Regional response to light illuminance across the human hypothalamus

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Abstract

Light exerts multiple non-image-forming biological effects on physiology including the stimulation of alertness and cognition. However, the subcortical circuitry underlying the stimulating impact of light is not established in humans. We used 7 Tesla functional magnetic resonance imaging to assess the impact of variations in light illuminance on the regional activity of the hypothalamus while healthy young adults (N=26; 16 women; 24.3 ± 2.9y) were completing two auditory cognitive tasks. We find that, during both the executive and emotional tasks, higher illuminance triggered an activity increase over the posterior part of the hypothalamus, which includes part of the tuberomamillary nucleus and the posterior part of the lateral hypothalamus. In contrast, increasing illuminance evoked a decrease in activity over the anterior and ventral parts of the hypothalamus, encompassing notably the suprachiasmatic nucleus and another part of the tuberomammillary nucleus. Critically, the performance of the executive task was improved under higher illuminance and was negatively correlated with the activity of the posterior hypothalamus area. These findings reveal the distinct local dynamics of different hypothalamus regions that underlie the impact of light on cognition.

55 **Introduction**

56 Light exerts multiple non-image-forming (NIF) biological effects that influence the quality of
57 sleep and wakefulness, and higher illuminance is known to stimulate alertness and cognition
58 (Campbell, Sharifpour, et al., 2023). The biological effects of light primarily rely on a subclass of
59 retinal ganglion cells that are intrinsically photosensitive (ipRGCs) because they express the
60 photopigment melanopsin, which is maximally sensitive to photons with wavelength ~480nm.
61 IpRGCs combine the light signalling of rods and cones to their intrinsic photosensitivity and,
62 collectively, the biological effects of light present a maximal sensitivity to the shorter blue
63 wavelength of visible light (Tri & Do, 2019). IpRGCs project to multiple subcortical brain areas and
64 their denser projections are found within the hypothalamus, particularly in nuclei involved in
65 sleep and wakefulness regulation (Scammell et al., 2017; Tri & Do, 2019). The suprachiasmatic
66 nucleus (SCN), which is the site of the principal circadian clock, receives the strongest inputs from
67 ipRGC inputs, over the anterior part of the hypothalamus (Hattar et al., 2006). Other nuclei also
68 receive ipRGC projections: the subparaventricular zone, one of the main output routes of the
69 SCN, the ventrolateral preoptic nucleus (VLPO) and the preoptic nucleus (PON) involved in sleep
70 initiation and also found in the anterior part of the hypothalamus; the lateral hypothalamus (LH),
71 site of the orexinergic wake-promoting neurons and melanin-concentrating hormone sleep-
72 promoting neurons, found in contrast over the lateral and posterior parts of the hypothalamus
73 (Scammell et al., 2017; Tri & Do, 2019).

74 The brain circuitry underlying the biological effects of light has mostly been uncovered
75 in nocturnal rodent models (Campbell, Sharifpour, et al., 2023; Tri & Do, 2019). Translation to
76 diurnal human beings, where the later maturation of the cortex allows for complex cognitive
77 processing (Braak & Del Tredici, 2015), remains scarce. In particular, whether hypothalamus nuclei
78 contribute to the stimulating impact of light on cognition in humans is not established.

We addressed this question using ultra-high-field (UHF) 7 Tesla (7T) functional magnetic resonance imaging (fMRI) in healthy young adults exposed to light of various illuminance while engaged in two different auditory cognitive tasks. We find that higher illuminance increased the activity of the posterior part of the hypothalamus encompassing the mamillary bodies (MB) and parts of the LH and tuberomammillary nucleus (TMN). In contrast, higher illuminance decreased the activity over the anterior and ventral parts of the hypothalamus encapsulating notably the SCN and another part of the TMN. Critically, the pattern of modulation was consistent across the two cognitive tasks. Importantly, the performance of the complex cognitive task was improved under higher illuminance while the activity of the posterior part of the hypothalamus was correlated to task performance. The findings reveal the distinct local dynamics of different hypothalamus areas in response to changing illuminance that may contribute to light's impact on cognition.

Results

Twenty-six healthy young adults (16 women; 24.3 ± 2.9 y; **Suppl. Table 1**) completed two auditory cognitive tasks encompassing, respectively, the executive (Collette et al., 2005) and emotional (Grandjean et al., 2005) domains, while alternatively maintained in darkness or exposed to short periods (< 1 min) of light of four different illuminances (0.16, 37, 92, 190 melanopic equivalent daylight illuminance - mel EDI- lux; **Suppl. Table 2**) [**Fig.1**]. The hypothalamus of each participant was segmented into 5 subparts – inferior-anterior, superior-anterior, inferior-tubular, superior-tubular, and posterior [**Fig.2 A**] – so we could consistently extract the regional effect of illuminance change on fMRI blood-oxygen-level-dependent (BOLD) signal over most of the hypothalamus volume.

The impact of illuminance variations on the activity of the hypothalamus is not uniform

The main analyses aimed at isolating differences in the overall impact of illuminance changes among the 5 hypothalamus subparts. For each subpart, we extracted an index of the illuminance impact as their average regression coefficients between their responses to the tasks and the illuminance levels. These analyses showed significant differences between the hypothalamus subparts for the executive (generalized linear mixed models (GLMM); main effect of the subparts; $p = 0.002$) and emotional (GLMM; main effect of the subparts; $p < 0.0001$) tasks, revealing that, during both tasks, the variations in illuminance affected the activity of the 5 hypothalamus subparts differently [**Fig.2 B, C**; **Table 1**]. A nominal main effect of the task was detected for the emotional task [$p = 0.049$; Table 1] but not for the n-back task. For both tasks, there was no significant main effect for any of the other covariates and post hoc analyses showed that the index of the illuminance impact was consistently different in the posterior hypothalamus subpart compared to the other subparts [$p_{corrected} \leq 0.05$, **Table 1**]. Importantly, whole-brain analyses confirmed that increasing illuminance resulted in a local increase and decrease of activity that could be detected, respectively, over the posterior and inferior subparts of the hypothalamus [**Fig.2 D-G**]. This shows that our results do not come from a relatively unspecific and widespread increase in BOLD signal surrounding the hypothalamus subparts and that the effect of light was most prominent over the posterior and inferior-anterior subparts.

Opposite dynamics between the posterior and inferior/anterior hypothalamus at higher illuminance

This prompted us to assess the activity of the hypothalamus subparts under each illuminance to detail the different regional activity dynamics across the hypothalamus. The statistical analyses confirmed that the activity dynamics across illuminance levels differed between the 5 subparts during the executive and the emotional tasks (GLMM; subparts-by-illuminance interaction; $p = 0.041$) tasks [**Fig.2 H-K**; **Table 2**]. Post hoc contrasts first considered the impact of the changes in illuminance within each subpart (**Suppl. Tables 3, 4**). The activity of the posterior hypothalamus

subpart significantly ($p < 0.05$) increased under the highest illuminance (190 mel EDI) compared with darkness for both tasks and with the lower illuminances (37 and 92 mel EDI lux) for the emotional task. In contrast, for both tasks, the activity in the inferior-anterior and inferior-tubular hypothalamus subparts significantly ($p < 0.05$) decreased under the highest illuminance compared with darkness, and with lower illuminances for the emotional task. Finally, the activity of the superior anterior hypothalamus subpart decreased under higher illuminance during the emotional but not the executive task, while the activity of the fifth hypothalamus subpart, the superior tubular subpart, was not significantly affected by illuminance changes in either task.

Post hoc analyses also yielded several significant differences between hypothalamus subparts ($p < 0.05$) (**Table 2**; **Suppl. Tables 5, 6**). For both tasks, the activity of the posterior hypothalamus subpart was consistently significantly higher than the activity inferior-tubular subpart under the highest illuminances (92 and 190 mel EDI lux). For the executive task, the activity of the posterior hypothalamus subpart was also significantly higher than the superior-anterior subpart under the highest illuminances (92 and 190 mel EDI lux). For the emotional task, the activity of the posterior hypothalamus subpart was also significantly higher than the superior-anterior subpart under the highest illuminances (190 mel EDI lux), while the activity superior-tubular hypothalamus subpart was significantly higher than the activity of the inferior-tubular, inferior-anterior and superior-anterior hypothalamus subparts (92 and/or190 mel EDI lux). The overall picture arising from these comparisons is that higher illuminance increased the activity of the posterior and superior hypothalamus subparts while it decreased the activity of the inferior and anterior hypothalamus subparts.

Performance to the executive task is improved by light and related to the activity of the posterior hypothalamus

Following these analyses, we explored whether the changes in activity across illuminances were related to cognitive performance. We first considered the more difficult (2-back) subtask of the

156 executive task as it requires higher cognitive functions (see method for a full rationale) (Collette
157 et al., 2005). The analysis revealed that accuracy to the executive task was high in all participants,
158 but accuracy to the more difficult subtask (2-back) improved with increasing illuminance (GLMM;
159 main effect of illuminance; F = 2.72; p = 0.034; Partial R2 215 = 0.1; **Fig.3 A**), controlling for age,
160 sex and BMI. Critically, the analysis also showed that performance under each illuminance was
161 significantly related to the activity of the posterior hypothalamus subpart (GLMM; main effect
162 of posterior subpart activity; F = 9.43; p = 0.0027; Partial R2 219 = 0.09). Surprisingly, the
163 association was negative (**Fig.3 B**), suggesting that the part of variance explained by the
164 hypothalamus subpart is distinct from the impact of light on performance. In contrast, no
165 significant association was found when considering the activity of the other four subparts
166 (GLMM; main effect of posterior subpart activity; F < 0.62; p > 0.4; **Fig.3 C,D**; **Suppl. Table 7**). We
167 went on and found that the accuracy to the simpler control subtask of the executive tasks (0-
168 back, see method) was not associated with the activity of the posterior hypothalamus subpart
169 (GLMM controlling for age, sex and BMI; main effect of subpart activity; F = 0.57; p = 0.45; **Fig.3**
170 **E**), suggesting that the association with performance is specific to the 2-back subtask.

171 In the last step, we explored the reaction times during the emotional task (accuracy to
172 the lure task is not meaningful). We found that reaction times to the emotional stimuli were not
173 significantly affected by illuminance (GLMM controlling for age, sex and BMI; main effect of
174 illuminance; F = 1.01; p = 0.41; **Fig.3 F**) and yet, they were significantly associated with the activity
175 of the posterior hypothalamus subpart across each illuminance (GLMM; main effect of subpart
176 activity; F = 4.34; p = 0.04; **Fig.3 G**). The association was positive meaning that reaction times
177 were longer if activity estimates were higher, which could indicate a reinforcement of the
178 emotional response characterized by longer reaction times (Grandjean et al., 2005). No such
179 significant association was detected when considering reaction times to the neutral items of the
180 task (GLMM controlling for age, sex and BMI; main effect of illuminance; F = 1.5; p = 0.21; main
181 effect of subpart activity; F = 0.28; p = 0.6; **Fig.3 H**).

Discussion

Animal research has established that the biological impact of light illuminance impinges on many subcortical structures, many of which regulate sleep and wakefulness (Campbell, Sharifpour, et al., 2023; Hattar et al., 2006; Scammell et al., 2017; Tri & Do, 2019). How these findings translate to human beings is not established. Here, we took advantage of the relatively high resolution and signal-to-noise ratio of UHF 7T fMRI to determine how illuminance affects the activity of the hypothalamus as, based on animal research, it receives the densest projections from ipRGCs (Hattar et al., 2006; Tri & Do, 2019). We find that the activity of the posterior part of the hypothalamus increases with increasing illuminance while, in contrast, the inferior and anterior hypothalamus show a seemingly opposite pattern and see their activity decrease under higher illuminance. The pattern of light-induced changes was consistent across an executive and an emotional task which consisted of block and an event-related fMRI design, respectively. This suggests that a robust anterior-posterior gradient of activity modulation by illuminance is present in hypothalamus across cognitive domains. Importantly, performance to the complex cognitive task was improved under higher illuminance and was correlated to the activity of the posterior part of the hypothalamus under the different illuminance, though negatively. The results demonstrate that the human hypothalamus does not respond uniformly to variations in illuminance while engaged in a cognitive challenge and suggest that the posterior part of the hypothalamus may be key in mediating the stimulating impact of light on cognition.

The different nuclei of the hypothalamus do not have clear contrast boundaries based on MRI signals (Billot et al., 2020). As a result, achieving nucleus resolution over the human hypothalamus even using UFH MRI remains out of reach (Sharifpour et al., 2022). Therefore, we cannot assign the effects we report to a specific nucleus. We can only speculate and present a selection of plausible scenarios that would need to be tested. The posterior part of the hypothalamus - delineated in each participant based on an automatic reproducible procedure

208 (Billot et al., 2020) - encompasses the MB as well as parts of the LH and the TMN. All these nuclei
209 could participate to the increased BOLD signal we detect under higher illuminance. The LH and
210 TMN, respectively, produce orexin and histamine, which are both known to promote
211 wakefulness, while animal histology reports direct projection of the ipRGCs to the LH (Hattar et
212 al., 2006; Scammell et al., 2017; Tri & Do, 2019). Orexin is a good candidate to constitute the
213 circadian signal that promotes wakefulness and to counter the progressive increase in sleep
214 needs with prolonged wakefulness (Zeitzer, 2013). Our data may therefore be compatible with
215 an increase in orexin release by the LH with increasing illuminance. In line with this assumption,
216 chemoactivation of ipRGCs lead to increase c-fos production, a marker of cellular activation, over
217 several nuclei of the hypothalamus, including the lateral hypothalamus (Milosavljevic et al.,
218 2016). If this initial effect of light we observe over the posterior part of the hypothalamus was
219 maintained over a longer period of exposure, this would stimulate cognition and maintain or
220 increase alertness (Campbell, Sharifpour, et al., 2023) and may also be part of the mechanisms
221 through which daytime light increases the amplitude in circadian variations of several
222 physiological features (Bano-Otalora et al., 2021; Dijk et al., 2012). It could then also be part of
223 the mechanisms through which evening light may disturb subsequent sleep (Chellappa et al.,
224 2013) when illuminance is higher than the recommended maximum of 10 mel EDI lux for evening
225 light (Brown et al., 2022). If the TMN was the hypothalamus nucleus underlying the regional
226 increase in the BOLD signal we report, it could confer a role to histamine in mediating the
227 stimulating impact of light. Of interest, the TMN receives orexin signal from the LH (Scammell et
228 al., 2019). Alternatively, our findings may suggest a role for the MBs in mediating the impact of
229 light on ongoing cognition, potentially influenced through its innervation by the TMN (Vann,
230 2010).

231 Previous research indicated that increasing illuminance reduced the activity of the
232 anterior part of the hypothalamus encompassing the SCN, either following the exposure to light
233 (Perrin et al., 2004) or during the exposure (Schoonderwoerd et al., 2022). We extend this finding

234 by showing that the significant decrease in activity extends beyond the inferior anterior
235 hypothalamus and therefore much beyond the SCN. Chemoactivation of ipRGCs in rodents led
236 to an increase activity of the SCN, over the inferior anterior hypothalamus, but had no impact on
237 the activity of the VLPO, over the superior anterior hypothalamus (Milosavljevic et al., 2016).
238 How our findings fit with these fine-grained observations and whether there are species-specific
239 differences in the responses to light over the different part of the hypothalamus remains to be
240 established. The inferior-tubular and inferior-anterior subparts of the hypothalamus – that we
241 isolated also based on an automatic reproducible procedure (Billot et al., 2020) - encompass
242 several nuclei such as notably the SCN, SON, ventromedial nucleus of the hypothalamus, arcuate
243 nucleus and part of the TMN. Again, all these nuclei may be involved in the reduction in BOLD
244 signal we observe at higher illuminance. In terms of chemical communication, these changes in
245 activity could be the results of an inhibitory signal from a subclass of ipRGCs, potentially through
246 the release aminobutyric acid (GABA), as a rodent study found that a subset of ipRGCs release
247 GABA at brain targets including the SCN (and intergeniculate leaflet and ventral lateral geniculate
248 nucleus), leading to a reduction in the ability of light to affect pupil size and circadian
249 photoentrainment (Sonoda et al., 2020). Whatever the signalling of ipRGC, our finding over the
250 anterior hypothalamus could correspond to a modification of GABA signalling of the SCN which
251 has been reported to have excitatory properties, such that the BOLD signal changes we report
252 may correspond to a reduction in excitation arising in part from the SCN (Albers et al., 2017).
253 Likewise, the SCN is also producing other neuropeptides that could affect its downstream
254 targets. As the inferior-tubular subpart of the hypothalamus also includes part of the TMN it may
255 be the TMN and its GABA production that is decreased by higher illuminance (Scammell et al.,
256 2019). The decrease in BOLD signal with increasing illuminance we report could therefore
257 arguably reflect a decreased inhibitory signal arising from the anterior and inferior nuclei of the
258 hypothalamus.

Importantly, none of the scenarios we elaborated on are mutually exclusive and we may have overlooked the potential implication of several nuclei as well as the cellular diversity of the nuclei of the hypothalamus (Adamantidis et al., 2019; Scammell et al., 2017). We further note that the anterior-superior hypothalamus subpart of the hypothalamus encompassing the VLPO and PON sees its activity decreasing under higher illuminance during the emotional task, similarly to the anterior-inferior and inferior-tubular areas. Likewise, similar to the posterior subpart, the activity of the superior-tubular hypothalamus subpart may be increased under higher illuminance during the emotional task. Whether this represents a task-specific effect arising, for instance, from differences in the salience of the auditory stimulus, remains to be determined.

Subcortical structures, and particularly those receiving direct retinal projections, including those of the hypothalamus, are likely to receive light illuminance signal first before passing on the light modulation to the cortical regions involved in the ongoing cognitive process (Campbell, Sharifpour, et al., 2023). A critical aspect of our results is that the performance to the 2-back (executive) subtask was significantly increased when exposed to higher illuminance light. The extent of this increase was limited, likely because performance was overall high at all illuminances, but was not detected for the simpler detection letter subtask (0-back). The result contrasts with many previous 3T MRI investigations on the biological effects of light on human brain function which did not report behavioural changes induced by repeated short exposures to light (e.g. (Vandewalle, Gais, et al., 2007; Vandewalle, Schmidt, et al., 2007; Vandewalle, Archer, et al., 2011) but see (Daneault et al., 2018; Vandewalle et al., 2006)). Our 7T MRI study, which includes a sample size larger than many of these previous studies, supports that BOLD fMRI is sensitive in detecting subtle impacts of light on the brain and that these detected changes can arguably contribute to the behavioural changes others reported using longer light exposure and other approaches (e.g.(Cajochen et al., 2011; Lockley et al., 2006) but see (Smolders et al., 2018)).

Importantly, we find that activity of the posterior hypothalamus subpart is negatively related to the performance to the executive task, making it unlikely that it mediates directly the positive impact of light on performance. The activity of the posterior hypothalamus was, however, associated with an increased behavioural response to emotional stimuli. The association between behaviour and the posterior hypothalamus is therefore likely to be complex and may depend on the context, with for instance different nuclei or neuronal populations contributing in some instances but not in others (Adamantidis et al., 2019; Scammell et al., 2019). It is likely also to work jointly with the decreased activity of the anterior/inferior hypothalamus we detected as well as with other non-hypothalamus subcortical structures regulating wakefulness to influence behaviour, which intrinsically primarily depends on cortical activity.

Future research may consider data-driven analyses of hypothalamus voxels time series as an alternative to the parcellation approach we adopted here. This may refine the delineation of the subparts of the hypothalamus undergoing decreased or increased activity with increasing illuminance. Future research should also assess the impact of light on other subcortical structures and on the entire subcortical network to determine how illuminance modifies their crosstalk as well as their interaction with the cortex, to eventually lead to behavioural impacts. These analyses could for instance address whether the regional changes in activity of the hypothalamus we find are upstream of the repeatedly reported impact of light illuminance on the activity of the pulvinar in the thalamus (Paparella et al., 2023; Vandewalle et al., 2006). Although it does not receive direct dense input from ipRGCs, it is likely to indirectly mediate the biological impact of light on ongoing cognitive activity (Paparella et al., 2023).

We based our rationale and part of our interpretations on ipRGC projections, which have been demonstrated in rodents to channel the NIF biological impact of light and incorporate the inputs from rods and cones with their intrinsic photosensitivity into a light signal that can impact the brain (Güler et al., 2008; Tri & Do, 2019). Given the polychromatic nature of the light we used, classical photoreceptors and their projections to visual brain areas are, however, very likely to

310 have directly or indirectly contributed to the modulation by light of the regional activity of the
311 hypothalamus. Furthermore, we cannot exclude that colour and/or spectral differences between
312 the orange and 3 blue-enriched light conditions may have contributed to our findings. Research
313 in rodent models demonstrated that variation in the spectral composition of light was perceived
314 by the suprachiasmatic nucleus to set circadian timing (Walmsley et al., 2015). No such
315 demonstration has, however, been reported yet for the acute impact of light on alertness,
316 attention, cognition or affective state. Future human studies could isolate the contribution of each
317 photoreceptor class to the impact of light on cognitive brain functions by manipulating prior light
318 history (Chellappa et al., 2014) or through the use of silent substitutions between metameric light
319 exposures (Viénot et al., 2012).

320 All these knowledge gaps are important to address because acting on light stands as a
321 promising means to reduce high sleepiness and improve cognitive deficits during wakefulness as
322 well as to facilitate sleep in the few hours preceding bedtime (Brown et al., 2022; Didikoglu et
323 al., 2023; Gooley et al., 2011; Munch et al., 2016; Riemersma-van der Lek et al., 2008;
324 Scheuermaier et al., 2018; Wirz-Justice et al., 2020). Light therapy is also a validated means to
325 improve mood and treat mood disorders (Glickman et al., 2006; Lam et al., 2016). Light
326 administration can also be considered a simple means to disturb the brain circuitry regulating
327 sleep and wakefulness such that it can provide insights about novel means to improve their
328 quality. For instance, if orexin and histamine were part of the mechanism through which natural
329 light affects brain functions, their administration may be the most ecological and/or natural
330 means to affect alertness and cognition. Likewise, as both orexin and histamine are targets for
331 the treatment of brain disorders, our findings could suggest that light may constitute a non-
332 pharmacological complementary intervention to compounds that are being developed to treat
333 arousal, sleep, or cognitive dysfunction in brain disorders (Ma et al., 2018). It remains, however,
334 premature in our view to base recommendations on the therapeutic use of light based on the
335 MRI findings gathered to date. Targeted lighting for interventions or for precise interference of

subcortical circuits will require a full understanding of how light affects the brain, particularly at the subcortical level. Our findings represent an important step towards this goal, at the level of the hypothalamus.

Materials and Methods

The data used in this paper arise from a large study that is leading to several publications and part of the methods have been published previously (Beckers et al., 2023; Campbell, Beckers, et al., 2023; Paparella et al., 2023). The protocol was approved by the Ethics Committee of the Faculty of Medicine at the University of Liège. Participants gave their written informed consent to take part in the study and received monetary compensation for their participation.

Participants. Thirty healthy young adults (19 women; 24.3 ± 2.9 y; **Suppl. Table S1**) were included in the analyses. Exclusion criteria were assessed through questionnaires and a semi-structured interview: history of psychiatric and neurological disorders, sleep disorders, use of psychoactive drugs or addiction; history of ophthalmic disorders or auditory impairments; colour blindness; night shift work during the last year or recent trans-meridian travel during the last 2 months; excessive caffeine (>4 caffeine units/day) or alcohol consumption (>14 alcohol units/week); medication affecting the central nervous system; smoking; pregnancy or breast-feeding (women); counter indication for MRI-scanning. All participants had to score < 18 on the 21-item Beck Anxiety Inventory (up to mild anxiety) (Beck, Epstein, et al., 1988), and <14 on the Beck Depression Inventory-II (up to mild depression) (Beck, Steer, et al., 1988), < 12 on the Epworth Sleepiness Scale (Johns, 1993), and < 8 on the Pittsburgh Sleep Quality Index (Buysse et al., 1989). Questionnaires further assessed chronotype with the Horne-Östberg questionnaire (Horne & Ostberg, 1976) and seasonality with the Seasonal Pattern Assessment Questionnaire (Rosenthal & Bradt, 1984), but the latter two questionnaires were not used for the inclusion of the participants.

361 For each task, 4 datasets were missing or had corrupt data such that 26 participants were
362 included in the analyses of each task (23 participants had valid datasets for both tasks). For the
363 emotional task, two participants' data failed the MRI quality control (QC) check, and the other
364 two participants were excluded as they did not complete the entire task. For the executive task,
365 four of the participants' data failed the MRI QC check. **Suppl. Table S2** summarises participants'
366 characteristics respective to each task.

367 **Overall Protocol.**_Participants completed an MRI session at least one week before the
368 experiment during which structural images of the brain were acquired and which served as
369 habituation to the experimental conditions. Participants maintained a loose sleep-wake schedule
370 (± 1h from the habitual sleep/wake-up time) during the 7 days preceding the fMRI experiment
371 to warrant similar circadian entrainment across participants and avoid excessive sleep loss while
372 maintaining realistic real-life conditions (verified using sleep diaries and wrist actigraphy - AX3
373 accelerometer, Axivity, United Kingdom). Volunteers were requested to refrain from all caffeine
374 and alcohol-containing beverages, and extreme physical activity for 3 days before participating
375 in the fMRI acquisitions. Data acquisitions took place in Liège, Belgium, between December 2020
376 and May 2023.

377 Participants arrived at the laboratory 1.5 to 2h after habitual wake time for the fMRI
378 scan. They were first exposed for 5 min to a bright polychromatic white light (1000 lux) and then
379 maintained in dim light (< 10 lux) for 45 min to standardise the participant's recent light history.
380 During this period participants were given instructions about the fMRI cognitive tasks and
381 completed practice tasks on a luminance-controlled laptop (< 10 lux). The fMRI session consisted
382 of participants completing three auditory cognitive tasks while alternatively maintained in
383 darkness or exposed to light: an executive task (25 min), an emotional task (20 min) and an
384 attentional task (15 min) [**Fig.1 A**]. The executive task was always completed first, as it was the
385 most demanding task. The order of the following two tasks was counterbalanced. Because it
386 included only 3 light conditions (see below) instead of 5 for the other two tasks, the attentional

task was not included in the present analyses. An eye-tracking system (EyeLink 1000Plus, SR Research, Ottawa, Canada) was monitored for proper eye opening during all data acquisitions.

Light exposure. An 8-m long MRI-compatible optic fibre (1-inch diameter, Setra Systems, MA, USA) transmitted light from a light box (SugarCUBE, Ushio America, CA, USA) to the dual end of the fibre which was attached to a stand fitted at the back of the MRI coil that allowed reproducible fixation and orientation of the optic fibre ends. The dual branches illuminated the inner walls of the head coil to ensure relatively uniform and indirect illumination of participants' eyes. A filter wheel (Spectral Products, AB300, NM, USA) and optical fibre filters (monochromatic narrowband orange filter - 589mn; full width at half maximum: 10 nm - or a UV highpass filter - 433–1650nm) were used to create the light conditions needed for the experiment (see **Fig.1 B and Suppl. Table 2** for in-detail light characteristics).

Illuminance and spectra could not be directly measured within the MRI scanner due to the ferromagnetic nature of measurement systems. The coil of the MRI and the light stand, together with the lighting system were therefore placed outside of the MR room to reproduce the experimental conditions of the in a completely dark room. A sensor was placed 2 cm away from the mirror of the coil that is mounted at eye level, i.e. where the eye of the first author of the paper would be positioned, to measure illuminance and spectra. The procedure was repeated 4 times for illuminance and twice for spectra and measurements were averaged. This procedure does not take into account inter-individual variation in head size and orbit shape such that the reported illuminance levels may have varied slightly across subjects. The relative differences between illuminance are, however, very unlikely to vary substantially across participants such that statistics consisting of tests for the impact of relative differences in illuminance were not affected. The detailed values reported in Supplementary Table 2 were computed combining spectra and illuminance using the excel calculator associated with a published work (Lucas et al., 2014).

412 Blue-enriched light illuminances were set according to the technical characteristics of
413 the light source and to keep the overall photon flux similar to prior 3T MRI studies of our team
414 (between ~10^{12} and 10^{14} ph/cm²/s) (Vandewalle et al., 2010; Vandewalle, Hébert, et al., 2011).
415 The orange light was introduced as a control visual stimulation for potential secondary whole-
416 brain analyses. For the present region of interest analyses, we discarded colour differences
417 between the light conditions and only considered illuminance as indexed by mel EDI lux. This
418 constitutes a limitation of our study as it does not allow attributing the findings to a particular
419 photoreceptor class.

420 For the executive and emotional task, the light conditions consisted of three different
421 illuminance of a white, blue-enriched polychromatic LED light (37, 92, 190 mel EDI lux; 6500K)
422 and one illuminance level of monochromatic orange light (.16 mel EDI lux; 590nm full width at
423 half maximum - FWHM: 10 nm). For the present analyses, we discarded colour differences
424 between the light conditions and only considered illuminance as indexed by mel EDI lux,
425 constituting a limitation of our study. In the executive task, participants were exposed to 30s to
426 70s (median 30s) of light blocks separated by 10s of darkness (< 0.1 lux) and the light blocks were
427 repeated 11 times for each light condition. For the emotional task, participants were exposed to
428 30 to 40s (median 35s) light blocks separated by 20s of darkness (< 0.1 lux) and the light blocks
429 were repeated five times for each light condition.

430 The attentional task only included a single illuminance level of the blue-enriched
431 polychromatic LED light (92 mel EDI lux) and one illuminance level of the monochromatic orange
432 light (.16 mel EDI lux), otherwise, the task would have been too long (> 30 min). Participants were
433 exposed to 30s of light blocks separated by 10s of darkness (<0.1 lux). The light blocks were
434 repeated 7 times for each light condition. As mentioned above it is not considered for the present
435 analyses.

436 **Cognitive Tasks**

437 Prior work of our team showed that the n-back task and emotional task included in the present
438 protocol were successful probes to demonstrate that light illuminance modulates cognitive
439 activity, including within subcortical structures (though resolution did not allow precise isolation
440 of nuclei or subparts) (e.g. (Vandewalle et al., 2010; Vandewalle, Schmidt, et al., 2007)). When
441 taking the step of ultra-high-field imaging, we therefore opted for these tasks as our goal was to
442 show that illuminance affects brain activity across cognitive domains while not testing for task-
443 specific aspects of these domains.

444 Auditory cognitive tasks. The tasks were programmed with Opensesame (3.2.8) (Mathôt
445 et al., 2012). Participants heard the auditory stimuli through MR-compatible earbuds
446 (Sensimetrics, Malden, MA). Before starting the tasks, to ensure optimal auditory perception of
447 task stimuli, participants set the volume through a volume check procedure. Participants used
448 an MRI-compatible keypad to respond to task items (Current Designs, Philadelphia, PA), which
449 was placed in the participant's dominant hand. The tasks were separated by about 5 minutes in
450 near darkness, to recalibrate the eye tracking system and to clarify instructions about the next
451 task to the participant.

452 **Executive task.** The task consisted of an auditory variant of the n-back task (Collette et al., 2005)
453 with a working memory 2-back task and a control letter detection 0-back task. Participants were
454 either asked to detect whether the current item was identical to the letter presented 2-items
455 earlier (2-back) or whether the current item consisted of the letter "K" (0-back) or using the
456 keypad (one button for "yes", one button for "no"). A block design was used for this task in which
457 each block included 15 items and lasted 30s. Task blocks were separated by 10-20s rest periods
458 and were preceded by an auditory instruction (500 ms) indicating the type of task to be
459 completed. Task levels were pseudo-randomised across the 4 light conditions with 3 blocks of 0-
460 back and 4 blocks of 2-back per light condition (see **Fig.1 C**).

461 **Emotional Task.** The task consisted of gender discrimination of auditory vocalizations that were
462 either pronounced with emotional or neutral prosody (Grandjean et al., 2005). Participants were

463 asked to use the keypad to indicate what they believed the gender of the person pronouncing
464 each token was. The gender classification was a lure task ensuring participants paid attention to
465 the auditory stimulation. The purpose of the task was to trigger an emotional response as
466 participants were not told that part of the stimuli was pronounced with angry prosody. The 240
467 auditory stimuli were pronounced by professional actors (50% women) and consisted of three
468 meaningless words ("goster", "niuvenci", "figotleich"). The stimuli were expressed in either an
469 angry or neutral prosody, which has been validated by behavioural assessments (Banse & Scherer,
470 1996) and in previous experiments (Grandjean et al., 2005; Sander et al., 2005; Vandewalle et al.,
471 2010). The stimuli were also matched for the duration (750 ms) and mean acoustic energy to
472 avoid loudness effects. During each 30 to 40-s light block, four angry prosody stimuli and four
473 neutral prosody stimuli were presented in a pseudorandom order and delivered every 3 to 5
474 seconds. A total of 160 distinct voice stimuli (50% angry; 50% neutral) were distributed across
475 the four light conditions. The darkness period separating each light block contained two angry
476 and two neutral stimuli. A total of 80 distinct voice stimuli (50% angry; 50% neutral) were
477 distributed across the darkness periods [see **Fig.1 D**].

478 **Data acquisition**

479 The MRI data were acquired in a 7T MAGNETOM Terra MR scanner (Siemens Healthineers,
480 Erlangen, Germany) with a 32-channel receive and 1-channel transmit head coil (Nova Medical,
481 Wilmington, MA, USA). Dielectric pads (Multiwave Imaging, Marseille, France) were placed
482 between the subject's head and receiver coil to homogenize the magnetic field of Radio
483 Frequency (RF) pulses.

484 Multislice T2*-weighted fMRI images were obtained with a multi-band Gradient-
485 Recalled Echo - Echo-Planar Imaging (GRE-EPI) sequence using axial slice orientation (TR = 2340
486 ms, TE = 24 ms, FA = 90°, no interslice gap, in-plane FoV = 224 mm × 224 mm, matrix size = 160
487 × 160 × 86, voxel size = 1.4 × 1.4 × 1.4 mm^3). To avoid saturation effects, the first three scans
488 were discarded. To correct for physiological noise in the fMRI data the participants' pulse and

489 respiration movements were recorded using a pulse oximeter and a breathing belt (Siemens
490 Healthineers, Erlangen, Germany). Following the fMRI acquisition a 2D GRE field mapping
491 sequence to assess B0 magnetic field inhomogeneity with the following parameters: TR = 5.2 ms,
492 TEs = 2.26 ms and 3.28 ms, FA = 15°, bandwidth = 737 Hz/pixel, matrix size = 96 × 128, 96 axial
493 slices, voxel size = (2x2x2) mm^3, acquisition time = 1:38 min, was applied.

494 For the anatomical image, a high-resolution T1-weighted image was acquired using a
495 Magnetization-Prepared with 2 RApid Gradient Echoes (MP2RAGE) sequence: TR = 4300 ms, TE
496 = 1.98 ms, FA = 5°/6°, TI = 940ms/2830 ms, bandwidth = 240 Hz, matrix size = 256x256, 224 axial
497 slices, acceleration factor = 3, voxel size = (0.75x0.75x0.75) mm^3.

498 **Data Processing**

499 For the MP2RAGE images, the background noise was removed using an extension (extension:
500 https://github.com/benoitberanger/mp2rage) of Statistical Parametric Mapping 12 (SPM12;
501 https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) under Matlab R2019 (MathWorks, Natick,
502 Massachusetts) (O'Brien et al., 2014). Then the images were reoriented using the
503 'spm_auto_reorient' function
504 (https://github.com/CyclotronResearchCentre/spm_auto_reorient) and corrected for intensity
505 non-uniformity using the bias correction method implemented in the SPM12 "unified
506 segmentation" tool (Ashburner & Friston, 2005). To ensure optimal co-registration, brain
507 extraction was done using SynthStrip (Hoopes et al., 2022) in Freesurfer
508 (http://surfer.nmr.mgh.harvard.edu/). The brain-extracted T1-images were used to create a T1-
509 weighted group template using Advanced Normalization Tools (ANTs,
510 http://stnava.github.io/ANTs/) prior to normalization to the Montreal Neurological Institute
511 (MNI) space using ANTs (1mm^3 voxel; MNI 152 template). The hypothalamus of each participant
512 was segmented within 1mm^3 MNI 152 template into 5 subparts - inferior anterior, superior
513 anterior, inferior tubular, superior tubular, posterior [cf. **Fig.2 A**] using an automatic
514 computational approach (Billot et al., 2020).

For the EPI images, auto reorientation was applied on the images first. Then, voxel-displacement maps were computed from the phase and magnitude images associated with B0 map acquisition (taken right after the task), using the SPM fieldmap toolbox. To correct for head motion and static and dynamic susceptibility-induced variance, the "Realign & Unwarp" of SPM12 was then applied to the EPI images. The realigned and distortion-corrected EPI images then underwent brain extraction using the SynthStrip and then the final images were smoothed with a Gaussian kernel characterized by a FWHM = 3mm. The first level analyses were performed in the native space to prevent any possible error that may be caused by co-registration.

Statistical analyses

The whole-brain univariate analyses consisted of a general linear model (GLM) computed with SPM12. For the executive task, task blocks and light blocks were modelled as block functions. For the emotional task, the auditory stimuli were modelled as stick functions. For both tasks, a high-pass filter with a 256s cut-off was applied to remove low-frequency drifts. For both tasks, stick or block functions were convolved with the canonical hemodynamic response function. Movement and physiological parameters (cardiac, and respiration), which were computed with the PhysIO Toolbox (Translational Neuromodeling Unit, ETH Zurich, Switzerland), were included as covariates of no interest (Kasper et al., 2017).

Two separate analyses were completed. In the main analyses, we sought to test whether brain responses during the tasks were modulated by overall changes in illuminance level. The regressors of task blocks or events were accompanied by a single parametric modulation regressor corresponding to the light melanopic illuminance level (.16, 37, 92, 190 mel EDI). The contrasts of interest consisted of the main effects of the parametric modulation. In the subsequent post hoc analysis, we estimated the responses to the stimuli under each light condition. Separate regressors modelled each task's block or event type under each light condition (0, 0.16, 37, 92, 190 mel EDI). The contrasts of interest consisted of the main effects of each regressor.

The output masks of the segmentation procedure we used to extract regression betas associated with each of the hypothalamus subparts using the REX Toolbox (https://web.mit.edu/swg/software.htm) (Duff et al., 2007). Betas were averaged (mean) within each subpart and then across the homologous subparts of each hemisphere. In the main analyses this yielded 1 activity estimate per stimulus type and per hypothalamus subpart (i.e. 10 per individual), while in the subsequent analyses, we obtained 5 activity estimates per stimulus type and per subpart (50 per individual).

For visualization of whole-brain results over the entire sample, all statistical maps obtained from the first level analysis were first transferred to the group template space and then the MNI space (1x1x1mm^3 image resolution). All the registration steps were performed with ANTs. The visualisation was focused on the hypothalamus regions to assess whether increasing illuminance resulted in a local increase and/ or decrease of beta estimates within the hypothalamus or whether beta estimates were mainly influenced by a relatively unspecific and widespread increase in BOLD signal surrounding the hypothalamus.

Statistical analyses of the activity of the hypothalamus subparts were performed in SAS 9.4 (SAS Institute, NC, USA). Analyses consisted of Generalised Linear Mixed Models (GLMM) with the subject as a random factor (intercept and slope) and were adjusted for the dependent variable distribution. As the main statistical analysis was completed for each task, the significance threshold was corrected for multiple comparisons and was set at $p < 0.025$. Direct post hoc of the main analyses were corrected for multiple comparisons using a Tukey adjustment. The subsequent more detailed analyses were considered as post hoc that were not corrected for multiple comparisons ($p < 0.05$). To detect outlier values within the data sets, Cook's distance > 1 was used for exclusion. No outliers were detected for activity estimates of both tasks, while four outlier values were removed from the analyses of the 2-back and 0-back performance.

The main analyses included the activity estimates modulated by light illuminance as a dependent variable and the hypothalamus subpart and stimulus type (2-back/0-back - neutral/emotional) as repeated measures (autoregressive (1) correlation), together with age, sex and BMI as covariates. The second set of post hoc GLMM analyses included the activity estimates of the hypothalamus subparts as the dependent variable and hypothalamus subpart, stimulus type and illuminance (0, 0.16, 37, 92, 190 mel EDI lux) as the repeated measures (autoregressive (1) correlation), together with age, sex, and BMI as covariates and interaction term between illuminance and hypothalamus subpart. The final set of analyses included performance metrics as dependent variables (accuracy to the 2-back or 0-back task - as percentage of correct responses; reaction time – ms - to emotional or neutral stimuli during the emotional task) and included the same repeated measures and covariates ads in the preceding set as well as activity of the relevant hypothalamus subpart.

Optimal sensitivity and power analyses in GLMMs remain under investigation (e.g. (Kain et al., 2015)). We nevertheless computed a prior sensitivity analysis to get an indication of the minimum detectable effect size in our main analyses given our sample size. According to G*Power 3 (version 3.1.9.4) (Erdfelder et al., 2009), taking into account a power of 0.8, an error rate α of 0.025 (correcting for 2 tasks), and a sample of 26 allowed us to detect large effect sizes $r > 0.54$ (two-sided; absolute values; CI: 0.19–0.77; $R^2 > 0.29$, R^2 CI: 0.04–0.59) within a multiple linear regression framework including one tested predictor (illuminance effect) and three covariates (age, sex and BMI).

Data and code availability statement

The processed data and analysis scripts supporting the results included in this manuscript are publicly available via the following open repository: https://gitlab.uliege.be/CyclotronResearchCentre/Public/xxxx (the repository will be created with the version of records).

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Figures and Tables

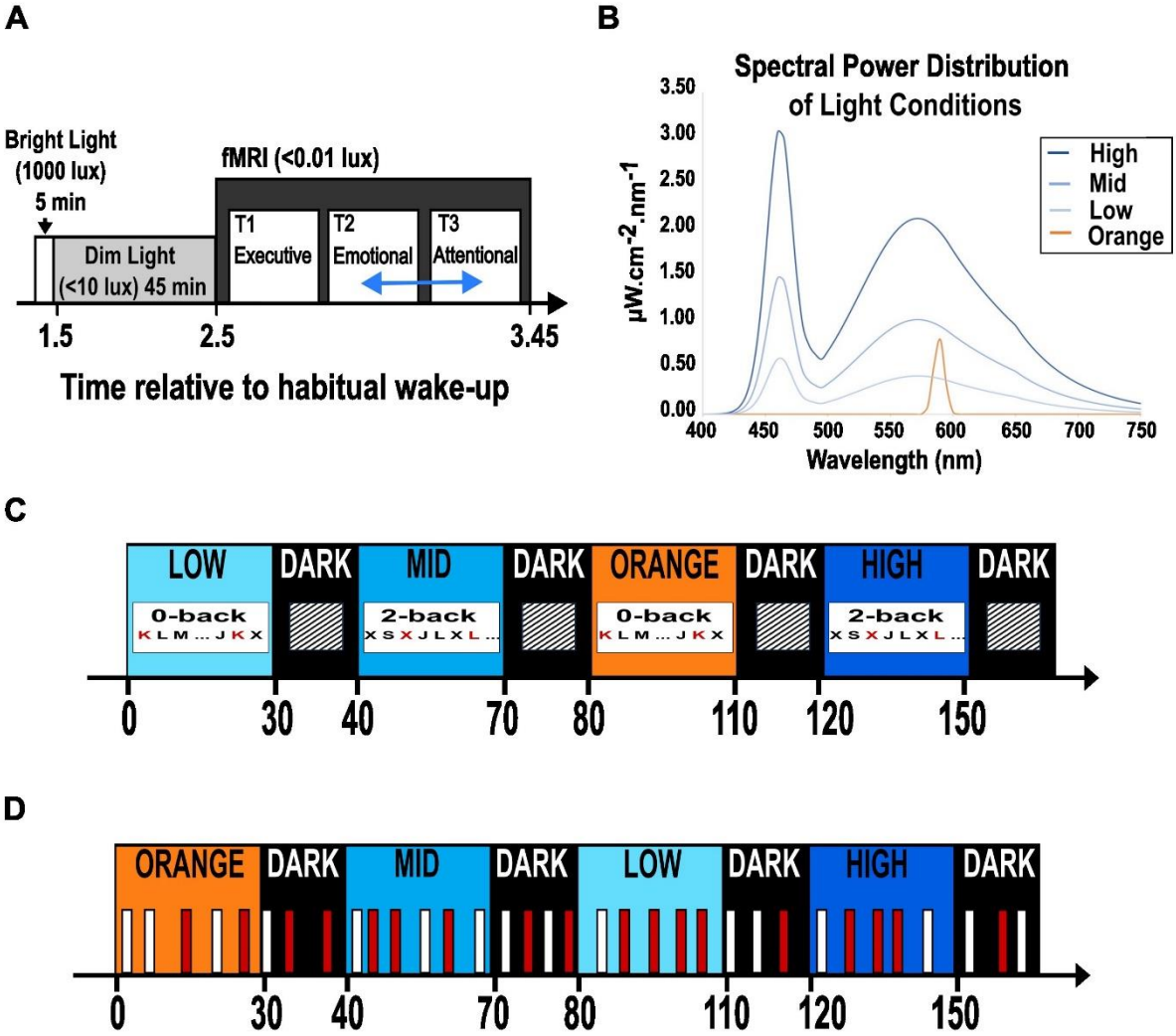
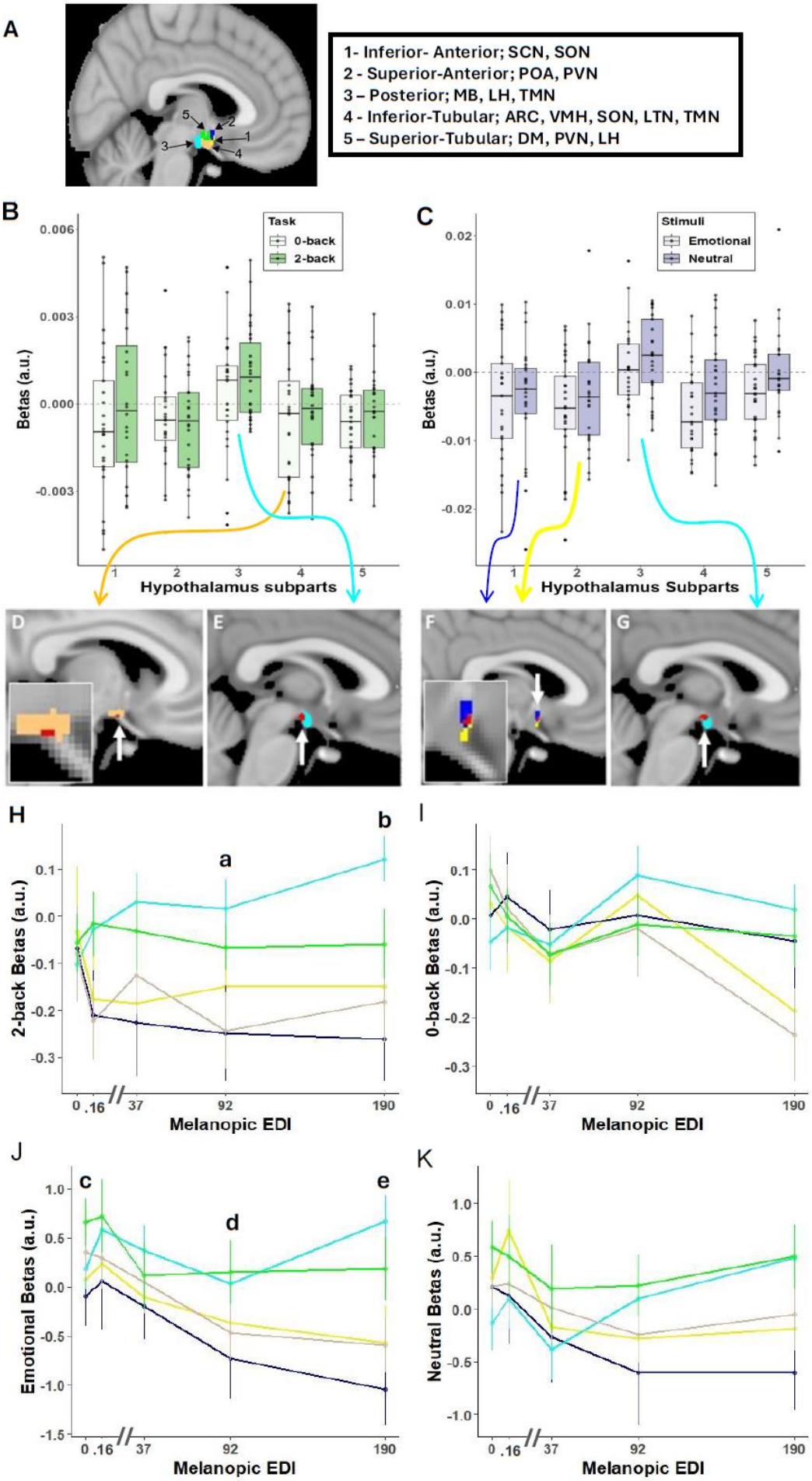


Figure 1. Experimental protocol.

(A) Overall timeline. After prior light history standardisation, participants performed executive (always first), emotional and attentional tasks (pseudo-randomly 2nd or 3rd, blue arrow). As the attentional task included fewer light conditions, it is not considered in the present manuscript (see methods for more details).

(B) Spectral power distribution of light exposures. Monochromatic orange: 0.16 mel EDI lux; Polychromatic, blue-enriched light (6500K); LOW, MID, HIGH: 37, 92, 190 mel EDI lux. For the present analyses, we discarded colour differences between the light conditions and only considered illuminance as indexed by mel EDI lux, constituting a limitation of our study. See **Suppl. Table 2** for full details).

(C-D) Tasks procedures. Time is reported in seconds relative to session onset; participants were pseudo-randomly exposed to the 4 light conditions. **(C)** Executive task: alternation of letter detection blocks (0-back) and working memory blocks (2-back). **(D)** Emotional task: lure gender discrimination of vocalizations (50% angry (red), 50% neutral (white).


A
1- Inferior- Anterior; SCN, SON
2 - Superior-Anterior; POA, PVN
3 – Posterior; MB, LH, TMN
4 - Inferior-Tubular; ARC, VMH, SON, LTN, TMN
5 – Superior-Tubular; DM, PVN, LH
B
Task
0-back
2-back
Betas (a.u.)
Hypothalamus subparts
C
Stimuli
Emotional
Neutral
Betas (a.u.)
Hypothalamus Subparts
D
E
F
G
H
2-back Betas (a.u.)
Melanopic EDI
I
0-back Betas (a.u.)
Melanopic EDI
J
Emotional Betas (a.u.)
Melanopic EDI
K
Neutral Betas (a.u.)
Melanopic EDI

844

845 **Figure 2. Illuminance impact on the hypothalamus subparts.**

846 **(A) Segmentation of the hypothalamus in five subparts in a representative participant.** The nuclei
847 encompassed by the different subparts are indicated in the right inset – according to (Billot et al., 2020).
848 ARC: arcuate nucleus; DMH; dorsomedial nucleus; LH lateral hypothalamus; LTN: lateral tubular nucleus;
849 MB: mamillary body; POA: preoptic area; PVN: paraventricular nucleus; PNH: posterior nucleus of the
850 hypothalamus; SCN: suprachiasmatic nucleus; SON: supraoptic nucleus; TMN: tuberomammillary nucleus;
851 VMN: ventromedial nucleus.

852 **(B-C)** Estimates (beta; arbitrary unit – a.u.) of the collective impact of illuminance variation on the activity
853 of each hypothalamus subpart (Refer to Table 1 full statistics). **(B)** Executive task: significant main effect
854 of hypothalamus subparts (p=0.002), no significant main of task type (p=0.4) or subpart-by-task-type
855 interaction (p=0.61). **(C)** Emotional task: significant main effect of hypothalamus subparts (p<.0001), and
856 of stimulus type (p=0.048) or subpart-by-stimulus-type interaction (p=0.74).

857 **(D-G)** Whole brain analyses of the collective impact of the variations in illuminance over the hypothalamus
858 area - for illustration. A local positive peak (red; $p_{uncorrected}$<0.001) was detected over the posterior
859 hypothalamus subpart (light blue) in executive **(E)** and emotional **(G)**. A local negative peak (red;
860 $p_{uncorrected}$<0.001) was detected over the inferior-tubular hypothalamus subparts (light orange) during the
861 executive task **(D)**, while local negative peak (red; $p_{uncorrected}$<0.001) was detected over the inferior-anterior
862 (yellow) and superior-anterior (blue) hypothalamus subparts during the emotional task **(F)** – insets
863 correspond to enlargements over the hypothalamus area. Arrows from panels B and C arise from and are
864 colour coded according to the hypothalamus subpart that is displayed in panels D to G. These results
865 indicate that our finding does not arise from a nearby "leaking“ activation/deactivation.

866 **(H-K)** Estimates of the impact of each illuminance on the activity of the hypothalamus subparts. (Refer for
867 Table 2 and Suppl. Tables 3/4/5/6 for full statistics) Activity dynamics across illuminance for each subpart
868 (colour code as in A). Results are displayed per task or stimulus type although no interactions with task or
869 stimulus type were detected. Significant illuminance-by-hypothalamus-subpart interactions were
870 detected for **(H-I)** the executive task (p=0.041) and **(J-K)** the emotional task (p=0.041). Small letter indicate
871 significant difference (p < 0.05) between the following subparts at illuminance: a. 92 mel EDI lux: posterior
872 vs. superior-anterior & inferior-tubular; b. 190 mel EDI lux: posterior vs. inferior-anterior, superior-anterior
873 & inferior-tubular; c. 0 mel EDI lux: posterior vs. superior-tubular; d. 92 mel EDI lux: posterior vs. superior-
874 anterior; superior-anterior vs. superior-tubular; e. 190 mel EDI lux: posterior vs. inferior-anterior,
875 superior-anterior & inferior-tubular; superior-tubular vs. superior-anterior , inferior-tubular & inferior-
876 anterior.

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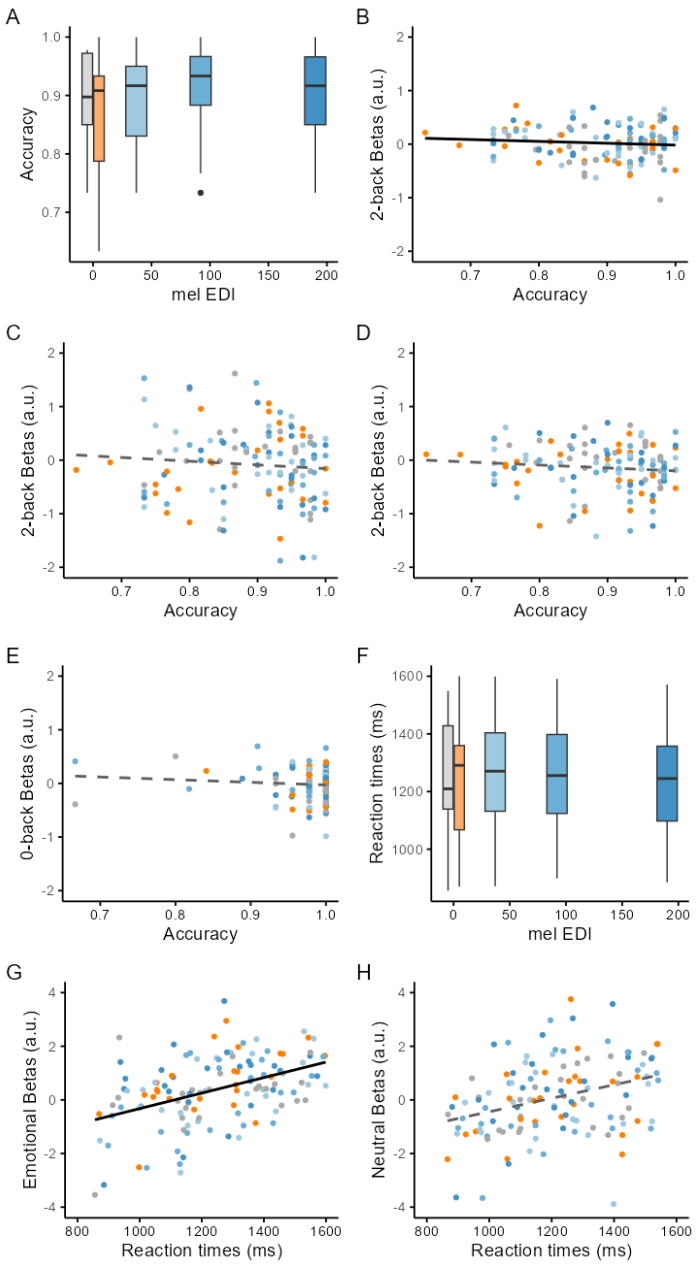

Figure 3. Impact of illuminance on performance and relationships with the activity of the posterior hypothalamus subpart.

(A) Accuracy (percentage of correct responses) to the 2-back increased with increasing illuminance ($p = 0.034$).

(B) Accuracy to the 2-back task is negatively correlated to the activity of the posterior hypothalamus subpart ($p = 0.0027$).

(C-D) Accuracy to the 2-back task is not correlated to the activity of the inferior-anterior **(C)** and inferior-tubular **(D)** hypothalamus subparts ($p > 0.4$). Association between superior-anterior and superior-tubular subparts are not displayed but were not significant ($p > 0.6$). See Suppl Table 7 for full details.

(E) Accuracy to the 0-back task is not correlated to the activity of the posterior hypothalamus subpart ($p = 0.45$).

(F) Reaction times to the emotional stimuli did not significantly change with increasing illuminance ($p = 0.41$).

(G) Reaction times to the emotional stimuli are correlated to the activity of the posterior hypothalamus subpart ($p = 0.04$) with higher activity associated to slower reaction times. **(H)** Reaction times to the neutral stimuli are not correlated to the activity of the posterior hypothalamus subpart ($p = 0.6$). Solid and dashed lines correspond to the significant and not significant linear regression lines, respectively.

Table 1. Differences between hypothalamus subparts in the collective impact of the variation in illuminance on their activity.

Executive task							
Main GLMM				**Pairwise comparisons**			
Effect	**F value (df)**	**P value***	**Partial R^2**	**Contrast#**	**t-value**	**$P_{uncorrected}$**	**$P_{corrected}$**
Hypothalamus subparts	4.36 (4,225)	**0.002**	**0.08**	1 vs. 2	-0.30	0.76	0.99
				1 vs. 3	-3.48	**0.0006**	**0.0056**
				1 vs. 4	< 0.01	0.99	1
Task	0.74 (1,25)	0.4		1 vs. 5	-0.57	0.57	0.98
Hypothalamus subparts x task type	0.68 (4,225)	0.61		2 vs. 3	-3.17	**0.0017**	**0.015**
				2 vs. 4	0.31	0.76	0.99
				2 vs. 5	-0.27	0.79	0.99
Age	0.33 (1,22)	0.57		3 vs. 4	3.48	**0.0006**	**0.0055**
BMI	0.59 (1,22)	0.45		3 vs. 5	2.54	**0.0041**	**0.033**
Sex	0.01 (1,22)	0.91		4 vs. 5	-0.5	0.57	0.98
Emotional task							
Main GLMM				**Pairwise comparisons**			
Effect	**F Value**	**P value***	**Partial R^2**	**Contrast#**	**t-value**	**$P_{uncorrected}$**	**$P_{corrected}$**
Hypothalamus subparts	9.38 (4,194)	**<.0001**	**0.22**	1 vs. 2	0.67	0.67	0.99
				1 vs. 3	-4.76	**< 0.0001**	**< 0.0001**
				1 vs. 4	0.00	0.99	1
Task	4.33 (1,25)	**0.048**	**0.15**	1 vs. 5	-1.88	0.06	0.33
Hypothalamus subparts x stimulus type	0.5 (4,194)	0.74		2 vs. 3	-5.43	**< 0.0001**	**0.0001**
				2 vs. 4	-0.66	0.51	0.96
				2 vs. 5	-2.54	**0.012**	0.086
Age	0.43 (1,22)	0.52		3 vs. 4	4.76	**< 0.0001**	**< 0.0001**
BMI	0.05 (1,22)	0.83		3 vs. 5	2.85	**0.0048**	**0.038**
Sex	1.47 (1,22)	0.24		4 vs. 5	-1.88	0.061	0.32

Outputs of the generalized linear mixed model (GLMM) with subject as the random factor (intercept and slope), and task and subpart as repeated measures (ar(1) autocorrelation).

* The corrected p-value for multiple comparisons over 2 tests is $p < 0.025$.

Refer to Fig.2A for correspondence of subpart numbers

Table 2. Statistical outputs of GLMM testing for differences between the activity of each subpart of the hypothalamus under each illuminance

Executive task							
Main GLMM				**Comparisons between subparts per illuminance #**			
Effect	**F-value (df)**	**P value**	**Partial R^2**	**Illuminance***	**contrast**	**t-value**	**p-value**
Subpart	1.4 (4,228)	0.23		92	2 vs. 3	-2.25	**0.025**
Illuminance	2.15 (4,1017)	0.073		92	3 vs. 4	2.58	**0.01**
				190	1 vs. 3	-2.80	**0.0053**
Task	3.24 (1,228)	0.073		190	2 vs. 3	-2.24	**0.025**
Subpart x Illuminance	1.7 (16,1017)	**0.041**	**0.09**	190	3 vs. 4	3.15	**0.0017**
Age	1.19 (1,22)	0.29					
BMI	0.01 (1,22)	0.9					
Sex	0.38 (1,22)	0.54					

Emotional task							
Main GLMM				**Comparisons between subparts per illuminance #**			
Effect	**F-value (df)**	**P value**	**Partial R^2**	**Illuminance***	**contrast**	**t-value**	**p-value**
Subpart	4.29 (4,229)	**0.0023**	**0.07**	0	3 vs. 5	-2.05	**0.04**
				92	2 vs. 3	-2.53	**0.012**
Illuminance	9.41 (4,1020)	**< 0.0001**	**0.035**	92	2 vs. 5	-2.96	**0.0032**
				190	1 vs. 3	-3.31	**0.001**
				190	2 vs. 3	-4.75	**< 0.0001**
Task	0.13 (1,229)	0.72		190	1 vs. 5	-2.5	**0.013**
				190	2 vs. 5	-4.04	**<0.0001**
				190	3 vs. 4	3.13	**0.0018**
Subpart x Illuminance	1.7 (16,1020)	**0.041**	**0.026**	190	4 vs. 5	-2.32	**0.021**
Age	0.59 (1,22)	0.45					
BMI	1.54 (1,22)	0.23					
Sex	0.05 (1,22)	0.83					

* illuminance in mel EDI lux

Only significant comparisons are reported in the main text. For the full table, including post hocs comparing light levels within a subpart, refer to **Suppl. Table 3/4/5/6/7**