RESEARCH ARTICLE

Impact of light on task-evoked pupil responses during cognitive tasks

Islay Campbell[1] | Elise Beckers[1,2] | Roya Sharifpour[1] | Alexandre Berger[1,3,4] |
Ilenia Paparella[1] | Jose Fermin Balda Aizpurua[1] | Ekaterina Koshmanova[1] |
Nasrin Mortazavi[1] | Siya Sherif[1] | Gilles Vandewalle[1]

[1]GIGA-Cyclotron Research Centre-In Vivo Imaging, University of Liège, Liège, Belgium

[2]Faculty of Health, Medicine and Life Sciences, School for Mental Health and Neuroscience, Alzheimer Centre Limburg, Maastricht University, Maastricht, The Netherlands

[3]Institute of Neuroscience (IoNS), Université Catholique de Louvain (UCLouvain), Brussels, Belgium

[4]Synergia Medical SA, Mont-Saint-Guibert, Belgium

Correspondence

Gilles Vandewalle and Islay Campbell, GIGA-Cyclotron Research Centre-In Vivo Imaging, Bâtiment B30, 8 Allée du Six Août, University of Liège-Sart Tilman, 4000 Liège, Belgium.
Email: gilles.vandewalle@uliege.be and icampbell@uliege.be

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Summary

Light has many non-image-forming functions including modulation of pupil size and stimulation of alertness and cognition. Part of these non-image-forming effects may be mediated by the brainstem locus coeruleus. The processing of sensory inputs can be associated with a transient pupil dilation that is likely driven in part by the phasic activity of the locus coeruleus. In the present study, we aimed to characterise the task-evoked pupil response associated with auditory inputs under different light levels and across two cognitive tasks. We continuously monitored the pupil of 20 young healthy participants (mean [SD] 24.05 [4.0] years; 14 women) whilst they completed an attentional and an emotional auditory task whilst exposed to repeated 30–40-s blocks of light interleaved with darkness periods. Blocks could either consist of monochromatic orange light (0.16 melanopic equivalent daylight illuminance (EDI) lux) or blue-enriched white light of three different levels [37, 92, 190 melanopic EDI lux; 6500 K]. For the analysis, 15 and then 14 participants were included in the attentional and emotional tasks, respectively. Generalised linear mixed models showed a significant main effect of light level on the task-evoked pupil responses triggered by the attentional and emotional tasks ($p \leq 0.0001$). The impact of light was different for the target versus non-target stimulus of the attentional task but was not different for the emotional and neutral stimulus of the emotional task. There is a smaller sustained pupil size during brighter light blocks but, a higher light level triggers a stronger task-evoked pupil response to auditory stimulation, presumably through the recruitment of the locus coeruleus.

KEYWORDS

functional MRI, light, locus coeruleus, melanopsin, non-image-forming, transient pupil response

1 | INTRODUCTION

The non-image-forming (NIF) system (also termed non-visual system) in the human retina detects environmental irradiance to mediate the influences of light on many NIF functions, including circadian entrainment (Berson et al., 2002), melatonin suppression (Brainard et al., 2001), pupillary light responses (Gamlin et al., 2007; Hattar et al., 2002), and stimulation of alertness and cognitive performance (Vandewalle et al., 2009). Light's influence on human alertness and cognition has been reported to be improved by high-intensity white light and short wavelength light, but the impact of light on cognition is complicated by being dependent on several factors, such as time of day, spectral composition, and intensity of the light source (Siraji et al., 2022).

The primary photoreceptors of the NIF system are intrinsically photosensitive retinal ganglion cells (ipRGCs) (Mure, 2021; Provencio et al., 2000), which express the photopigment melanopsin. Animal studies have established that the ipRGCs project to various subcortical brain regions, including the suprachiasmatic nucleus (SCN) of the hypothalamus, the site of the master circadian clock (Tri & Do, 2019). The exact brain pathways involved in light's NIF functions for humans is an area of continued and active research. The locus coeruleus (LC), in the brainstem, receives indirect inputs from the SCN, and it is hypothesised that the LC may be involved in mediating light's influence on alertness and cognition (Aston-Jones et al., 2001; Aston-Jones & Cohen, 2005; Vandewalle et al., 2009). The LC is central to cognition and alertness and a major source of noradrenaline (NA) in the brain (Aston-Jones & Cohen, 2005). A previous neuroimaging study, using a 3-Tesla magnetic resonance imaging (MRI) apparatus reported that an area of the brainstem consistent with the location of the LC is modulated by the wavelength of light whilst performing a non-visual cognitive task (Vandewalle et al., 2007). The LC is a small bilateral nucleus with a cylinder shape, ∼0.15 mm long and 2.5 mm in diameter (∼50.000 neurones in total), located in the brainstem (Keren et al., 2009). Due to its small size, and its deep location near the fourth ventricle, in vivo imaging of the LC is challenging such that it is difficult to assess its role in mediating the NIF impacts of light in humans. Here, we emphasise that variation in pupil size may be an accessible means to address this research question.

The autonomic nervous system regulates pupil size through the control of two muscles in the pupil, the iris sphincter muscle that causes the constriction of the pupil, and the dilatory muscle that promotes the dilation of the pupil (Larsen & Waters, 2018). Pupil size is dependent on the sympathovagal balance, with parasympathetic activity promoting pupil constriction through recruitment of the iris sphincter muscle via the midbrain Edinger–Westphal nucleus (EWN). Pupil dilation is dependent on the sympathetic system that starts at the hypothalamus and the LC, leading to the inhibition of the activity of the EWN causing pupil dilation through the constriction of the dilator muscle (Larsen & Waters, 2018; Mathôt, 2018). However, pupillary dilation can also be caused by inhibiting the parasympathetic constriction pathway, through LC activity inhibiting the EWN, causing relaxation of the constrictor muscles (Mathôt, 2018; Steinhauer et al., 2015). There is research that suggests that pupil dilation due to cognitive demand is due to inhibition of the parasympathetic pathway (Steinhauer et al., 2004). The interplay between the sympathetic and the parasympathetic systems determines the size of the pupil, with environmental irradiance, mental effort, and fatigue influencing the balance between the two systems (Larsen & Waters, 2018; Steinhauer et al., 2004; Wang et al., 2018). Change in pupil size can be described as a baseline response where pupil size is maintained for a longer period of time or a faster phasic response (Beatty, 1982).

There is evidence to suggest that fluctuations in pupil size is a proxy measure of the changes in brain arousal during cognitive activity. Specifically, the LC is proposed to be an important region in the control of pupil dilation and changes in pupil diameter have been hypothesised to be a readout of the activity of the NA neurones of the LC (Costa & Rudebeck, 2016; Joshi & Gold, 2020). The LC-NA system has two different modes, baseline tonic activity where there is continuous spiking, and phasic activity, characterised by brief bursts of high-frequency activity that can be spontaneous or in response to salient stimuli (Aston-Jones & Cohen, 2005). Evidence for the link between the LC and pupil size comes from the observation that the neuronal activity of the LC fluctuates almost simultaneously with changes in pupil diameter (Aston-Jones & Cohen, 2005). Further direct evidence comes from research showing that the spiking activity of the LC and the diameter of the pupil were also correlated during a decision-making task in monkeys (Varazzani et al., 2015). Also, spontaneous LC activity correlated with pupil size in monkeys performing a simple fixation task and an evoked pupil dilation occurred when the LC was electrically microstimulated. In addition, other brain areas (inferior colliculus, superior colliculus, anterior and posterior cingulate cortex) also show a less reliable association between pupil size and spontaneous LC activity, suggesting there is co-ordinated neuronal activity in brain areas through LC-mediated arousal (Aston-Jones & Cohen, 2005; Joshi et al., 2016; Nassar et al., 2012). The propagation of LC signal is slow to brain areas due to having unmyelinated projections (Aston-Jones et al., 1985). Furthermore, human studies combining functional MRI (fMRI) and pupillometry have found activations in the area of the brainstem compatible with the LC were linked to fluctuations in pupil diameter, during resting state and for a novelty detection task (de Gee et al., 2017; Murphy et al., 2014). The research highlights that changes in pupil diameter are a relatively reliable means to assess LC activity.

Changes in pupil diameter can also be induced in response to cognitive effort which can be triggered by external stimuli (Joshi & Gold, 2020; Mathôt, 2018). In response to an external task event, the pupil dilates and then constricts back to baseline. This pupil response to a task event is called the 'task-evoked pupil response' (TEPR). These TEPRs can also be influenced by factors such as the demand of the cognitive task and the performance (Aston-Jones & Cohen, 2005; Kahneman & Beatty, 1966). The exact mechanism of the link between the size of the pupil and the activity of the LC is still not known. However, studying TEPRs is nevertheless often considered a non-invasive means to determine the ongoing alterations in the LC phasic activity or arousal level during cognitive tasks.

The pupil is well known to adapt to changes in the light environment, with the pupil constricting at higher light levels mainly driven by the parasympathetic system and dilation mainly being driven by the sympathetic system in darkness (Joshi & Gold, 2020; Larsen & Waters, 2018). This light-induced constriction is maintained by ipRGCs, which innervate the pretectal olivary nucleus, which in turn project to the EWN leading to pupil constriction by parasympathetic drive (Joshi & Gold, 2020). However, whether the TEPRs are influenced by light's NIF effects is currently not known. We, therefore, decided to study the TEPRs under different light conditions. We measured pupil diameter during two cognitive tasks and examined the effect of light level, expressed in melanopic (mel) equivalent daytime illuminance (EDI) lux, on the TEPRs to auditory stimuli. We hypothesised that the TEPRs would be greater under higher irradiance levels

due to the stimulating NIF impact of light, potentially due to an increase in either sympathetic or parasympathetic drive. To test this hypothesis, we used eye tracking data from healthy young participants, who completed an attentional and an emotional auditory cognitive task during a fMRI recording whilst exposed to different light conditions.

2 | METHODS

2.1 | Participants

A total of 20 healthy participants (mean [SD] age 24.05 [4.0] years; 14 women) gave their written informed consent to take part in the study, which was approved by the Ethics Committee of the Faculty of Medicine of the University of Liège. The participants were assessed for the exclusion criteria with a semi-structured interview and questionnaires. None of the participants had a history of psychiatric and neurological disorders, sleep disorders, the use of psychoactive drugs or addiction. Participants had no history of night shift work during the last year or recent transmeridian travel during the last 2 months; excessive caffeine (>4 caffeine units/day) or alcohol consumption (>14 alcohol units/week); and were not taking medication or smoking. Their scores on the 21-item Beck Anxiety Inventory (Beck et al., 1988) and the Beck Depression Inventory-II (Beck et al., 1961) were minimal or mild (<17) and minimal (<14), respectively normal. Women were not pregnant or breastfeeding. Participants reported no history of ophthalmic disorders or auditory impairments and were screened for colour blindness. Due to technical issues (see below), 15 and 14 participants were, respectively, included in the analyses of the attentional and emotional tasks (Table 1).

Participants followed a loose sleep–wake schedule (±1 h from habitual bedtime/wake-up time) during the 7 days preceding the laboratory experiment to maintain realistic entrained life conditions and avoid excessive sleep restriction across all participants. Sleep–wake schedules were verified using wrist actigraphy and sleep diaries. They were asked to refrain from caffeinated and alcohol-containing beverages and excessive exercise for at least 3 days before the experiment. Participants were familiarised with the MRI environment 1 week before the experiment during an MRI session where structural images of the brain were acquired.

2.2 | Experimental protocol

Most participants ($N = 17$) arrived at the laboratory 1.5–2 h after habitual wake time, whilst a minority ($N =$ three) were admitted to the laboratory 1.5–2 h before habitual bedtime. The study will investigate the effect time-of-day (morning versus evening) has on light exposure on brain functions and behaviour in the future. For this paper, all results presented are controlled for time-of-day differences.

Participants were first exposed for 5 min to a bright white light (1000 lux) and were then maintained in dim light (<10 lux) for 45 min to standardise participant light history before the fMRI session (Figure 1a). During this period participants were given instructions about the fMRI cognitive tasks and completed practice tasks. The fMRI session consisted of participants completing an executive task (25 min), an attentional task (15 min), and an emotional task (20 min) (Figure 1b,c). Participants always completed the executive task first and then the order of the following two tasks was pseudo-randomised. Only the emotional and the attentional tasks are discussed in the present paper as they consisted of a stream of events, where each sound potential triggers a TEPR.

An MRI-compatible light system (Supplementary Figure S1) designed-in-laboratory was developed to ensure relatively uniform and indirect illumination of participants' eyes whilst in the MRI scanner. An 8-m long MRI-compatible dual-branched optic fibre (Setra Systems, MA, USA) transmitted light from a light box (SugarCUBE,

TABLE 1 Table of participants included in the analysis.

	Total participants	Oddball analysis	Emotional analysis
Number of participants	20	15	14
Age, years, mean (SD)	24.05 (4.00)	24.33 (4.15)	24.07 (4.41)
Sex, male, n	6	5	4
Mood, BDI-II score, mean (SD)	6.94 (5.57)	6.0 (4.78)	6.83 (6.01)
Anxiety, BAI score, mean (SD)	6.55 (5.98)	5.71 (4.06)	7.66 (6.71)
Sleep quality, PSQI score, mean (SD)	4.27 (2.88)	3.78 (1.92)	4.41 (3.31)
Seasonality, SPAQ score, mean (SD)	1.05 (0.80)	1 (0.78)	1.16 (0.83)
Chronotype, HO score, mean (SD)	48.5 (9.26)	47.42 (9.72)	47.58 (6.98)
Daytime sleepiness, ESS score, mean (SD)	6.27 (3.21)	6.35 (2.79)	6.75 (3.57)
Years of education, mean (SD)	14.35 (3.12)	14.84 (2.47)	13.72 (3.40)

Note: columns for total number of participants who completed the study, and the number of participants included for each task. Refer to the main text for references.

Abbreviations: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; ESS, Epworth Sleepiness Scale; HO, Horne and Östberg questionnaire; PSQI, Pittsburgh Sleep Quality Index; SPAQ, Seasonal Pattern Assessment Questionnaire.
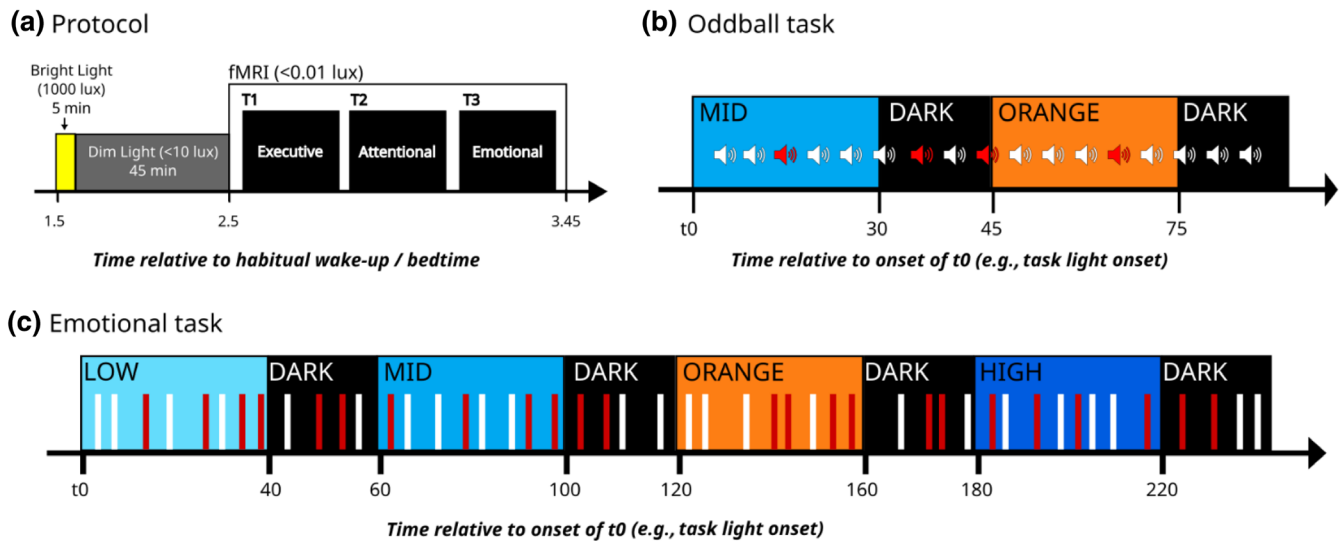
(a) Protocol

(b) Oddball task

(c) Emotional task

FIGURE 1 Experimental design. (a) General protocol. Time relative to scheduled wake-up/bedtime (h). Following standardisation of immediate prior light exposure (see Methods), participants performed an executive (not discussed in the present paper), an attentional and emotional task in functional magnetic resonance imaging (fMRI). (b) Detailed procedures of the attentional task (oddball). Time (s) relative to t0, a time point arbitrarily chosen as the light onset of the session. The task consisted of a stream of standard sounds (80%) and pseudo-randomly interspersed odd sounds (20%); participants were asked to identify the odd stimuli through a button press. Whilst completing the task participants were exposed to blue-enriched white light (BEL; 92 melanopic [mel] equivalent daylight illuminance [EDI] lux; 6500 K) (MID) and a monochromatic orange (0.16 mel EDI lux; 589mn) light. Light exposures lasted 30 s and were separated by 15-s periods of darkness. Odd (red) and standard (white) stimuli were equally distributed across the two light conditions and darkness. (c) Detailed procedures of the emotional task. Time (s) relative to t0, a time point arbitrarily chosen as the light onset of the session. The task consisted of a lure gender discrimination of auditory vocalisations of the three pseudo-word types ('goster', 'niuvenci', or 'figotleich') whilst exposed to the alternating white BEL of three different intensities (37, 92, 190 mel EDI lux; 6500 K) (LOW, MID, HIGH) and a monochromatic orange (0.16 mel EDI lux; 589mn) light. Light exposures lasted 30–40 s and were separated by 15–20-s periods of darkness. Untold to the participants, vocalisations were pronounced with angry (red bars) and neutral (white bars) prosody pseudo-randomly and equally distributed across the three light conditions.

Ushio America, CA, USA), that was stored in the MRI control room. The dual end of the optic fibre was attached to a light stand fitted at the back of the MRI coil. This allowed for equal illumination of the participants' eyes. A filter wheel (Spectral Products, AB300, NM, USA) and optical fibre filters (a monochromatic orange light filter [589mn; full width at half maximum: 10 nm] and a UV long bypass [433–1650 nm] filter) were used to create the light conditions needed for the experiment. Participants were asked to keep their eyes open and try not to blink too much during the cognitive tasks.

Both tasks were programmed with Opensesame (3.2.8) (Mathôt et al., 2012) and launched from a computer in the MRI control room. Participants heard the auditory stimuli through MR-compatible headphones (Sensimetrics, Malden, MA) and the volume was set by the participant before starting the tasks to ensure a good auditory perception of all the task stimuli. Participants used an MRI-compatible button box to respond to task items (Current Designs, Philadelphia, PA, USA). During the attentional task, participants were exposed to 30 s of light blocks separated by 15 s of darkness (<0.1 lux). The spectra of the lights were assessed at the level of the end of the optic fibre (AvaSpec-2048, Avantes, The Netherlands). Irradiance could not be measured directly in the magnet, but the light source was calibrated (840-C power meter, Newport, Irvine, CA, USA). The light conditions used were a polychromatic, blue-enriched white light emitting diode (LED) light (92 mel EDI lux; 6500 K) and a monochromatic orange light
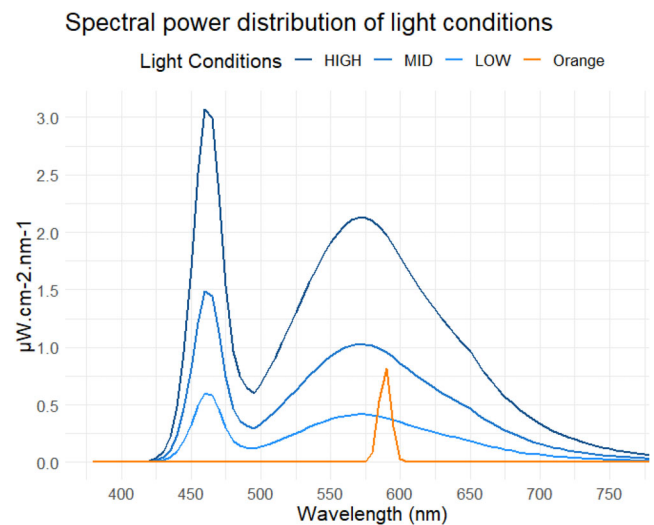
Spectral power distribution of light conditions

FIGURE 2 Spectral power distribution of light conditions. Orange: monochromatic orange light, 0.16 melanopic (mel) equivalent daylight illuminance (EDI) lux, 589 mn; blue-enriched white light (BEL) LOW, MID, and HIGH: light of three different intensities (37, 92, 190 mel EDI lux; 6500 K). See Table 2 for additional characteristics.

(0.16 mel EDI lux). The light blocks were repeated seven times for each light condition. During the emotional task, participants were

exposed to 30–40-s periods of light blocks separated by 20 s of darkness (<0.1 lux). The light conditions used were three different irradiances of a polychromatic, blue-enriched white LED light (37, 92, 190 mel EDI lux; 6500 K) and a monochromatic orange light (0.16 mel EDI lux) (Figure 2; Table 2). The light blocks were repeated five times for each light condition.

2.3 | Attentional task

The attentional task used was a mismatch negativity or oddball task (Kiehl & Liddle, 2003). Participants were asked to detect a rare randomly occurring target (or odd) item in a stream of frequent standard items. They used the keypad to report the detection of the odd items. Stimuli ($n = 315$) consisted of frequent standard (500 Hz, 100 ms) and odd tones (1000 Hz, 100 ms), presented 80% and 20% of the time, respectively, in a pseudo-randomised order. The inter-stimulus interval between stimuli was 2 s. Target and standard stimuli were equally distributed across the two light conditions and the separating darkness periods (Figure 1b). The instruction was to prioritise accuracy over rapidity when responding.

2.4 | Emotional task

The emotional task used was a gender discrimination of auditory vocalisations task (Banse & Scherer, 1996). Participants were asked to use the keypad to indicate what they believed the gender of the person pronouncing each token was. The gender classification was a lure task ensuring participants paid attention to the auditory stimulation. The purpose of the task was to trigger an emotional response as participants were not told that 50% of the stimuli were pronounced with angry prosodies. The 240 auditory stimuli were pronounced by professional actors (50% women) and consisted of three meaningless

words ('goster', 'niuvenci', 'figotleich'). The stimuli were expressed in either an angry or neutral prosody, which has been validated by behavioural assessments (Banse & Scherer, 1996) and in previous experiments (Grandjean et al., 2005; Sander et al., 2005). The stimuli were also matched for the duration (750 ms) and mean acoustic energy to avoid loudness effects. During each 30–40-s light block, four angry prosody stimuli and four neutral prosody stimuli were presented in a pseudo-random order and delivered every 3–5 s. A total of 160 distinct voice stimuli (50% angry; 50% neutral) were distributed across the four light conditions. The darkness period separating each light block contained two angry and two neutral stimuli. A total of 80 distinct voice stimuli (50% angry; 50% neutral) were distributed across the darkness periods (Figure 1c). Again, the instruction was to prioritise accuracy over rapidity when responding.

2.5 | Pupil

The right eye movements and the pupillary size was recorded continuously with an infrared eye tracking system (Eyelink-1000, SR Research, Osgoode, ON, Canada; sampling rate, 1000 Hz). Pupil data were analysed using MATLAB R2019b (MathWorks, Natick, MA, USA). Participants with >25% missing or corrupted eye-tracking data were excluded. Blink events were replaced with linear interpolation and the data were smoothed using the 'rlowess' a robust linear regression function. The total amount of interpolated data included was 21% ± 9% and 22% ± 9% for the attentional and the emotional task, respectively. The transient pupil response was computed as the change in the pupil diameter from before (baseline) and after (maximum) the auditory stimulus presentation. Baseline pupil diameter was computed as the mean pupil diameter over 1 s before stimuli onset. The maximum pupil diameter was defined as the maximum value over a 1.5 s window following sound onset. TEPRs were computed as the ratio between maximum and baseline diameter. For the attentional

TABLE 2 Light characteristics.

Characteristic	Low BEL	Mid BEL	High BEL	Monochromatic light (589 nm)
Photopic illuminance, lux	47	116	240	7.5
Peak spectral irradiance, nm	460	460	460	590
Melanopic EDI lux (ipRGCs)	37	92	190	0.16
Rhodopic EDI lux (rods)	39	97	201	0.94
Cyanopic EDI lux (S-cones)	32	79	163	0
Chloropic EDI lux (M-cones)	44	110	227	5
Erythropic EDI lux (L-cones)	46	113	233	8
Irradiance, $\mu W/cm^2$	15	36	75	1.4
Photon flux, $1/cm^2/s$	4.12E+13	1.02E+14	2.10E+14	4.24E+12
Log photon flux, $\log_{10}$ $(1/cm^2/s)$	13.61	14.01	14.32	12.63
Narrowband peak	–	–	–	589
Narrowband FWHM	–	–	–	10

Note: additional light characteristics of the two light sources used. Blue-enriched white light (BEL) (low, mid, and high) and monochromatic light (589 nm).
Abbreviations: EDI, equivalent daylight illuminance; FWHM, full width at half-maximum; ipRGCs, intrinsically photosensitive retinal ganglion cells.

task, one participant was excluded because they did not complete the entire attentional task and four were excluded as there was >25% missing or corrupt pupil data. Therefore, we included 15 participants in the analysis of the oddball task (Table 1). For the emotional task, two participants were excluded as there was >25% missing or corrupt pupil data. One participant was excluded because he did not complete the entire emotional task correctly and three were excluded due to problems with the eye-tracking system. Therefore, we included 14 participants in the analysis of the emotional task (Table 1).

2.6 | Statistical analyses

Statistical analyses were computed using the Statistical Analysis System (SAS) version 9.4 (SAS Institute, Cary, NC, USA) using individual TEPRs segregated per stimulus type and light condition. Values were considered outliers if they were > ± 3 standard deviations (SDs) across the entire dataset and were therefore removed. Analyses consisted of generalised linear mixed models (GLMM) seeking effects of light condition (i.e., mel EDI lux level) on the TEPRs. TEPRs were set as the dependent variable, with subject as a random factor (intercept), and light condition and stimulus type as repeated measures (autoregressive (1) correlation), together with the time of day, age, body mass index and sex as covariates. GLMM were adjusted for the dependent variable distribution. Post hoc contrasts were corrected for multiple comparisons using a Tukey adjustment.

3 | RESULTS

The performance of both tasks was high, with a mean (SD) 96.6% (0.5%) of detection of target sounds during the attentional (oddball) task and 93.9% (7.21%) button response during the emotional (gender classification) task. In line with the literature (Sander et al., 2005; Vandewalle et al., 2010), for the emotional task, reaction times (RTs) were faster for neutral stimuli with a mean (SD) of 1192 (182.8) ms compared to 1234 (199.8) ms RT for emotional prosody vocal stimulation ($p = 0.0004$) suggesting that the task was successful in triggering a differential response according to the emotional content. As no response was collected for the standard tone in the oddball task, RT could not be compared between stimulus types for the attentional task. Although not relevant to the task and not compromising any emotional effect (Grandjean et al., 2005), gender detection accuracy for the emotional task (mean [SD] 79% [11%]) was slightly lower than what has previously been reported for the task (Sander et al., 2005). For both tasks, there were no significant main effects of the light level on RTs ($F < 2.1$, $p ≥ 0.1$) and accuracy ($F < 2.1$, $p ≥ 0.1$), and there was no light exposure by stimulus type interaction for the emotional task ($F_{[4,34.04]} = 0.25$, $p = 0.9$). This was expected to ensure that behavioural performance differences unspecific to light exposure would significantly bias neuroimaging results (Paparella et al., 2023).

It is well established that pupil size changes in response to variations in environmental irradiance. In a joint paper
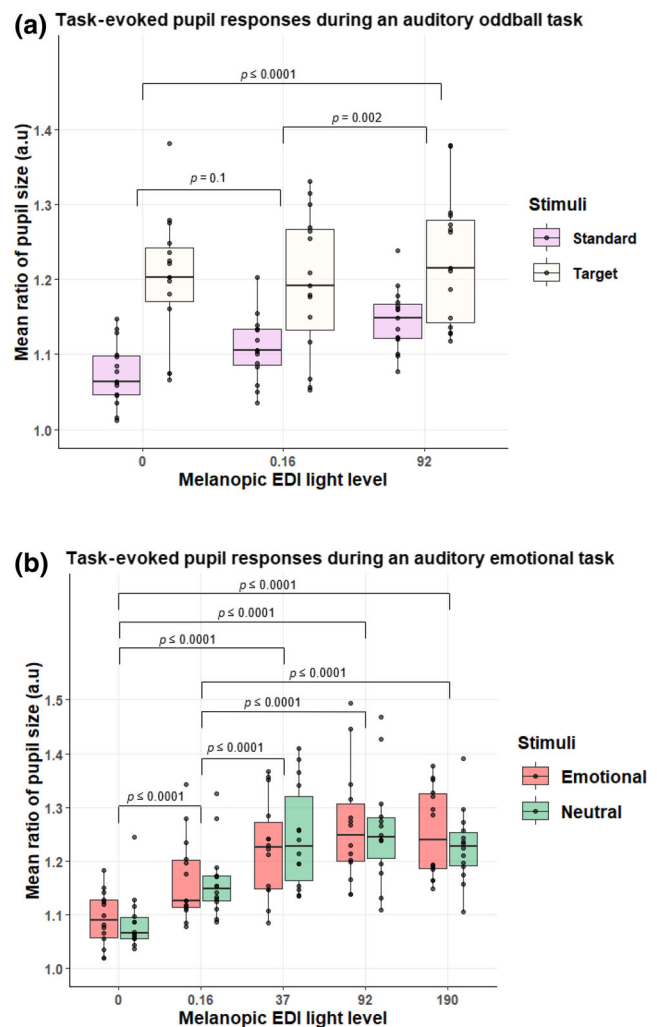

FIGURE 3   Task-evoked pupil response (TEPRs) across light conditions and stimulus type. (a) TEPRs under the different light conditions during the attentional (oddball) task ($N = 15$; mean [SD] age 24.33 [4.15] years; 10 women). Individual average TEPRs were computed per stimulus type and light condition. TEPRs were significantly higher for target versus standard stimulations ($p < 0.0001$), as well as under higher versus lower melanopic equivalent daylight illuminance (EDI) light levels ($p < 0.0001$). A significant light condition by stimulus type was also found ($p = 0.02$) and post hoc analyses indicated that TEPRs significantly increased with higher light irradiance for the standard but not the target stimulations. (b) TEPRs under different light levels during the emotional task ($N = 14$; mean [SD] age 24.0 [4.41] years; 10 women). Individual average TEPRs were computed per stimulus type and light condition. There was no significant difference between neutral and emotional stimulations ($p = 0.8$) whilst TEPRs were greater under higher versus lower melanopic light levels ($p < 0.0001$). There was no light condition by stimulus type interaction ($p = 0.7$).

(Beckers et al., 2023), we notably confirmed this and reported that the sustained constriction of the pupil increased with higher light levels in the same sample of participants who completed the same protocol. In contrast to the joint paper (Beckers et al., 2023), here, we consider whether changes in light conditions, as indexed by mel

EDI lux, impact the TEPRs for an attentional and emotional task. Both tasks consist of streams of events that putatively trigger TEPRs, and both have two types of auditory stimulations. We hypothesised that the TEPRs would be greater under higher light levels due to the stimulating NIF impact of light.

To characterise the effect of light conditions on TEPRs for the attentional task, an initial GLMM was conducted with TEPRs during the oddball task as the dependent variable. The results yielded significant main effects of stimulus type (target and standard tones; $F_{[1,1548]} = 189.27$, $p \leq 0.0001$) and light condition ($F_{[2,1548]} = 13.71$, $p \leq 0.0001$). Importantly, the GLMM detected a significant interaction between stimulus type and light condition ($F_{[2,1548]} = 3.65$, $p = 0.02$) (Figure 3a). Post hoc analyses first indicated that TEPRs were larger for target versus standard stimuli ($p \leq 0.0001$). They further indicated that TEPRs were smaller during darkness as compared to the blue-enriched white light condition (92 mel EDI lux; $p \leq 0.0001$) but TEPRs during darkness were not significantly different when compared to the orange (0.16 mel EDI lux; $p = 0.1$) light condition. However, TEPRs were significantly larger under the blue-enriched white light (92 mel EDI lux; $p = 0.002$) when compared to the orange light (0.16 mel EDI lux). Finally, post hoc analyses indicated that TEPRs significantly increased with higher light irradiance for the standard ($p \leq 0.0001$) but not the target stimuli ($p > 0.2$).

The second GLMM, with TEPRs during the emotional task as the dependent variable, led to a significant main effect of light condition ($F_{[4,1072]} = 77.78$, $p \leq 0.0001$). Despite there being a qualitative difference between angry and neutral stimuli, there was no significant main effect of stimulus type ($F_{[1,1072]} = 0.06$, $p = 0.8$) (Figure 3b). In addition, there was no interaction between stimulus type and light condition ($F_{[4,1073]} = 0.5$, $p = 0.7$). Post hoc analysis showed a significant difference between darkness and all four light conditions ($p \leq 0.0001$), as well as between the orange (0.16 mel EDI lux) light and the blue-enriched white light conditions (37, 92, 190 mel EDI lux; $p \leq 0.0001$). There was no significant difference between the blue-enriched white light conditions (37, 92, 190 mel EDI lux; $p \geq 0.7$).

4 | DISCUSSION

The TEPRs consist of transient pupil dilations triggered by the processing of stimulations over diverse cognitive domains. They are considered to be at least in part driven by a transient increase in the phasic activity of the LC-NA system and potentially other brain areas (Joshi et al., 2016; Larsen & Waters, 2018). In the present study, we tested whether the TEPRs evoked by auditory stimulus during two cognitive tasks would be larger under higher ambient light levels, when the parasympathetic drive to the pupil is high, to investigate whether light's NIF impacts on cognitive brain activity could potentially be mediated through the LC. To test this hypothesis, we analysed eye tracking data from young healthy participants who completed an attentional and an emotional cognitive task during an fMRI protocol whilst exposed to different light conditions. The results reveal that when there is a smaller sustained pupil size at higher light levels

(Beckers et al., 2023), the TEPRs to auditory stimulus were larger under higher light irradiances, as indexed by mel EDI lux. Although this main finding was detected for both the attentional and emotional tasks, we further observed task-specific differences in the impact light irradiance has on the different types of stimuli of each task.

The LC is involved in the processing of salient events through an increase in its phasic activity (Berridge & Waterhouse, 2003). The oddball task, which mimics novelty/salience detection has been previously used to assess the phasic activity of the LC (Rajkowski et al., 1994), whilst the LC is also known to be important for emotional processing (Aston-Jones & Cohen, 2005; Bradley et al., 2008). The oddball task was reported to trigger TEPRs (both in the visual and auditory modality) that were larger for the odd target stimuli, which is in line with our findings (Gilzenrat et al., 2010; Murphy et al., 2014). Similarly, TEPRs were also reported using emotional tasks (Aston-Jones & Cohen, 2005; Bradley et al., 2008). Pupil size depends on the parasympathetic–sympathetic balance and transient pupil dilation is thought to reflect an increase in arousal due to an increase in the sympathetic tone (Larsen & Waters, 2018). Although recent investigations have indicated that it is likely not the sole driver of transient pupil dilation, in vivo animal studies support that transient increases in pupil size were directly related to the firing of the neurones of the LC (Costa & Rudebeck, 2016). Our findings could suggest therefore that the phasic activity of the LC related to an ongoing cognitive process is likely to be affected by changes in ambient light level. Light is known to increase arousal and have wake-promoting effects and can cause the activation of the pupil dilation pathway via the LC, through indirect sympathetic influence by stimulating the SCN, and the dorsomedial hypothalamus (Mathôt, 2018). The LC could also cause pupil dilation via sympathetic drive by its projection to the intermediolateral column and potential through projections to the superior colliculus (Mathôt, 2018; Szabadi, 2018). Alternatively, our results could be interpreted as transient inhibition of the parasympathetic constriction pathway, through EWN inhibition by the LC, leading to an increase in pupil dilation under higher light levels (Steinhauer et al., 2015). Transient inhibition of parasympathetic signal may indeed be the primary pathway involved in pupil dilation caused by arousal and cognition (Steinhauer et al., 2004; Szabadi, 2018).

The LC is a good candidate to mediate the impact of light on human alertness and cognition through an effect on other subcortical and cortical structures (Aston-Jones & Cohen, 2005). The thalamus pulvinar could likely be one of these downstream structures, as it is the most consistently affected by light in previous investigations on the impact of light on non-visual cognitive brain activity (Vandewalle et al., 2009). Other structures and nuclei, e.g., within the hypothalamus or basal forebrain, could also be implicated, whilst the recruitment of limbic and cortical areas would depend on the ongoing cognitive processes (Gaggioni et al., 2014). Our results indicate that the impact of increasing light level is stronger for standard compared with target stimulation. We interpret this as a ceiling effect for TEPRs elicited by target stimulations that cannot be further increased, whilst the milder TEPRs triggered by standard stimulations in darkness or at lower light levels can continue to be increased under higher ambient

light. In line with this interpretation, the impact of light on non-visual cognitive brain activity was previously found to be reduced in the evening during the wake-maintenance zone, when the endogenous circadian signal promoting wakefulness is strong and therefore when alertness could not be further increased by lights influence (Vandewalle et al., 2011). In contrast, light's impact was increased in the morning following sleep deprivation, when the circadian signal is weaker but the need for sleep is high due to sleep loss. Therefore, alertness can benefit from the external stimulating impact of light (Vandewalle et al., 2011). If our interpretation is correct, this could mean that light can only affect the activity of the LC when it is not already highly recruited by the processing of a salient stimulation. Even though the average TEPR to target stimuli remains stable across light conditions, the variance of TEPR was larger for target stimuli. We cannot rule out that it contributed to the absence of difference between light conditions for target stimuli.

The situation is different if we consider the emotional task as we find no difference between the TEPRs triggered by the emotional and neutral simulations. This could call into question the emotional valence of the stimuli included in the task. However, the emotional task has been previously extensively validated and was successful in triggering differential brain responses to emotional versus neutral stimulations, including in studies interested in the NIF effects of light (Banse & Scherer, 1996; Grandjean et al., 2005; Vandewalle et al., 2010). We also find that RTs were significantly slower in response to emotional versus neutral stimulations, which is in line with the literature and supports that the emotional valence of the stimuli was perceived by the participants (Sander et al., 2005; Vandewalle et al., 2010). Yet, the emotional response may not be strong and/or different enough from the response to neutral stimuli to be detected with 15 subjects. Auditory emotional stimuli are indeed considered to be less effective at provoking an emotional response when compared to visual emotional stimuli (Bradley et al., 2008). It may also be that the unexpected occurrence of neutral stimulations (stimulations were pseudo-randomly delivered every 3–5 s) triggers a TEPR that is similar to the emotional stimuli. Our results further indicate that given the relatively mild response elicited in darkness or at lower light levels, TEPRs could be increased by increasing light levels. The maximum increase seems to be reached already with the lower level of polychromatic, blue-enriched white light (37 mel EDI lux) to ceiling thereafter. Interestingly, the maximum TEPRs for both the oddball and emotional tasks seem to lay on average around 1.25, i.e., a 25% increase on average in pupil size compared to baseline (cf. Figure 2).

4.1 | Study limitations

We emphasise that our study has limitations. The light conditions included do not allow for determining which of the human photoreceptors are mostly contributing to the TEPRs. Rods, cones, and ipRGCs could equally be involved with differential recruitment at the different light levels we used (Mure, 2021). Future research could use metameric light sources with which the wavelength compositions can be manipulated to differentially recruit one photoreceptor type whilst leaving the others relatively similarly recruited (Viénot et al., 2012).

We are also unable to say conclusively to what extent the sympathetic and/or parasympathetic system contributes to the increase in TEPRs under higher light levels. The LC is considered the centre point of the NA pupil control pathway and contains sympathetic and parasympathetic premotor neurones (Szabadi, 2018). Yet other nuclei may affect pupil size and TEPRs and contribute to our results (Joshi et al., 2016). We stress that we did not have access to the brain activity associated with TEPRs. The assumptions made regarding the recruitment of the LC can only be verified using the fMRI data acquired simultaneously with the pupil data. Further research using drugs that lead to the alteration of pupil size control, through the modification of the activity/transmission of the sympathetic or parasympathetic NA neurones may elucidate the contribution of sympathetic or parasympathetic systems to increase in TEPRs under higher light levels (Steinhauer et al., 2015).

Finally, during a goal-oriented task, the phasic activity of the LC facilitates task-related behaviours to optimise performance, and tonic activity is involved in task disengagement and search for alternative behaviours. Switching between these two modes allows to maximise utility (Aston-Jones & Cohen, 2005). Therefore, it can be hypothesised that we only investigated the phasic activity of the LC, as both tasks used in the study are stream-of-conscious tasks and do not involve the exploration of alternative behaviours at the cost of task performance. However, we cannot rule out the possibility of tonic activity affecting the results.

5 | CONCLUSION

Overall, this study shows that the NIF impacts of light can be detected when focusing on pupil size with transient pupil dilation induced by increasing light levels. This is true for two different auditory cognitive tasks whilst increased transient pupil dilation may only be possible if TEPRs are not already at maximum. Future research is needed to conclude if it is the sympathetic or parasympathetic drive that is causing the increase in TEPRs under higher light levels. There is a putative link between LC phasic activity and transient pupil dilation (Costa & Rudebeck, 2016), alternatively, transient pupil dilation may be due to the transient inhibition of the parasympathetic signal (Steinhauer et al., 2015). The results presented here provide further support for the involvement of the LC in the stimulating impact of light on alertness and cognition.

AUTHOR CONTRIBUTIONS

Islay Campbell: Conceptualization; methodology; investigation; formal analysis; writing – original draft; writing – review and editing. **Elise Beckers:** Conceptualization; investigation; writing – review and editing. **Roya Sharifpour:** Investigation; writing – review and editing. **Alexandre Berger:** Investigation; writing – review and editing. **Ilenia Paparella:** Investigation; writing – review and editing. **Jose Fermin Balda**

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA 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/fasst/pupil_and_light.

ORCID

Islay Campbell https://orcid.org/0000-0003-4497-6673
Elise Beckers https://orcid.org/0000-0002-5523-1741

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