori, and I. Homma, “Effects of left amygdala lesions on respiration, skin conductance, heart rate, anxiety, and activity of the right amygdala during anticipation of negative stimulus,” *Behavior modification*, vol. 27, no. 5, p. 607, 2003.
[115] A. Michimori, K. Araki, and H. Hagiwara, “Effects of illuminance level on alertness levels and sympathetic activities,” presented at the the 11th Annual Meeting of the Association of Professional Sleep Societies (APSS), 1997, vol. 466, p. 183.
[116] E. Troncoso, M. Rodríguez, and M. Feria, “Light-induced arousal affects simultaneously EEG and heart rate variability in the rat,” *Neuroscience letters*, vol. 188, no. 3, pp. 167-170, 1995.
[117] M. Stanciu, D. Faur, and A. Boev, “ECG measurements and acquisition system for heart rate variability analysis,” presented at the the

6th International Conference on Electromechanical and Power Systems, Chisinau, Moldova, 2007.
[118] C. R. Galbrecht and R. A. Dykman, "On the scoring of heart rate: reply to criticisms," *Psychophysiology*, vol. 2, no. 1, pp. 42-46, 1965.
[119] M. Malik et al., "Heart rate variability: standards of measurement, physiological interpretation, and clinical use," *Circulation*, vol. 93, no. 5, pp. 1043-1065, 1996.
[120] M. A. Peña, J. C. Echeverría, M. T. García, and R. González-Camarena, "Applying fractal analysis to short sets of heart rate variability data," *Medical and Biological Engineering and Computing*, vol. 47, no. 7, pp. 709-717, 2009.
[121] K. Jaywoo, L. Mi-hee, L. Hyoung-Ki, C. Kiwan, B. Seokwon, and K. Sangryong, "Heart rate monitor for portable MP3 player," presented at the the 27th Int Conf of the IEEE EMBS, Shanghai, China, 2005, pp. 5207-5210.
[122] W. W. Grings and M. E. Dawson, *Emotions and bodily responses: A psychophysiological approach*. Academic Press New York, 1978.
[123] E. Duffy, "The psychological significance of the concept of," *Psychological Review*, vol. 64, no. 5, pp. 265-275, 1957.
[124] M. E. Dawson, A. M. Schell, and D. L. Filion, "The electrodermal system," in *Handbook of psychophysiology*, vol. 2, Cambridge, UK: Cambridge University Press, 2000, pp. 200-223.
[125] R. Edelberg, "Electrical properties of the skin," in *Methods in psychophysiology*, Baltimore, MA: Williams and Wilkin, 1967, pp. 1-53.
[126] R. M. Stern, W. J. Ray, and K. S. Quigley, *Psychophysiological recording*. USA: Oxford University Press, 2001.
[127] C. Karenbach, *Ledalab-a software package for the analysis of phasic electrodermal activity*. Technical report, Allgemeine Psychologie, Institut für Psychologie, 2005.
[128] D. T. Lykken and P. H. Venables, "Direct measurement of skin conductance: A proposal for standardization," *Psychophysiology*, vol. 8, no. 5, pp. 656-672, 1971.
[129] M. Atienza, J. L. Cantero, R. Stickgold, and J. Allan Hobson, "Eyelid movements measured by Nightcap predict slow eye movements during quiet wakefulness in humans," *Journal of sleep research*, vol. 13, no. 1, pp. 25–29, 2004.
[130] C. Cajochen, S. B. S. Khalsa, J. K. Wyatt, C. A. Czeisler, and D. J. Dijk, "EEG and ocular correlates of circadian melatonin phase and human performance decrements during sleep loss," *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, vol. 277, no. 3, p. 640, 1999.
[131] M. F. Marmor and E. Zrenner, "Standard for clinical electro-oculography," *Documenta Ophthalmologica*, vol. 85, no. 2, pp. 115-124, 1993.
[132] G. B. Arden and J. H. Kelsey, "Changes produced by light in the standing potential of the human eye," *The Journal of Physiology*, vol. 161, no. 2, p. 189, 1962.
[133] B. Lam, *Electrophysiology of Vision: Clinical Testing and Applications*, vol. 1. CRC Press, 2005.
[134] K. Hyoki, M. Shigeta, N. Tsuno, Y. Kawamuro, and T. Kinoshita, "Quantitative electro-oculography and electroencephalography as indices of alertness," *Electroencephalography and clinical Neurophysiology*, vol. 106, no. 3, pp. 213-219, 1998.
[135] S. L. Foote, G. Aston-Jones, and F. E. Bloom, "Impulse activity of locus coeruleus neurons in awake rats and monkeys is a function of sensory stimulation and arousal," *Proceedings of the National Acad-*

emy of Sciences of the United States of America, vol. 77, no. 5, p. 3033, 1980.

[136] C. W. Berridge, M. E. Page, R. J. Valentino, and S. L. Foote, "Effects of locus coeruleus inactivation on electroencephalographic activity in neocortex and hippocampus," *Neuroscience*, vol. 55, no. 2, pp. 381-393, 1993.

[137] T. P. Jung, S. Makeig, M. Stensmo, and T. J. Sejnowski, "Estimating alertness from the EEG power spectrum," *Biomedical Engineering, IEEE Transactions on*, vol. 44, no. 1, pp. 60-69, 2002.

[138] P. Badia, B. Myers, M. Boecker, J. Culpepper, and J. R. Harsh, "Bright light effects on body temperature, alertness, EEG and behavior," *Physiology & behavior*, vol. 50, no. 3, pp. 583-588, 1991.

[139] J. K. Wyatt, A. R. D. Cecco, C. A. Czeisler, and D. J. Dijk, "Circadian temperature and melatonin rhythms, sleep, and neurobehavioral function in humans living on a 20-h day," *American Journal of Physiology- Regulatory, Integrative and Comparative Physiology*, vol. 277, no. 4, p. 1152, 1999.

[140] S. Makeig and T. P. Jung, "Tonic, phasic, and transient EEG correlates of auditory awareness in drowsiness," *Cognitive Brain Research*, vol. 4, no. 1, pp. 15-25, 1996.

[141] E. M. Reiman, R. D. Lane, C. Van Petten, and P. A. Bandettini, "Positron emission tomography and functional magnetic resonance imaging," in *Handbook of Psychophysiology*, Cambridge, UK: Cambridge University Press, 2000, pp. 85-118.

[142] T. Wittlinger, I. Martinovic, A. Moritz, and S. Romanzetti, "Evaluation of the Spatial Resolution with 1.5-4 Tesla in a Stenosis Model," *Asian Cardiovascular and Thoracic Annals*, vol. 14, no. 5, p. 387, 2006.

[143] T. Fujiwara et al., "Performance evaluation of a large axial field-of-view PET scanner: SET-2400W," *Annals of nuclear medicine*, vol. 11, no. 4, pp. 307-313, 1997.

[144] K. Ishii et al., "First achievement of less than 1 mm FWHM resolution in practical semiconductor animal PET scanner," *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*, vol. 576, no. 2-3, pp. 435-440, 2007.

[145] J. R. Stickel and S. R. Cherry, "High-resolution PET detector design: modelling components of intrinsic spatial resolution," *Physics in medicine and biology*, vol. 50, p. 179, 2005.

[146] V. Menon and S. Crottaz-Herbette, "Combined EEG and fMRI studies of human brain function," *International Review of Neurobiology*, vol. 66, pp. 291-321, 2005.

[147] L. De Lecea et al., "The hypocretins: hypothalamus-specific peptides with neuroexcitatory activity," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 95, no. 1, p. 322, 1998.

[148] S. Cortese, E. Konofal, and M. Lecendreux, "Alertness and feeding behaviors in ADHD: does the hypocretin/orexin system play a role?," *Medical Hypotheses*, vol. 71, no. 5, pp. 770-5, 2008.

[149] J. M. Cedarbaum and G. K. Aghajanian, "Afferent projections to the rat locus coeruleus as determined by a retrograde tracing technique," *The Journal of Comparative Neurology*, vol. 178, no. 1, pp. 1-15, 1978.

[150] T. L. Horvath et al., "Hypocretin (orexin) activation and synaptic innervation of the locus coeruleus noradrenergic system," *The Journal of Comparative Neurology*, vol. 415, no. 2, pp. 145–159, 1999.

[151] L. Bayer et al., "Orexins (hypocretins) directly excite tuberomammillary neurons," *European Journal of Neuroscience*, vol. 14, no. 9, pp. 1571–1575, 2001.

[152] H. S. Lee, S. H. Park, W. C. Song, and B. D. Waterhouse, "Retrograde study of hypocretin-1 (orexin-A) projections to subdivisions of the dorsal raphe nucleus in the rat," *Brain research*, vol. 1059, no. 1, pp. 35–45, 2005.

[153] S. Burlet, C. J. Tyler, and C. S. Leonard, "Direct and indirect excitation of laterodorsal tegmental neurons by hypocretin/orexin peptides: implications for wakefulness and narcolepsy," *Journal of Neuroscience*, vol. 22, no. 7, p. 2862, 2002.

[154] A. Yamanaka, Y. Muraki, N. Tsujino, K. Goto, and T. Sakurai, "Regulation of orexin neurons by the monoaminergic and cholinergic systems," *Biochemical and biophysical research communications*, vol. 303, no. 1, pp. 120-129, 2003.

[155] M. A. Kim, H. S. Lee, B. Y. Lee, and B. D. Waterhouse, "Reciprocal connections between subdivisions of the dorsal raphe and the nuclear core of the locus coeruleus in the rat," *Brain research*, vol. 1026, no. 1, pp. 56–67, 2004.

[156] J. De Keyser, G. Ebinger, and G. Vauquelin, "Evidence for a widespread dopaminergic innervation of the human cerebral neocortex," *Neuroscience letters*, vol. 104, no. 3, pp. 281-285, 1989.

[157] Y. P. Hou, I. D. Manns, and B. E. Jones, "Immunostaining of cholinergic pontomesencephalic neurons for [alpha] 1 versus [alpha] 2 adrenergic receptors suggests different sleep-wake state activities and roles," *Neuroscience*, vol. 114, no. 3, pp. 517–521, 2002.

[158] G. Engberg and T. H. Svensson, "Pharmacological analysis of a cholinergic receptor mediated regulation of brain norepinephrine neurons," *Journal of Neural Transmission*, vol. 49, no. 3, pp. 137-150, 1980.

[159] H. Haas and P. Panula, "The role of histamine and the tuberomamillary nucleus in the nervous system," *Nature Reviews Neuroscience*, vol. 4, no. 2, pp. 121-130, 2003.

[160] H. Ericson, A. Blomqvist, and C. Köhler, "Brainstem afferents to the tuberomammillary nucleus in the rat brain with special reference to monoaminergic innervation," *The Journal of Comparative Neurology*, vol. 281, no. 2, pp. 169-192, 1989.

[161] S. M. Reppert and D. R. Weaver, "Coordination of circadian timing in mammals," *Nature*, vol. 418, no. 6901, pp. 935–941, 2002.

[162] V. M. Cassone, M. J. Chesworth, and S. M. Armstrong, "Entrainment of rat circadian rhythms by daily injection of melatonin depends upon the hypothalamic suprachiasmatic nuclei," *Physiology & behavior*, vol. 36, no. 6, pp. 1111-1121, 1986.

[163] L. Ruggiero, C. N. Allen, R. L. Brown, and D. W. Robinson, "Research mice with early retinal degeneration show differences in neuropeptide expression in the suprachiasmatic nucleus," *Behavioral and Brain Functions*, vol. 36, no. 6, pp. 1-7, 2010.

[164] M. E. Harrington, "The ventral lateral geniculate nucleus and the intergeniculate leaflet: interrelated structures in the visual and circadian systems," *Neuroscience & Biobehavioral Reviews*, vol. 21, no. 5, pp. 705–727, 1997.

[165] K. Edelstein and S. Amir, "The role of the intergeniculate leaflet in entrainment of circadian rhythms to a skeleton photoperiod," *Journal of Neuroscience*, vol. 19, no. 1, p. 372, 1999.

[166] C. B. Saper, J. Lu, T. C. Chou, and J. Gooley, "The hypothalamic integrator for circadian rhythms," *TRENDS in Neurosciences*, vol. 28, no. 3, pp. 152–157, 2005.

[167] A. H. Luo and G. Aston-Jones, “Circuit projection from suprachiasmatic nucleus to ventral tegmental area: a novel circadian output pathway,” *European Journal of Neuroscience*, vol. 29, no. 4, pp. 748–760, 2009.

[168] D. S. Charney, C. Grillon, and J. D. Bremner, “Review: The Neurobiological Basis of Anxiety and Fear: Circuits, Mechanisms, and Neurochemical Interactions (Part I),” *The Neuroscientist*, vol. 4, no. 1, p. 35, 1998.

[169] E. J. Van Bockstaele, E. E. O. Colago, and R. J. Valentino, “Amygdaloid corticotropin-releasing factor targets locus coeruleus dendrites: substrate for the co-ordination of emotional and cognitive limbs of the stress response,” *Journal of neuroendocrinology*, vol. 10, no. 10, pp. 743-758, 1998.

[170] G. Vandewalle et al., “Spectral quality of light modulates emotional brain responses in humans,” *Proceedings of the National Academy of Sciences*, vol. 107, no. 45, pp. 19549-19554, Oct. 2010.

[171] H. J. Suk and H. Irtel, “Emotional response to simple color stimuli,” *Kansai Eng*, vol. 7, no. 2, pp. 181-188, 2008.

[172] D. M. Berson, “Strange vision: ganglion cells as circadian photoreceptors,” *TRENDS in Neurosciences*, vol. 26, no. 6, pp. 314–320, 2003.

[173] M. G. Figueiro, A. Bierman, B. Plitnick, and M. S. Rea, “Preliminary evidence that both blue and red light can induce alertness at night,” *BMC neuroscience*, vol. 10, no. 1, p. 105, 2009.

[174] L. A. Segall, A. Milet, F. Tronche, and S. Amir, “Brain glucocorticoid receptors are necessary for the rhythmic expression of the clock protein, PERIOD2, in the central extended amygdala in mice,” *Neuroscience letters*, vol. 457, no. 1, pp. 58-60, 2009.

[175] D. H. Loh et al., “Rapid changes in the light/dark cycle disrupt memory of conditioned fear in mice,” *PloS one*, vol. 5, no. 9, pp. 227-234, 2010.

[176] N. Goel, T. M. Lee, and L. Smale, “Suprachiasmatic nucleus and intergeniculate leaflet in the diurnal rodent Octodon degus: retinal projections and immunocytochemical characterization,” *Neuroscience*, vol. 92, no. 4, pp. 1491-1509, 1999.

[177] J. L. Price and W. C. Drevets, “Neurocircuitry of mood disorders,” *Neuropsychopharmacology*, vol. 35, no. 1, pp. 192–216, 2009.

[178] P. J. Lang et al., “Emotional arousal and activation of the visual cortex: an fMRI analysis,” *Psychophysiology*, vol. 35, no. 2, pp. 199-210, 1998.

[179] R. D. Lane et al., “Neuroanatomical correlates of pleasant and unpleasant emotion,” *Neuropsychologia*, vol. 35, no. 11, pp. 1437–1444, 1997.

[180] L. Eiseman, *Color : Messages & Meanings*. Gloucester: Hand Books Press, 2006.

[181] F. H. Mahnke, *Color, environment, and human response*. Van Nostrand Reinhold New York, 1996.

[182] M. Hemphill, “A Note on Adults’ Color–Emotion Associations,” *The Journal of genetic psychology*, vol. 157, no. 3, pp. 275-280, 1996.

[183] L. B. Wexner, “The degree to which colors (hues) are associated with mood-tones,” *Journal of Applied Psychology*, vol. 38, no. 6, pp. 432-435, 1954.

[184] N. Kaya and H. H. Epps, “Relationship between color and emotion: A study of college students.,” *College Student Journal*, vol. 38, no. 3, pp. 396-406, 2004.

[185] L. Laufer, E. Lang, L. Izso, and E. Nemeth, "Psychophysiological effects of coloured lighting on older adults," *Lighting Research and Technology*, vol. 41, no. 4, pp. 371-378, Aug. 2009.
[186] K. L. Phan, T. Wager, S. F. Taylor, and I. Liberzon, "Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI," *Neuroimage*, vol. 16, no. 2, pp. 331–348, 2002.
[187] L. Pessoa, S. Japee, D. Sturman, and L. G. Ungerleider, "Target visibility and visual awareness modulate amygdala responses to fearful faces," *Cerebral Cortex*, vol. 16, no. 3, p. 366, 2006.
[188] P. Vuilleumier, "How brains beware: neural mechanisms of emotional attention," *Trends in Cognitive Sciences*, vol. 9, no. 12, pp. 585-594, Dec. 2005.
[189] L. A. Benevento and J. H. Fallon, "The ascending projections of the superior colliculus in the rhesus monkey (Macaca mulatta)," *The Journal of Comparative Neurology*, vol. 160, no. 3, pp. 339-361, 1975.
[190] M. F. Folstein and R. Luria, "Reliability, validity, and clinical application of the Visual Analogue Mood Scale," *Psychological Medicine*, vol. 3, no. 4, pp. 479-486, 1973.
[191] G. S. Lall et al., "Distinct contributions of rod, cone, and melanopsin photoreceptors to encoding irradiance," *Neuron*, vol. 66, no. 3, pp. 417–428, 2010.
[192] J. Nathan et al., "Scotopic and photopic visual thresholds and spatial and temporal discrimination evaluated by behavior of mice in a water maze," *Photochemistry and photobiology*, vol. 82, no. 6, pp. 1489-1494, 2006.
[193] D. M. McNair, M. Lorr, and L. F. Droppleman, "Manual for the profile of mood states," *San Diego, CA: Educational and Industrial Testing Service*, vol. 1981, p. 1992, 1971.
[194] H. C. Thorne, K. H. Jones, S. P. Peters, S. N. Archer, and D. J. Dijk, "Daily and seasonal variation in the spectral composition of light exposure in humans," *Chronobiology International*, vol. 26, no. 5, pp. 854-866, 2009.
[195] J. A. Horne and O. Ostberg, "A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms.," *International Journal of Chronobiology*, vol. 4, no. 2, p. 97, 1976.
[196] D. Dumortier, B. Coutelier, T. Faulcon, and F. V. Roy, "PHOTOLUX: a new luminance mapping system based on Nikon Coolpix digital cameras," *Lux Europa*, 2005.
[197] *Criteria for a recommended standard: occupational exposure to carbon dioxide*. National Institute for Occupational Safety and Health, 1976, p. 179.
[198] M. Hebert, S. K. Martin, C. Lee, and C. I. Eastman, "The effects of prior light history on the suppression of melatonin by light in humans," *Journal of pineal research*, vol. 33, no. 4, pp. 198-203, 2002.
[199] R. G. Foster and L. Kreitzman, *Rhythms of Life: The Biological Clocks That Control the Daily Lives of Every Living Thing*. London: Profile Books, 2004.
[200] A. Hedge, *Biological Rhythms: DEA 325*. Cornell University, 1999.
[201] S. Fleischer, H. Krueger, and C. Schierz, "Effect of brightness distribution and light colours on office staff," in *The 9th European Lighting Conference Proceeding Book of Lux Europa*, 2001, pp. 77-80.
[202] W. van Bommel, "Dynamic lighting at work - both in level and colour," presented at the CIE 2006 Ottawa, Ottawa, 2006.
[203] T. H. Monk, "The post-lunch dip in performance," *Clinics in Sports Medicine*, vol. 24, no. 2, p. e15-e23, 2005.

[204] "ICNIRP. Guidelines on Limits of Exposure to BroadBand Incoherent Optical Radiation (0.38 to 3μm)," *Health Physics*, vol. 73, no. 3, pp. 539-554, 1997.

[205] J. P. Niskanen, M. P. Tarvainen, P. O. Ranta-aho, and P. A. Karjalainen, "Software for advanced HRV analysis," *Computer methods and programs in biomedicine*, vol. 76, no. 1, pp. 73-81, 2004.

[206] Y. C. Arai et al., "The influence of acupressure at extra 1 acupuncture point on the spectral entropy of the EEG and the LF/HF ratio of heart rate variability," *Evidence-Based Complementary and Alternative Medicine*, vol. 2011, pp. 1-6, 2008.

[207] R. N. Golden et al., "The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence," *American Journal of Psychiatry*, vol. 162, no. 4, p. 656, 2005.

[208] T. Partonen and J. Lönnqvist, "Bright light improves vitality and alleviates distress in healthy people," *Journal of Affective disorders*, vol. 57, no. 1-3, pp. 55-61, 2000.

[209] C. Grillon and M. Davis, "Fear potentiated startle conditioning in humans: Explicit and contextual cue conditioning following paired versus unpaired training," *Psychophysiology*, vol. 34, no. 4, pp. 451-458, 1997.

[210] A. G. Nasello, C. Machado, J. F. Bastos, and L. F. Felicio, "Sudden darkness induces a high activity-low anxiety state in male and female rats," *Physiology & behavior*, vol. 63, no. 3, pp. 451-454, 1998.

Aalto-DD 72/2011

ISBN 978-952-60-4249-7 (pdf)
ISBN 978-952-60-4248-0
ISSN-L 1799-4934
ISSN 1799-4942 (pdf)
ISSN 1799-4934

Aalto University
School of Electrical Engineering
Department of Electronics, Lighting Unit
www.aalto.fi

BUSINESS + ECONOMY

ART + DESIGN + ARCHITECTURE

SCIENCE + TECHNOLOGY

CROSSOVER

DOCTORAL DISSERTATIONS