

1 Evidence that homeostatic sleep regulation depends on ambient illuminance levels

2

3 Christian Cajochen^{1,2}, Carolin Reichert^{1,2}, Micheline Maire³, Luc J M Schlangen⁴, Christina
4 Schmidt⁵, Antoine U Viola⁶, Virginie Gabel⁷

5

- 6 1. Centre for Chronobiology, Psychiatric Hospital of the University of Basel, Switzerland
- 7 2. Transfaculty Research Platform Molecular and Cognitive Neurosciences, University of
8 Basel, Switzerland
- 9 3. Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland.
- 10 4. Intelligent Lighting Institute, School of Innovation Sciences, Department of Human
11 Technology Interaction, Eindhoven University of Technology, The Netherlands
- 12 5. GIGA-Research, Cyclotron Research Centre-In Vivo Imaging Unit, University of Liège,
13 Belgium; Psychology and Neuroscience of Cognition Research Unit (PsyNCog), Faculty of
14 Psychology and Educational Sciences, University of Liège, Belgium
- 15 6. PPRS-Research, Colmar, France
- 16 7. Department of Psychiatry and Behavioral Sciences, Stanford University, Palo Alto CA

17

18 **Keywords:** circadian timing system, EEG, spectral analysis, sleepiness, melanopic equivalent
19 daylight illuminance, melatonin, slow-wave activity

20 **Corresponding author:**

21 Christian Cajochen, PhD

22 Centre for Chronobiology

23 Psychiatric Hospital of the University of Basel,

24 Wilhelm Kleinstr. 27

25 CH-4002 Basel, Switzerland

26 TEL: +41613255318

27 FAX: +41 613255577

28 Email: christian.cajochen@upk.ch

29 **Abstract**

30 We examined whether the ambient illuminance during extended wakefulness modulates the
31 homeostatic increase in human deep sleep [i.e. slow wave sleep (SWS) and
32 electroencephalographic (EEG) slow-wave activity (SWA)] in healthy young and older
33 volunteers.

34 Thirty-eight young and older participants underwent 40 hours of extended wakefulness [i.e.
35 sleep deprivation (SD)] once under dim light (DL: 8 lux, 2800K), and once under either white
36 light (WL: 250 lux, 2800K) or blue-enriched white light (BL: 250 lux, 9000K) exposure. Subjective
37 sleepiness was assessed hourly and polysomnography was quantified during the baseline night
38 prior to the 40-h SD and during the subsequent recovery night.

39 Both the young and older participants responded with a higher homeostatic sleep response to
40 40-h SD after WL and BL than after DL. This was indexed by a significantly faster intra-night
41 accumulation of SWS and a significantly higher response in relative EEG SWA during the
42 recovery night after WL and BL than after DL for both age groups. No significant differences
43 were observed between the WL and BL condition for these two particular SWS and SWA
44 measures. Subjective sleepiness ratings during the 40-h SD were significantly reduced under
45 both WL and BL compared to DL, but were not significantly associated with markers of sleep
46 homeostasis in both age groups.

47 Our data indicate that not only the duration of prior wakefulness, but also the experienced
48 illuminance during wakefulness affects homeostatic sleep regulation in humans. Thus, working
49 extended hours under low illuminance may negatively impact subsequent sleep intensity in
50 humans.

51

52 Introduction

53 It is firmly established that human sleep regulation is under the control of the circadian timing
54 system and an hourglass process keeping track of prior sleep-wake history as conceptualized in
55 the two-process model of sleep regulation (for a review see [1]). In fact, the amount of time
56 spent awake prior to sleep onset is the most important determinant of sleep intensity in
57 mammals [2]. Sleep homeostasis can be accurately tracked, quantified and modelled by
58 electroencephalographic (EEG) slow-wave activity (SWA) during non-rapid eye movement
59 (NREM) sleep [3], which is considered an important marker for optimal brain functioning [4].
60 Later studies refined the homeostatic sleep-wake process with respect to its brain topography,
61 with frontal brain areas more susceptible in their response to prior wake duration [5,6] and also
62 with respect to experience-dependent aspects during wakefulness. Thus, superimposed on the
63 global homeostatic regulation of SWA, local SWA increases have been reported to depend on
64 scheduled activity/experience such as physical activity [7], learning [8], and stress [9] volunteers
65 or animals were exposed to prior sleep. Along these lines, Tononi and Cirelli have proposed the
66 synaptic homeostasis hypothesis (SHY), which assumes that sleep serves to re-establish
67 synaptic processes which have been challenged by different experiences during prior
68 wakefulness (for a review see [10]). According to the SHY, “sleep is the price to pay for waking
69 plasticity, to avoid runaway potentiation, decreased signal-to-noise ratio, and impaired learning
70 due to saturation” [10].

71 Interestingly, the potential impact on sleep homeostatic aspects of environmental factors such
72 as light, noise and temperature experienced during extended wakefulness have, to our best
73 knowledge, not yet been investigated systematically under controlled laboratory conditions in
74 humans. Light is of particular interest, since, besides its function for vision, it also activates non-
75 image forming brain regions implicated in the regulation of circadian rhythms, mood, sleep and
76 learning (for a review see [11]). In addition, humans living in modern societies are spending
77 more time indoors under rather dim light conditions [12], which potentially exacerbates when
78 working extended hours, particularly during the night. Thus, here we investigated whether
79 different ambient lighting conditions experienced during extended wakefulness impact on sleep
80 homeostatic regulation. The rationale for this study was twofold: First, we have evidence that

81 evening lighting conditions modulate EEG SWA during subsequent sleep after a normal waking
82 day [13-15] and second, sleep homeostatic processes change with age, such that the relative
83 SWA response to sleep loss is diminished in frontal brain areas in older compared to young
84 healthy volunteers [16]. Thus, we hypothesized 1.) that the increase in frontal EEG SWA after
85 sleep loss is more pronounced after experienced illuminance levels at 250 lux than after
86 experienced dim illuminance at < 8 lux in both healthy young and older volunteers, and 2.) that
87 the light induced enhancement in the EEG SWA response is stronger in young than older
88 participants.

89

90 **Results and Discussion**

91 As expected - confirming numerous previous reports (as an example [16,17]) - sleep was more
92 consolidated after 40-h of SD in the recovery night when compared to the baseline night as
93 indexed by more SWS at the expense of stage 2, stage 1 and wakefulness leading to a
94 significantly higher sleep efficiency in the recovery night (factor 'night-type': $F_{1,127}$ at least 46.5,
95 p at least 0.001). The response of sleep architecture to the 40-h SD was rather similar in the
96 young and older volunteers, with the exception for stage 3 (factor 'age': $F_{1,33} = 20.0$, $p=0.001$)
97 and stage 4 (factor 'age': $F_{1,33} = 16.6$, $p=0.002$) as well as rapid eye movement (REM) sleep
98 (factor 'age': $F_{1,33} = 4.4$, $p=0.04$). In general, older people showed a stronger increase in stage 3
99 sleep in response to 40-h SD, while the young, reacted with a more pronounced increase in
100 stage 4 sleep [see relative changes in sleep architecture (recovery minus baseline night), Table
101 1]. This was most likely due to a reduced amplitude in sleep EEG delta waves normally occurring
102 with healthy ageing (for a review see [18,19]). A significance for the factor 'light condition' ($F_{2,50}$
103 $= 3.3$, $p=0.04$) was only found for stage 4 sleep, yielding a higher relative

Age group	Young			Older			Light cond	Age	Light cond x Age
Light condition	Dim Light	White Light	Blue Light	Dim Light	White Light	Blue Light			
TST (min)	26.2 ± 6.0	30.8 ± 8.9	33.7 ± 9.9	12.9 ± 5.1	36.6 ± 15.2	26.6 ± 9.6	n.s.	n.s.	n.s.
SE (%)	3.0 ± 0.7	5.3 ± 2.0	4.2 ± 1.2	3.0 ± 1.0	6.5 ± 2.7	5.8 ± 1.7	0.08	n.s.	n.s.
MT (%)	-0.1 ± 0.1	0.0 ± 0.1	-0.2 ± 0.2	0.3 ± 0.1	0.4 ± 0.1	0.3 ± 0.2	n.s.	*	n.s.
Wake (%)	-3.4 ± 0.8	-7.2 ± 3.0	-5.2 ± 1.6	-4.8 ± 1.4	-10.2 ± 5.0	-8.8 ± 2.5	0.08	n.s.	n.s.
Stage 1 (%)	-3.2 ± 0.6	-2.5 ± 0.8	-3.0 ± 0.8	-2.2 ± 0.8	-4.5 ± 1.4	-3.9 ± 1.9	n.s.	n.s.	n.s.
Stage 2 (%)	-4.5 ± 0.9	-5.2 ± 1.4	-5.5 ± 1.1	-6.5 ± 2.3	-6.2 ± 2.6	-7.6 ± 2.2	n.s.	n.s.	n.s.
Stage 3 (%)	0.6 ± 0.7	1.9 ± 1.0	0.2 ± 0.7	5.0 ± 1.4	6.1 ± 1.1	4.8 ± 1.3	n.s.	*	n.s.
Stage 4 (%)	6.9 ± 0.7	6.7 ± 0.8	8.8 ± 0.7	2.7 ± 0.9	2.8 ± 0.8	4.0 ± 2.0	*	*	n.s.
SWS (%)	7.5 ± 1.0	8.6 ± 1.3	8.9 ± 0.8	7.7 ± 1.7	8.9 ± 1.3	8.9 ± 1.7	n.s.	n.s.	n.s.
NREMS (%)	3.0 ± 1.0	3.4 ± 1.4	3.5 ± 1.1	1.1 ± 1.1	2.8 ± 1.8	1.2 ± 2.1	n.s.	n.s.	n.s.
REMS (%)	0.2 ± 0.7	-1.0 ± 1.2	-0.5 ± 0.8	1.0 ± 1.3	1.7 ± 1.9	2.7 ± 1.3	n.s.	*	n.s.
S1 Latency (min)	-3.9 ± 4.5	0.1 ± 2.6	3.4 ± 2.2	8.3 ± 2.2	0.3 ± 5.8	5.4 ± 3.5	n.s.	n.s.	*
S2 Latency (min)	-0.4 ± 2.6	-0.7 ± 2.8	3.0 ± 2.3	10.0 ± 2.3	3.7 ± 3.9	4.8 ± 3.2	n.s.	0.07	*
REMS Latency (min)	-39.7 ± 8.6	-30.1 ± 16.1	-28.7 ± 9.9	-14.8 ± 6.8	-9.8 ± 16.3	-13.0 ± 6.6	n.s.	0.08	n.s.

104

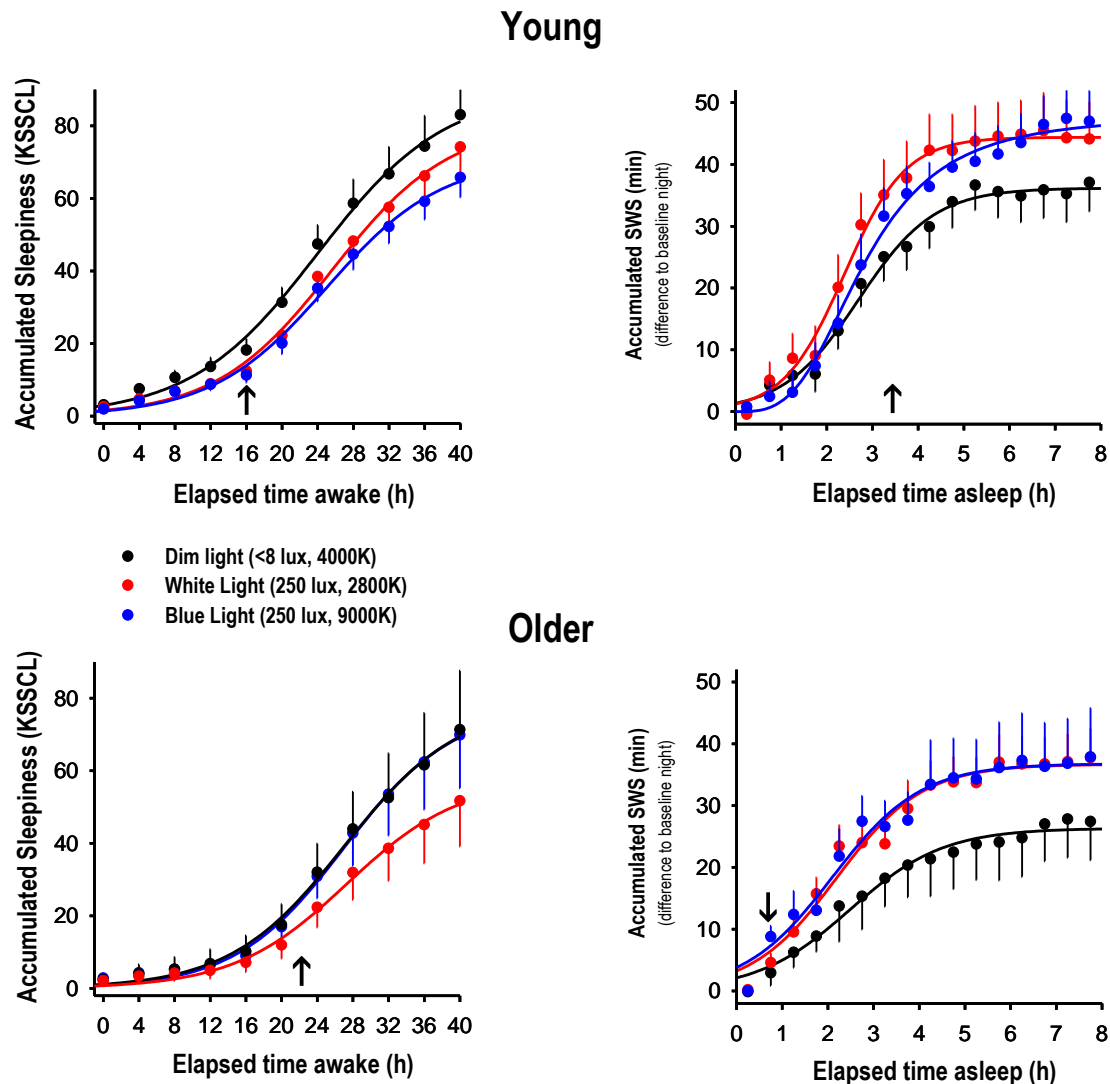
105

106 **Table 1:** Difference in sleep variables between the recovery and baseline night in minutes for
107 TST (total sleep time), S1 (sleep stage 1) latency, S2 (sleep stage 2) latency, and REMS (rapid eye
108 movement sleep) latency; and in percentages of TST for Stages 1 to 4 sleep, NREMS (non-rapid
109 eye movement sleep), REMS, wake and MT (movement time). SE (sleep efficiency) was
110 calculated as the ratio of the duration between lights off and lights on (i.e. bedtime) and
111 TST*100 (mean values, SEM) per light condition and age group. The last 3 columns depict
112 significances for the factors 'light condition', 'age' and their interaction term assessed via the
113 mixed linear model (* $p < 0.05$; n.s. = not significant, see methods for more information).

114

115 increase after WL and BL compared to DL in both age groups. In addition, we found a significant
116 interaction between 'age group' and 'light condition', for sleep latency to stage 1 ($F_{2,51} = 4.2$,
117 $p = 0.02$) and latency to stage 2 ($F_{2,51} = 4.0$, $p = 0.02$) respectively (Table 1). Unexpectedly, unlike
118 the young volunteers, the older volunteers did not fall asleep faster after 40-SD, particularly
119 after DL. However, this is in agreement with a previous report by Münch et al. 2004 [16], who
120 also found no reduction in sleep latency after 40-SD in older but young participants in a very
121 similar study design setting. We further analyzed the intra-sleep build-up of slow wave sleep
122 (SWS) and found a significantly faster accumulation of SWS in WL and BL compared to DL in
123 both age groups (Figure 1, right panels). Mixed model analyses per 15-min time interval
124 including the factors

125



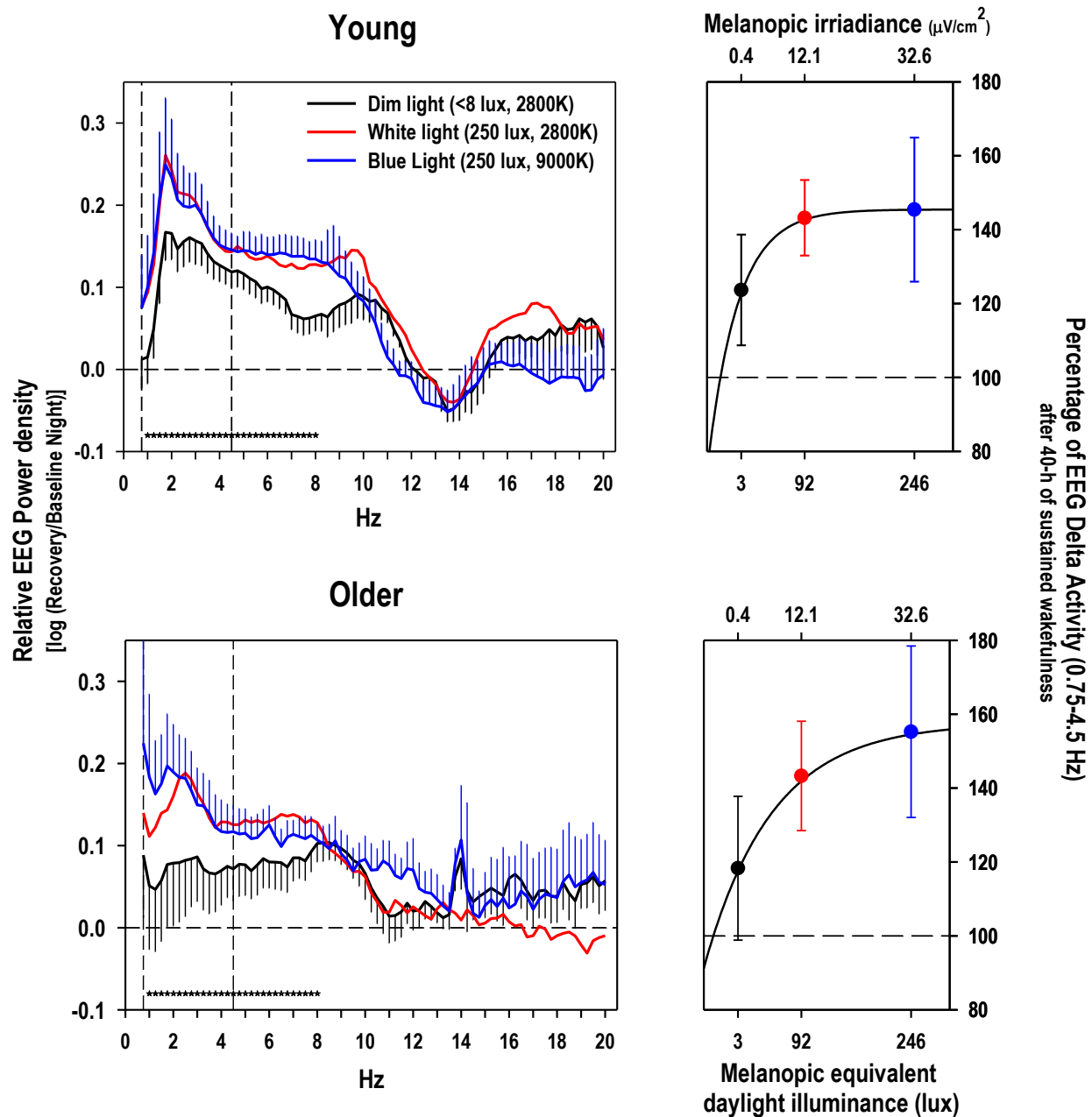
126

127 **Figure 1.** Accumulation curves of subjective sleepiness (KSSCL ratings) and SWS (min) across the
 128 40-h SD and across the recovery night after 40-h SD under dim light (black), white light (red)
 129 and blue-enriched white light (blue); mean values + or – SEM per age group. The arrows on the
 130 abscissa indicate the time point of the first occurrence of a significant difference between DL
 131 and BL or WL respectively.

132

133 ‘age’ and ‘light condition’, yielded significance for the factor ‘light condition’ starting 3.5 hours
 134 after lights off for the young, and after 75 minutes after lights off in the older (arrows in Figure
 135 1, right-hand panels). The factors ‘age’ and the interaction ‘age x light condition’ did not reach

136 significant levels in any of the time intervals. Thus, SWS accumulation during the night, a sleep
137 homeostatic marker, was more pronounced in WL and BL than in DL in both age groups.
138 To further corroborate our hypothesis, we calculated EEG power spectra during NREM sleep in
139 the range of 0.75 and 20 Hz during the recovery night and expressed them relative to the
140 corresponding values during the baseline night (Figure 2, left-hand panels).
141 Mixed model analyses on the relative EEG activity per single frequency bin yielded a significant
142 effect of the factor 'light condition' in the range of 1 to 8 Hz (p at least 0.04) independent of the
143 factor 'EEG derivation' and 'age'. The factor 'light condition' was also significant for the
144 collapsed frequency bins in the range from 0.75 to 4.5 Hz, the SWA band, (factor 'light
145 condition', $F_{2,224} = 5.72$; $p = 0.004$) and the collapsed frequency bins in the theta range from 4.75
146 to 8 Hz, (factor 'light condition', $F_{2,224} = 9.4$; $p = 0.0001$). *Post-hoc* comparisons for each age group
147 separately indicated a significantly stronger increase in relative EEG SWA after WL than after DL
148 ($p = 0.0005$) for the young participants, while the difference between BL and DL did not reach
149 significance, probably due to the higher inter-participant variability in the BL than in the WL
150 data in the



151

152 **Figure 2.** Left-hand panels: relative EEG power density during NREM sleep during the recovery
 153 night with respect to the baseline night (log ratio) in the frequency range from 0.75 to 20 Hz in
 154 the young and older group (mean values + or - SEM, black DL, red WL and in blue BL, for the
 155 sake of clarity, the SEMs for the WL condition were omitted). Right-hand panels: Percentage of
 156 NREMS EEG SWA in the range of 0.75-4.5 Hz during the recovery night after 40-h SD in DL
 157 (black), WL (red), and BL (blue); mean values \pm SEMs, 100%= value during the corresponding
 158 baseline night) plotted against melanopic equivalent daylight illuminance in lux, the new

159 standard for ipRGCs driven light responses [http://www.cie.co.at/publications/cie-system-](http://www.cie.co.at/publications/cie-system-metrology-optical-radiation-iprgc-influenced-responses-light-0)
160 [metrology-optical-radiation-iprgc-influenced-responses-light-0](http://www.cie.co.at/publications/cie-system-metrology-optical-radiation-iprgc-influenced-responses-light-0). The light induced rise in EEG
161 SWA response to 40-h SD was fitted by using an exponential rise function with 3 parameters:
162 $f=y_0+a*(1-\exp(-b*x))$ on the mean values.

163
164 young group (Figure 2, left-hand panel). For the older group, only the difference in relative EEG
165 SWA between BL and DL yielded significance ($p=0.04$, Figure 2, right-hand panel). Very similar
166 results were found for the *post-hoc* comparisons for the EEG theta band (data not reported).

167 Due to the fact that Gabel et al. 2017 [20] reported significantly lower sleepiness levels in the
168 course of the 40-h SD under both WL and BL compared to DL in the same study, we
169 reconfirmed this result by accumulating ratings on the Karolinska Sleepiness Symptoms
170 Checklist (KSSCL) across the 40-h SD in both age groups (Figure 1, left-hand panel). Subjective
171 symptoms of sleepiness were significantly reduced in both BL and WL compared to DL after 16
172 hours of prior wakefulness in the young. In the older, only the difference between DL and WL
173 yielded significance after 22 hours of prior wakefulness. Furthermore, we tested whether these
174 difference in subjective sleepiness were related to the observed changes in the EEG SWA
175 response to sleep deprivation under differential lighting conditions, and did not find a
176 significant correlation between the light induced alerting effect during wakefulness and the
177 light-induced difference in EEG SWA response thereafter ($r = -0.03$, $p=0.83$, Spearman rank
178 correlation). In addition, we correlated sleepiness ratings during each 2-h time interval with
179 relative EEG SWA and did not find consistent associations between those measures, neither a
180 difference for either the light condition and age group (data not shown). All of this makes it
181 unlikely that the more pronounced EEG SWA response after WL's and BL's was related to the
182 alerting properties of light seen during the previous 40-h SD [20].

183 Based on our stringently controlled laboratory data, we have first evidence that homeostatic
184 regulation of human sleep is modulated by prior light exposure levels, which indicates that
185 environmental factors during wakefulness shape human sleep architecture. This goes in line
186 with a recent sleep study performed in a nocturnal primate in the wild, reporting major
187 influences of environmental factors (i.e. light and temperature) on monophasic sleep and

188 activity patterns [21]. In a human field study, Wams et al. 2017 [22] found that individuals
189 exposed to higher maximal light intensities experienced larger subsequent SWS accumulation,
190 similarly as reported here. However, in their observational study prior wakefulness was not
191 manipulated, and EEG delta activity was not measured. Therefore, in their study, one cannot
192 rule out whether prior sleep had an influence on subsequent light exposure. It remains unclear
193 whether their result reflects an effect of prior light exposure on sleep homeostasis or rather an
194 alternation in the circadian phase angle of entrainment. Furthermore, in their study both REM
195 sleep and wake accumulation were reported to be affected by light exposure. In contrast, in our
196 study we can rule out effects of sleep on future light exposures and changes in circadian phase,
197 since sleep-wake timing was controlled for, and we have no indication that circadian melatonin
198 phase was altered between the three light conditions [20]. Furthermore, only stage 4 sleep and
199 EEG power density in the delta and theta range was significantly affected by the factor 'light
200 condition' in our study, while REM sleep and wakefulness during sleep was not. All of this let us
201 assume that the different lighting conditions during the 40-h SD impacted on the homeostatic
202 aspect of sleep regulation.

203 We could not confirm our second hypothesis that the increase in the homeostatic sleep
204 response by light is stronger in the young than older participants. Although, we confirmed the
205 well-known age-related reduction in SWS and the age-related increase in wakefulness after
206 sleep onset, the relative increase in both indices of sleep homeostasis (i.e. SWS and EEG SWA)
207 was similarly enhanced after 40-h SD in WL and BL in both age groups. Thus, we corroborate
208 the fact that homeostatic aspects of sleep regulation are fully operational in healthy ageing,
209 despite lower EEG SWA levels and more wakefulness after sleep onset [18,19].

210 Sleep alterations after exposures to differential light modalities in the evening have been
211 frequently reported, most of them showing acute alerting responses to light extending over
212 into the night sleep episode as verified by longer sleep latencies, reduced EEG SWA in the first
213 cycle or REM sleep alterations [13,14,16,23]. To our best knowledge however, there is not yet a
214 study looking at extended light exposures (i.e. 40 h) and its repercussions on subsequent sleep.
215 Thus, although participants rated themselves less sleepy under WL and BL compared to DL in
216 our study [20], which can be related to a tonic and less so to an acute alerting response to light,

217 we did not find any significant association between how sleepy our participants felt during the
218 40-h SD and their homeostatic sleep response afterwards. This indicates that subjective
219 alertness ratings, although showing an increase across the 40-SD, may not be a good predictor
220 for homeostatic sleep regulation in the subsequent recovery night.

221 It is usually assumed that melatonin suppression by light is predominantly mediated via
222 intrinsically photosensitive ganglion [(ipRGCs, for a review see [24]), by activation of the
223 photopigment melanopsin already at rather low irradiances [25,26]. If this also holds for the
224 light induced increase in EEG SWA response to SD, one could have expected a stronger effect
225 after BL than WL, since melanopsin excitation was a 2.7 fold stronger in BL than WL (32.6 vs.
226 $12.1 \mu\text{W}/\text{cm}^2$ melanopic irradiance or 246 vs. 91.6 melanopic daylight equivalent illuminance).
227 However, we did not find any significant differences between WL and BL in both age groups
228 neither for stage 4 sleep, or SWS accumulation or relative EEG SWA. Thus, it could be that our
229 observed light effects on electrophysiological correlates of sleep homeostasis were not
230 mediated via melanopsin or that the response did already saturate out at the light level (i.e.
231 250 photopic lux) used in our study. Indeed, saturation of the melatonin response to
232 polychromatic light was reported to be at $36.6 \mu\text{W}/\text{cm}^2$ melanopsin weighted irradiance in
233 young volunteers in the absence of a mydriatic [27,28]. Thus, at our calculated $32.6 \mu\text{W}/\text{cm}^2$
234 melanopsin weighted irradiance for the BL condition, we were probably already approaching
235 the saturation part of the dose-response curve (Figure 2, right-hand panels). In other words, at
236 light intensities of 250 photopic lux, a difference between 2500 and 9000 Kelvin does not elicit
237 a differential response in melatonin suppression (see [20]) and EEG SWA homeostasis. In fact,
238 the spectral composition (colour and/or correlated colour temperature) of light exposure can
239 be more important at low ambient light levels (< 200 lux): after passing a certain threshold of
240 brightness a particular response can reach saturation, thus making the actual spectral
241 composition above this brightness less relevant for the response-size.

242 Our data can be interpreted in the light of the SHY hypothesis assuming a use-dependent
243 aspect of synaptic usage during wakefulness, which needs recovery or downscaling during
244 subsequent sleep [10]. Along these lines, we speculate that the experienced ambient light
245 intensity modulates “synaptic load” during wakefulness, being higher in a brighter than dim

246 environment, and eventually leading to more EEG SWA in the subsequent night. This is in line
247 with data in mice which demonstrated that sustained neuronal activation induced by active
248 exploration in awake animals leads to an increase in SWA during subsequent sleep [29]. If this
249 was true, also a more local response in EEG SWA should be expected, as demonstrated in
250 several studies on use-dependent aspects of sleep regulation [7,8,30,31]. However, in contrast
251 to these studies, in our study light exposure was not aimed at providing unilateral sensory
252 stimulation and therefore did not lead to a local EEG response- at least in our 12-channel EEG
253 recordings-, but rather led to a global EEG SWA response in all electrodes. This would favor the
254 idea of a general increase in synaptic upscaling or more EEG activation, which may have been
255 preceded by a general increase in alertness during the 40-SD.

256 Since specific brain regions responsible for homeostatic sleep regulation *per se* have to our
257 knowledge not yet been assured, it is difficult to explain how light modifies sleep homeostasis
258 on the neuroanatomical/neurophysiological level. Based on data in mice showing that
259 melanopsin regulates both sleep-promoting and arousal-promoting responses to light [32], one
260 could assume that ipRGC stimulation through light, particularly in the short-wavelength range,
261 relays to the SCN and thereof to lateral hypothalamic (LH) areas for its arousal-mediating
262 effects [33]. Conversely, light without strong short-wavelength components may decrease LH
263 neuronal activity allowing for increased activity within the ventrolateral preoptic neurons, an
264 important sleep-promoting area. However, how different wavelengths of light activate specific
265 pathways for arousal promotion in humans remains elusive. Interestingly, it has been recently
266 discovered that distinct ipRGC subpopulations mediate light's acute effect on sleep through a
267 circuitry distinct from that of circadian photoentrainment [34]. This corroborates how
268 important the role of the daily cycle of light intensity is in shaping temporal sleep-activity
269 patterns independent of circadian photoentrainment but directly via current ecological and
270 physiological settings [35].

271

272 **Summary and Conclusion**

273 Our data show that the light environment impacts on human homeostatic sleep regulation
274 independent of circadian effects. This adds to the growing insight that besides its impact on

275 circadian physiology, light is an important environmental factor in shaping sleep-wake
276 behaviour. Our results may have important ramifications when it comes to designing light
277 solutions that support alertness or sleep promotion, while minimizing effects on the circadian
278 timing system.

279 **Methods**

280

281 *Ethical Approval*

282 All participants gave written informed consent for inclusion before they participated in the
283 study. The study protocol, screening questionnaires and consent forms were approved by the
284 local ethics committee (EKBB/Ethikkommission beider Basel, Switzerland, Project identification
285 code: 247/11), and conformed to the Declaration of Helsinki.

286

287 *Study volunteers*

288 Potential study volunteers completed a general medical questionnaire, the Epworth Sleepiness
289 Scale (ESS), the Horne Ostberg Morningness Eveningness Questionnaire (MEQ), the Munich
290 Chronotype Questionnaire (MCTQ), the Pittsburgh Sleep Quality Index (PSQI), and Beck
291 Depression Inventory II (BDI-II). Based on the participants' questionnaire data, only participants
292 fulfilling the inclusion criteria [for details see [20]] were selected for study participation. In a
293 next step, we ruled out sleep disturbances, and tested the volunteers' ability to sleep in a new
294 environment by letting them sleep one night at our Centre for Chronobiology with the entire
295 polysomnographic (PSG) setup. In addition, each participant underwent a medical screening
296 including an ophthalmologic examination (i.e. visual field, colour vision, pupillary reflex).
297 Female study participants took a pregnancy test and completed the study during the luteal
298 phase of their menstrual cycle. The experimental part of the study started one week before the
299 in-laboratory part, during which the volunteers were asked to abstain from excessive alcohol
300 and caffeine consumption and to maintain a rather regular sleep-wake cycle (i.e. 8-h sleep at
301 night within a regular bedtime +/- 30 min and no daytime napping) to ensure proper circadian
302 entrainment of the sleep-wake cycle with the light-dark cycle. Compliance was verified via the
303 use of wrist actigraphs (Actiwatch L, Cambridge Neurotechnologies, Cambridge, UK) and self-
304 reported sleep logs. Thirty-eight healthy volunteers finally met all inclusion criteria out of an
305 initial 650 potential participants. The young group comprised 26 participants between 20 and
306 35 years (11 females, 16 males, mean age (SE): 24.96 (0.58) years) and the older group included

307 12 participants between 55 and 75 years (3 females and 9 males, mean age (SE): 63.58 (1.27)
308 years). For more information please refer to table 3 of [20].

309

310 *Study design and light settings*

311 The entire in-laboratory part of the study lasted 62 hours, which included a 6-h baseline
312 evening episode, an 8-h baseline night sleep episode (BL), a 40-h total sleep deprivation (SD)
313 followed by an 8-h recovery sleep episode (RC), all scheduled according to the individual's usual
314 bedtime. Each participant lived in a single windowless and sound-attenuated bedroom, which
315 was temperature and humidity controlled without any access to time-of-day information. Visits
316 to the bathroom were allowed via a corridor outside the bedroom under dim light conditions (<
317 8 lux) only with blackened goggles. Immediately, upon scheduled raise time from the 8-h
318 baseline night (lights on), the light treatment started with a 40-h fluorescent white light
319 exposure under 3 different conditions: a control dim light (DL: <8 lux, 4000 K) condition, a white
320 light (WL: 250 lux, 2800 K) and a blue enriched white light (BL: 250 lux, 9000 K) condition. The
321 illuminance readings were taken vertically at the eye position of the participant (for the spectral
322 characteristics please see figure 4 of [15]). The lamps in each test room were provided by
323 Philips (Philips Lighting, Eindhoven, The Netherlands) and comprised 2700 K fluorescent tubes
324 (Master TL5 HO 54w/827) and 17000 K fluorescent tubes (Master TL5 HO Activiva Active 54w
325 1sl). The test rooms are uniformly painted with high reflective white painting providing a
326 homogenous light distribution. However, ambient reflections and optical conditions resulted in
327 an effective colour temperature that deviated from the values above. We effectively measured
328 4000 K for the DL and WL condition, and 9000 K for the BL condition. The irradiance in the DL
329 condition was 0.0024 mW/cm²; photon irradiance: 6.58863E+16 photons/m²s, while in the WL
330 condition: 0.07 mW/cm²; photon irradiance: 2.00E+18 photons/m²s, and in the BL condition:
331 0.087 mW/cm²; photon irradiance: 2.30E+18 photons/m²s. According to the new standard
332 [http://www.cie.co.at/publications/cie-system-metrology-optical-radiation-iprgc-influenced-responses-](http://www.cie.co.at/publications/cie-system-metrology-optical-radiation-iprgc-influenced-responses-light-0)
333 [light-0](http://www.cie.co.at/publications/cie-system-metrology-optical-radiation-iprgc-influenced-responses-light-0) mentioned in [36], photoreceptor weighted irradiance for melanopsin was 0.4 μW/cm²
334 (2.93 melanopic equivalent daylight illuminance) for DL, 12.1 μW/cm² (91.61 melanopic
335 equivalent daylight illuminance) and 32.6 μW/cm² (246 melanopic equivalent daylight

336 illuminance for BL. Since recent evidence shows that melanopsin is the main driver for
337 melatonin suppression in humans ([25,26]), we did not calculate dose response relationships
338 with the other alpha-opic irradiances.

339 Study volunteers needed to participate in at least two light conditions, while one was always
340 the control DL condition. Out of the 26 young participants: 18 (12 m and 6 f) participated in all
341 three lighting conditions (i.e. DL, WL, and BL): 6 with the following order: DL,BL,WL; 4 with
342 WL,BL,DL; 3 with DL,WL,BL; 2 with WL,DL,BL; 1 with WL,DL,BL; 1 with BL,DL,WL, and 1 with
343 BL,WL,DL. The remaining 9 (4m and 5f) young participated in two lighting conditions [i.e. DL and
344 (WL or BL)]: 3 with the following order: BL,DL; 2 with DL,WL; 2 with WL,DL, and 2 with DL,WL.
345 Out of the 12 older participants, 9 (7 m and 2 f) participated in all three lighting conditions (i.e.
346 DL, WL, and BL): 3 with the following order: WL,DL,BL; 2 with DL,BL,WL; 1 with DL,WL,BL; 1
347 BL,WL,DL; 1 with WL,BL,DL, and 1 with BL,DL,WL. The remaining 3 (2 m and 1 F) older
348 participated in two lighting conditions [i.e. DL and (WL or BL)]: 2 with the following order:
349 DL,WL; and 1 with DL,BL. The participants were not allowed to use any light-emitting electronic
350 devices such as smartphones, tablets or laptops during their entire stay in the laboratory.
351 Standardized meals were provided every 2 hours during scheduled wakefulness and controlled
352 for their caloric content. Participant's movements in their room were reduced to a minimum,
353 and they were regularly asked to take scheduled computer tests (illuminance due to screen
354 usage <10 lx) and bathroom visits. Following activities during scheduled wakefulness during all
355 lighting conditions were allowed: reading, listening to music, writing or drawing, knitting, doing
356 puzzles, and talking to the study helpers. At any time, they did not have access to devices which
357 could connect to the internet nor to other light emitting devices except for the monitor of the
358 testing computer.

359

360 *Polysomnographic (PSG) recordings*

361 The PSG was continuously recorded during the entire 62-h stay in the laboratory. The PSG
362 recording system (Vitaport Ambulatory system (Vitaport-3 digital recorder TEMEC Instruments
363 BV, Kerkrade, the Netherlands) included 12 EEG derivations (Fz, F3, F4, Cz, C3, C4, Pz, P3, P4,

364 Oz, O1, O2) referenced against linked mastoids (A1 and A2), two electrooculograms, one
365 bipolar submental electromyogram, and one bipolar electrocardiogram. After low pass filtering
366 all signals at 30 Hz (fourth order Bessel type anti-aliasing, total 24 dB/Oct, time constant of 1s),
367 online digitization with a 12 bit AD converter (0.15 μ V/bit) with a sampling rate of 128 Hz for
368 the EEG, the raw signals were stored on a flash RAM card. A single experienced sleep technician
369 (M.F. see acknowledgments) scored the sleep stages per 20-s epochs according to the standard
370 criteria. The EEG was subjected to spectral analysis using a fast Fourier transformation (FFT;
371 Hanning 4-s window). EEG power spectra were computed during Non-rapid eye movement
372 (NREM) sleep in the frequency range from 0 to 20 Hz, by averaging artifact-free 4-s epochs
373 were averaged across 20-s epochs for each EEG derivation. All PSG recordings were manually
374 inspected for artifacts EEG channel losses etc., resulting in a total n= 24 for DL, n=18 for WL,
375 n=19 for BL in the young, and a n= 12 for DL, n=11 for WL, and n=8 BL for the older participants.

376

377 *Subjective sleepiness*

378 Subjective sleepiness was rated by the volunteers on the Karolinska sleepiness symptoms check
379 list (KSSCL) [37] at 30-min intervals.

380 *Statistical analysis*

381 A mixed-model analysis of variance for repeated measures (PROC MIXED, statistical package
382 SAS [version 9.1; SAS Institute, Cary, NC, USA]) with the between factor “age” (young [Y], older
383 [O]), and the within factors “night-type” (baseline night [BL], recovery night [RC]), and “light
384 condition” (dim light [DL], blue-enriched white light [BL] versus white light [WL]) was calculated
385 for the following endpoints: individual sleep variables derived from sleep scoring (table 1), EEG
386 power density in the frequency bins from 0.75-20 Hz and EEG slow-wave activity (SWA, EEG
387 power density in the 0.75-4.5 Hz range). The factor “study participant” was defined as random
388 and a compound symmetry or an autoregressive model [ar (1)] for equidistant time series was
389 chosen as a covariance structure. The Least squares means statement was applied for *post-hoc*
390 comparisons.

391

392

393 **Acknowledgments**

394 We thank Dr. Krebs for medical screenings, Claudia Renz, Marie-France Dattler and all the
395 helpers for their help in data acquisition, and the volunteers for participating in this demanding
396 study. This research was supported by the Velux Foundation Switzerland and Philips, The
397 Netherlands and in part by the Swiss National Foundation (#310030_130689; P1BSP1-155209).

398

399 **Conflict of interest**

400 C.C. has had the following commercial interests in the last two years (2017–2018) related to
401 lighting: honoraria, travel, accommodation and/or meals for invited keynote lectures,
402 conference presentations or teaching from Toshiba Materials, Velux, Firalux, Lighting Europe,
403 Electrosuisse, Novartis, Roche, Elite, Servier, and WIR Bank. C.C. is a member of the Daylight
404 Academy.

405 L.J.M.S. was an employee of Philips Lighting/Signify, the Netherlands until July 2019. His current
406 TU/e position is partially funded by Signify.

407 M.M., A.U.V., and C.S do not report any conflict of interest

408 V.G. does not report any conflict of interest related to lighting.

409

410 **References**

411

- 412 1. Borbely, A.A.; Daan, S.; Wirz-Justice, A.; Deboer, T. The two-process model of sleep regulation: a
413 reappraisal. *J Sleep Res* **2016**, *25*, 131-143.
- 414 2. Campbell, S.S.; Tobler, I. Animal sleep: a review of sleep duration across phylogeny.
415 *Neuroscience and biobehavioral reviews* **1984**, *8*, 269-300.
- 416 3. Achermann, P.; Dijk, D.J.; Brunner, D.P.; Borbely, A.A. A model of human sleep homeostasis
417 based on EEG slow-wave activity: quantitative comparison of data and simulations. *Brain*
418 *research bulletin* **1993**, *31*, 97-113.
- 419 4. Lesku, J.A.; Vyssotski, A.L.; Martinez-Gonzalez, D.; Wilzeck, C.; Rattenborg, N.C. Local sleep
420 homeostasis in the avian brain: convergence of sleep function in mammals and birds?
421 *Proceedings. Biological sciences* **2011**, *278*, 2419-2428, doi:10.1098/rspb.2010.2316.
- 422 5. Werth, E.; Achermann, P.; Borbely, A.A. Fronto-occipital EEG power gradients in human sleep. *J*
423 *Sleep Res* **1997**, *6*, 102-112.
- 424 6. Cajochen, C.; Foy, R.; Dijk, D.J. Frontal predominance of a relative increase in sleep delta and
425 theta EEG activity after sleep loss in humans. *Sleep research online : SRO* **1999**, *2*, 65-69.
- 426 7. Kattler, H.; Dijk, D.J.; Borbely, A.A. Effect of unilateral somatosensory stimulation prior to sleep
427 on the sleep EEG in humans. *J Sleep Res* **1994**, *3*, 159-164.
- 428 8. Huber, R.; Ghilardi, M.F.; Massimini, M.; Tononi, G. Local sleep and learning. *Nature* **2004**, *430*,
429 78-81, doi:10.1038/nature02663.
- 430 9. Meerlo, P.; Pragt, B.J.; Daan, S. Social stress induces high intensity sleep in rats. *Neurosci Lett*
431 **1997**, *225*, 41-44.
- 432 10. Tononi, G.; Cirelli, C. Sleep and synaptic down-selection. *The European journal of neuroscience*
433 **2019**, 10.1111/ejn.14335, doi:10.1111/ejn.14335.
- 434 11. LeGates, T.A.; Fernandez, D.C.; Hattar, S. Light as a central modulator of circadian rhythms, sleep
435 and affect. *Nature reviews. Neuroscience* **2014**, *15*, 443-454, doi:10.1038/nrn3743.
- 436 12. Crowley, S.J.; Molina, T.A.; Burgess, H.J. A week in the life of full-time office workers: work day
437 and weekend light exposure in summer and winter. *Applied ergonomics* **2015**, *46 Pt A*, 193-200,
438 doi:10.1016/j.apergo.2014.08.006.
- 439 13. Cajochen, C.; Dijk, D.J.; Borbely, A.A. Dynamics of EEG slow-wave activity and core body
440 temperature in human sleep after exposure to bright light. *Sleep* **1992**, *15*, 337-343.
- 441 14. Chellappa, S.L.; Steiner, R.; Oelhafen, P.; Lang, D.; Gotz, T.; Krebs, J.; Cajochen, C. Acute exposure
442 to evening blue-enriched light impacts on human sleep. *J Sleep Res* **2013**, *22*, 573-580,
443 doi:10.1111/jsr.12050.
- 444 15. Munch, M.; Kobiacka, S.; Steiner, R.; Oelhafen, P.; Wirz-Justice, A.; Cajochen, C. Wavelength-
445 dependent effects of evening light exposure on sleep architecture and sleep EEG power density
446 in men. *American journal of physiology. Regulatory, integrative and comparative physiology*
447 **2006**, *290*, R1421-1428, doi:10.1152/ajpregu.00478.2005.
- 448 16. Munch, M.; Knoblauch, V.; Blatter, K.; Schroder, C.; Schnitzler, C.; Krauchi, K.; Wirz-Justice, A.;
449 Cajochen, C. The frontal predominance in human EEG delta activity after sleep loss decreases
450 with age. *The European journal of neuroscience* **2004**, *20*, 1402-1410, doi:10.1111/j.1460-
451 9568.2004.03580.x.

- 452 17. Aeschbach, D.; Cajochen, C.; Landolt, H.; Borbely, A.A. Homeostatic sleep regulation in habitual
453 short sleepers and long sleepers. *The American journal of physiology* **1996**, *270*, R41-53,
454 doi:10.1152/ajpregu.1996.270.1.R41.
- 455 18. Cajochen, C.; Munch, M.; Knoblauch, V.; Blatter, K.; Wirz-Justice, A. Age-related changes in the
456 circadian and homeostatic regulation of human sleep. *Chronobiology international* **2006**, *23*,
457 461-474, doi:10.1080/07420520500545813.
- 458 19. Dijk, D.J.; Duffy, J.F.; Czeisler, C.A. Contribution of circadian physiology and sleep homeostasis to
459 age-related changes in human sleep. *Chronobiology international* **2000**, *17*, 285-311.
- 460 20. Gabel, V.; Reichert, C.F.; Maire, M.; Schmidt, C.; Schlangen, L.J.M.; Kolodyazhniy, V.; Garbazza,
461 C.; Cajochen, C.; Viola, A.U. Differential impact in young and older individuals of blue-enriched
462 white light on circadian physiology and alertness during sustained wakefulness. *Scientific reports*
463 **2017**, *7*, 7620, doi:10.1038/s41598-017-07060-8.
- 464 21. Reinhardt, K.D.; Vyazovskiy, V.V.; Hernandez-Aguilar, R.A.; Imron, M.A.; Nekaris, K.A.
465 Environment shapes sleep patterns in a wild nocturnal primate. *Scientific reports* **2019**, *9*, 9939,
466 doi:10.1038/s41598-019-45852-2.
- 467 22. Wams, E.J.; Woelders, T.; Marring, I.; van Rosmalen, L.; Beersma, D.G.M.; Gordijn, M.C.M.; Hut,
468 R.A. Linking Light Exposure and Subsequent Sleep: A Field Polysomnography Study in Humans.
469 *Sleep* **2017**, *40*, doi:10.1093/sleep/zsx165.
- 470 23. Chang, A.M.; Aeschbach, D.; Duffy, J.F.; Czeisler, C.A. Evening use of light-emitting eReaders
471 negatively affects sleep, circadian timing, and next-morning alertness. *Proceedings of the*
472 *National Academy of Sciences of the United States of America* **2015**, *112*, 1232-1237,
473 doi:10.1073/pnas.1418490112.
- 474 24. Spitschan, M. Melanopsin contributions to non-visual and visual function. *Current Opinion in*
475 *Behavioral Sciences* **2019**, *30*, 67-72.
- 476 25. Allen, A.E.; Hazelhoff, E.M.; Martial, F.P.; Cajochen, C.; Lucas, R.J. Exploiting metamerism to
477 regulate the impact of a visual display on alertness and melatonin suppression independent of
478 visual appearance. *Sleep* **2018**, *41*, doi:10.1093/sleep/zsy100.
- 479 26. Souman, J.L.; Borra, T.; de Goijer, I.; Schlangen, L.J.M.; Vlaskamp, B.N.S.; Lucassen, M.P. Spectral
480 Tuning of White Light Allows for Strong Reduction in Melatonin Suppression without Changing
481 Illumination Level or Color Temperature. *Journal of biological rhythms* **2018**, *33*, 420-431,
482 doi:10.1177/0748730418784041.
- 483 27. Nowozin, C.; Wahnschaffe, A.; Rodenbeck, A.; de Zeeuw, J.; Hadel, S.; Kozakov, R.; Schopp, H.;
484 Munch, M.; Kunz, D. Applying Melanopic Lux to Measure Biological Light Effects on Melatonin
485 Suppression and Subjective Sleepiness. *Current Alzheimer research* **2017**, *14*, 1042-1052,
486 doi:10.2174/1567205014666170523094526.
- 487 28. Zeitzer, J.M.; Dijk, D.J.; Kronauer, R.; Brown, E.; Czeisler, C. Sensitivity of the human circadian
488 pacemaker to nocturnal light: melatonin phase resetting and suppression. *The Journal of*
489 *physiology* **2000**, *526 Pt 3*, 695-702, doi:10.1111/j.1469-7793.2000.00695.x.
- 490 29. Rodriguez, A.V.; Funk, C.M.; Vyazovskiy, V.V.; Nir, Y.; Tononi, G.; Cirelli, C. Why Does Sleep Slow-
491 Wave Activity Increase After Extended Wake? Assessing the Effects of Increased Cortical Firing
492 During Wake and Sleep. *The Journal of neuroscience : the official journal of the Society for*
493 *Neuroscience* **2016**, *36*, 12436-12447, doi:10.1523/JNEUROSCI.1614-16.2016.
- 494 30. Landsness, E.C.; Ferrarelli, F.; Sarasso, S.; Goldstein, M.R.; Riedner, B.A.; Cirelli, C.; Perfetti, B.;
495 Moisello, C.; Ghilardi, M.F.; Tononi, G. Electrophysiological traces of visuomotor learning and
496 their renormalization after sleep. *Clinical neurophysiology : official journal of the International*
497 *Federation of Clinical Neurophysiology* **2011**, *122*, 2418-2425, doi:10.1016/j.clinph.2011.05.001.
- 498 31. Cajochen, C.; Di Biase, R.; Imai, M. Interhemispheric EEG asymmetries during unilateral bright-
499 light exposure and subsequent sleep in humans. *American journal of physiology. Regulatory,*

- 500 *integrative and comparative physiology* **2008**, *294*, R1053-1060,
501 doi:10.1152/ajpregu.00747.2007.
- 502 32. Pilorz, V.; Tam, S.K.; Hughes, S.; Pothecary, C.A.; Jagannath, A.; Hankins, M.W.; Bannerman,
503 D.M.; Lightman, S.L.; Vyazovskiy, V.V.; Nolan, P.M., et al. Melanopsin Regulates Both Sleep-
504 Promoting and Arousal-Promoting Responses to Light. *PLoS biology* **2016**, *14*, e1002482,
505 doi:10.1371/journal.pbio.1002482.
- 506 33. Cajochen, C.; Chellappa, S.L. Commentary: Melanopsin Regulates Both Sleep-Promoting and
507 Arousal-Promoting Responses to Light. *Frontiers in neural circuits* **2016**, *10*, 94,
508 doi:10.3389/fncir.2016.00094.
- 509 34. Rupp, A.C.; Ren, M.; Altimus, C.M.; Fernandez, D.C.; Richardson, M.; Turek, F.; Hattar, S.;
510 Schmidt, T.M. Distinct ipRGC subpopulations mediate light's acute and circadian effects on body
511 temperature and sleep. *eLife* **2019**, *8*, doi:10.7554/eLife.44358.
- 512 35. Hazlerigg, D.G.; Tyler, N.J.C. Activity patterns in mammals: Circadian dominance challenged.
513 *PLoS biology* **2019**, *17*, e3000360, doi:10.1371/journal.pbio.3000360.
- 514 36. Spitschan, M.; Stefani, O.; Blattner, P.; Gronfier, C.; Lockley, S.W.; Lucas, R.J. How to Report Light
515 Exposure in Human Chronobiology and Sleep Research Experiments. *Clocks & sleep* **2019**, *1*, 280-
516 289, doi:10.3390/clockssleep1030024.
- 517 37. Akerstedt, T.; Gillberg, M. Subjective and objective sleepiness in the active individual. *The*
518 *International journal of neuroscience* **1990**, *52*, 29-37, doi:10.3109/00207459008994241.

519