



International Commission on Illumination  
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DOI 10.25039/x051.2025/e7t6e3

This article is also published as part of:

Proceedings of the CIE 2025 Midterm Meeting Vienna, Austria, July 4-11, 2025:  
Scientific Conference (July 7-9, 2025)

DOI 10.25039/x051.2025

in

Proceedings of the CIE (International Commission on Illumination)

ISSN no. 3061-015X (print), 3061-0168 (online)

The paper has undergone double-blind peer review and its final version has been presented at the CIE 2025 Midterm Meeting, Vienna, Austria, July 4–11, 2025.

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## EFFECTIVENESS OF LIGHT IN ENHANCING WORKING MEMORY THROUGH MELANOPsin STIMULATION VARIES WITH AGING

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### Abstract

Light is essential for vision but also regulates functions unrelated to image formation such as circadian rhythm, mood but also cognition. Short wavelengths of visible light have been shown to modulate alertness and working memory by activating intrinsically photosensitive retinal ganglion cells through a photopigment called melanopsin. Here, we investigated how this memory-enhancing effect of light varies with aging. We compared short wavelengths of visible light (blue) exposition and long wavelengths of visible light (red) exposition impact on short term and working memory and found that the most effective exposition light in enhancing working memory depended on aging (blue light for young individuals and red light for older individuals). In addition, electrodermal activity was found to be a possible good indicator of the amount of light perceived and received on the retina.

*Keywords: Photometry, Light, Melanopsin, Working Memory, Electrodermal activity*

### 1 Introduction

Intrinsically photosensitive retinal ganglion cells (ipRGCs) projections to the suprachiasmatic nucleus (SCN) in regions dedicated to learning raised to the idea that ipRGCs may be involved in non-visual functions in particular in cognition and memory processes [1]. Blue light exposure with a peak at 480nm – wavelength that stimulates a photopigment, melanopsin, contained in ipRGCs – increased brain activity in visually blind individuals during working memory tasks, supporting the idea that light stimulates cognitive processes independently of vision [2]. In addition, blue light exposure increased working memory performances compared to control lights exposure in young and old adults even if this enhancing effect was lower in old adults [3]. Interestingly, in this study light impacted similarly aged individuals with natural yellowing lenses and those with intraocular lens replacements after cataract surgery. Moreover, light exposure before learning can also enhance memory consolidation in declarative [4] and motor tasks [5].

More and more evidences states the effect of blue light or blue-enriched light on cognitive functions via the stimulation of ipRGCs but the boundaries of the action of ipRGCs on memory remain unclear. Furthermore, only few studies investigated the effect of light on memory as a function of age. In this study, we aimed to explore how aging influences the effects of light on cognitive processes and the extents of light's impact on memory. Specifically, we investigated whether short-term memory is affected and which phases of working memory are influenced by light exposure and aging. We compared the effects of blue light (480 nm) and red light (620-660 nm) on behavioural and physiological responses during auditory and visual cognitive tasks in both young and older healthy participants.

## 2 Study

### 2.1 Method

A population 16 old participants ( $75.3 \pm 3.1$  years) and 16 young participants was included in this study. Two young participants were excluded of the analysis; resulting in 14 young participants analysed ( $26.7 \pm 4.52$  years). They were all part of the SilverSight cohort opulation ( 350 enrolled subjects) at the Vision Institute - Quinze-Vingts National Ophthalmology Centre, in Paris, were voluntary and gave informed consent for inclusion based on the following criteria: i) normal or corrected to normal vision ii) no history of neurological disorder iii) and no extreme chronotype: Horne-Östberg Morningness-Eveningness Questionnaire [6] score between 42 and 67.

A power analysis was conducted to determine the sample size with R and the library *pwr*. The effect size was first estimated from data measured in previous studies. [3, 7]. Mean reaction time difference between blue and control light on working memory task was larger than 15 ms with a standard deviation lower than 50ms leading to a Cohen's effect size of 0.3 ( $f^2=0.09$ ). To achieve 95% statistical power, and  $\alpha=0.05$  with a repeated measure ANOVA with 5 repetitions, a sample size of at least 15 participants was needed for each group.

Experiments were planned between March 2021 and December 2021. On a first visit, participants were familiarised to the different neuropsychological tasks. The second and third visits took placed one week apart, at a fixed time (9 or 10:30 a.m). The participants were asked to wear blue cut filters from the time they woke up to their arrival at the laboratory, where they were installed in a dim room. After 15 minutes of pre-exposure amber light, participants were exposed to monochromatic blue light (480 nm) or red control light (620-660nm). The blue and red lights were equalized in luminance and density photonic flux (illuminance=157 lux, log photon irradiance=18,44  $\text{ph.s}^{-1}.\text{m}^{-2}$ ).

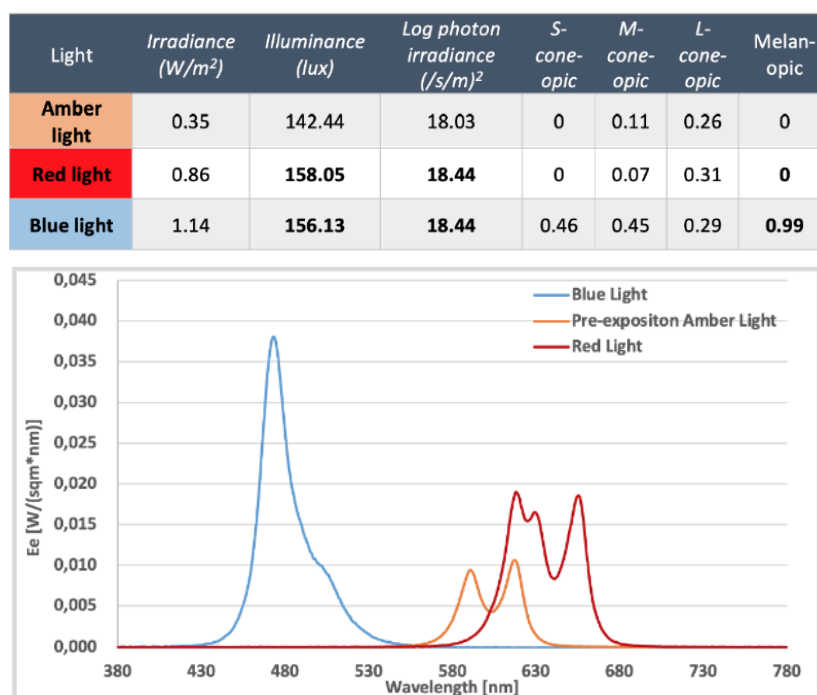


Figure 1 – Lights characteristics

During light exposure, participants performed neuropsychological tasks. *Auditory tasks* (GO/NO GO, 0-back, 2-back) respectively engaged participants' inhibition, attention and working memory. An *auditory verbal short-term memory task*, adapted from the California Verbal Learning version II Task, evaluate participants' short-term memory. Finally, an adapted version of *Visual delayed Matching-to-Sample* (dMTS) from Beatty et al. aimed to investigate the different phases of visual working memory [8]. The visual modality of this newly designed task allowed to distinguish encoding, maintenance, updating and

retrieval phases of working memory, and staircase procedures were introduced to enable it without using neuroimaging.

Electrodermal activity was recorded with Empatica E4 wristband to assess participants' emotional state and help to distinguish the action of ipRGCs from the visual perception. Recordings could be exploited on only of 4 young participants and 4 aged participants. In addition, questionnaires assessed the subjective arousal state (Karolinska Sleepiness Scale). Subjective light perception was finally also evaluated after 30 minutes of light exposition.

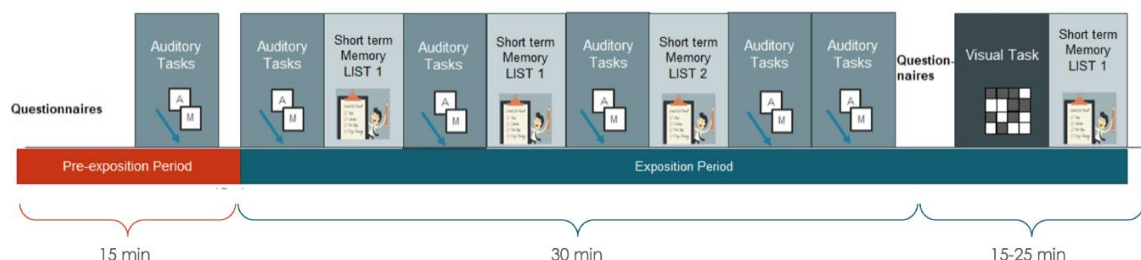


Figure 2 – Experimental protocol

## 2.2 Results

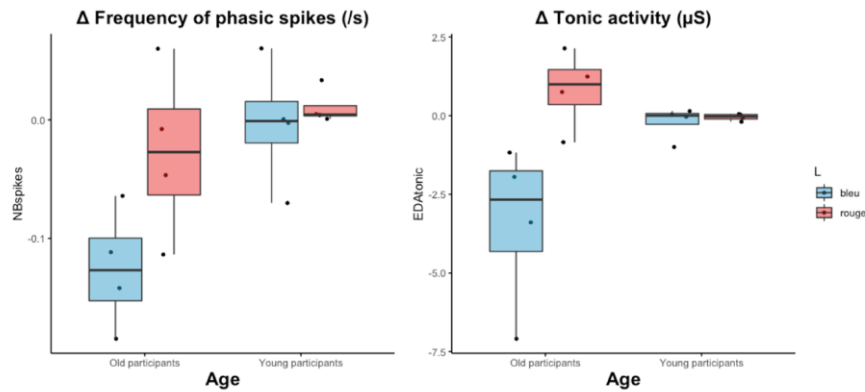
### 2.2.1 Subjective & physiological results

Young participants' subjective sleepiness after 30 minutes-light exposure tends to be higher for red vs. blue light ( $t = 1.99$ ,  $p$ -value = 0.068), which is consistent with the way they subjectively perceived the lights. They evaluated the awakening effect of blue light stronger than the one of red light ( $t=2.3$ ,  $p=0.03$ ). On the contrary, old participants did not perceived any differences between the two lights and their subjective sleepiness after 30 minutes exposure did not differ with the light

	Young participants (n=14)			Old participants (n=16)		
	Blue light exposure Mean±SD	Red light exposure Mean±SD	Statistics	Blue light exposure Mean±SD	Red light exposure Mean±SD	Statistics
Baseline KSS	6.6 ± 1.5	6.1 ± 0.9	$t=0.9$ , $p=0.36$	7.4 ± 0.9	6.9 ± 1.5	$t=1.5$ , $p=0.15$
After exposure KSS	<b>6.5 ± 1.2</b>	<b>5.5 ± 1.1</b>	<b><math>t=2.0</math>, <math>p=0.07 +</math></b>	7.3 ± 1.1	7.1 ± 1.7	$t=0.9$ , $p=0.36$
Subjective awakening effect of light	<b>4.8 ± 1.6</b>	<b>3.3 ± 1.3</b>	<b><math>t=2.3</math>, <math>p=0.03 *</math></b>	6.1 ± 1.8	5.5 ± 1.9	$t=1.2$ , $p=0.25$
Subjective pleasantness effect of light	4.2 ± 1.8	3.0 ± 2.0	$t=1.5$ , $p=0.15$	3.8 ± 2.7	4.0 ± 2.1	$t=-0.2$ , $p=0.83$

Table 1 – Descriptive statistics

In parallel, young participants did not present a different electrodermal activity according to light exposure while phasic spikes frequency and tonic activity amplitude of the normalized electrodermal activity of old participants were significantly lower (paired t-test adjusted with holm method, respectively  $t=-4.16$ ,  $p=0.012$  and  $t=-4.22$ ,  $p=0.029$ ) when exposed to blue light.

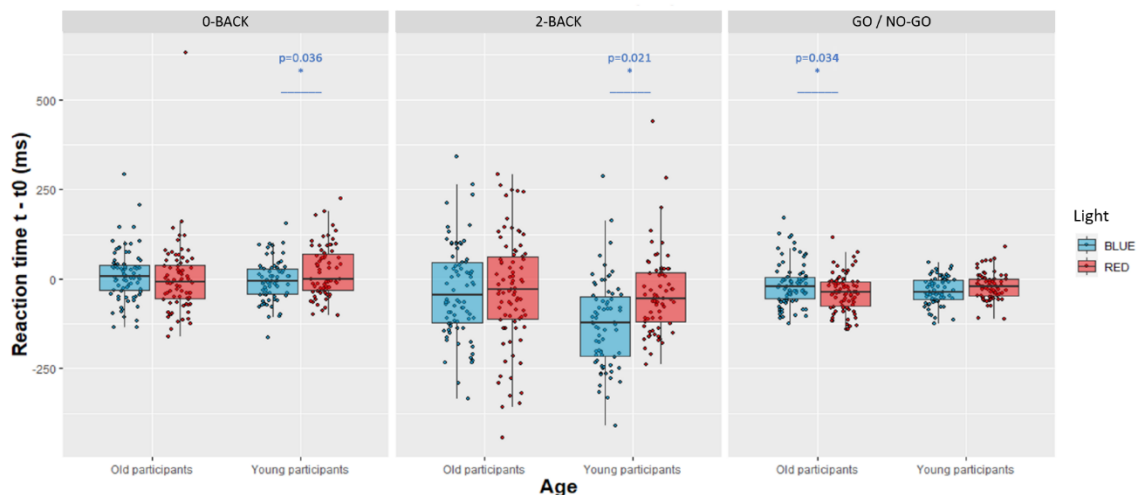


**Figure 2 – Frequency of EDA phasic spikes and EDA tonic activity amplitude as a function of light group and age group of participants.**

## 2.2.2 Behavioral results

The results of each participant on the auditory tasks (0-back, 2-back, and GO-NO GO tasks) during the washout period (pre-exposure) are subtracted from their results during the light exposure period. This normalisation helps eliminate biases related to daily conditions or emotions that are unrelated to the light exposure itself.

Young participants responded faster to the 0-BACK (repeated measures ANOVA,  $F=5.49$ ,  $p=0.036$ ) and 2-BACK tasks (repeated measures ANOVA,  $F=6.63$ ,  $p=0.021$ ) under blue light compared to red light, with an improved accuracy on the 2-BACK task (repeated measures ANOVA,  $F=5.45$ ,  $p=0.011$ ). In contrast, old participants displayed shorter response times when exposed to red light during the GO/NO-GO task (repeated measures ANOVA,  $F=5.45$ ,  $p=0.034$ ) but no significant differences were observed in attention and working memory tasks.



**Figure 4 – Reaction Time [Exposition – Pre-exposition] to 0-Back (0B), 2-Back (2B) and GO-NO GO tasks as a function of age group and light group**

In addition, young participants tended to get a lower encoding threshold time when exposed to blue light compared to red light (paired T-test, respectively  $t=-1.8$ ,  $p=0.1$ ) but a higher interstimulus threshold time under blue light exposure vs red light exposure (paired T-test, respectively  $t=-1.9$ ,  $p=0.08$ ). Threshold encoding time of old participants was significantly lower

when they were exposed to red light compared to blue light (paired T-test,  $t=2.63$ ,  $p=0.016$ ), i.e., aged participants needed less time to encode the presented stimulus when exposed to red light vs blue light. No significant difference has been observed for maintenance threshold time with light conditions in young nor old participants.

Light effect	Young participants (n=14)			Old participants (n=16)		
	Blue light exposure Mean±SD	Red light exposure Mean±SD	Statistics	Blue light exposure Mean±SD	Red light exposure Mean±SD	Statistics
Encoding Threshold Time (ms)	<b>37 ± 27</b>	<b>71 ± 60</b>	<b>t=-1.8, p=0.1 +</b>	<b>924 ± 464</b>	<b>609 ± 340</b>	<b>t=2.7, p=0.016 *</b>
Inter-Stimulus Threshold Time (ms)	<b>174 ± 259</b>	<b>77 ± 195</b>	<b>t=1.9, p=0.08 +</b>	879 ± 1138	435 ± 589	t=1.5, p=0.14
Maintenance Threshold Time (ms)	61400 ± 11575	61900 ± 11566	t=-0.2, p=0.84	20906 ± 13640	25218 ± 18290	t=-1.0, p=0.33

**Table 2 – Statistics of light effects to the encoding, inter-stimulus and maintenance time thresholds in young and old participants.**

Finally, no light effect was seen in the short-term memory task neither in young (paired t-test,  $t=0.06$ ,  $p=0.81$ ) nor in old participants (paired t-test,  $t=0.41$ ,  $p=0.53$ ).

### 3 Discussion

Young individuals responded faster when exposed to blue vs red light to a sustained attention task (0-Back), in line with previous studies [9, 10]. As expected, they also responded faster and more accurately to the auditory working memory task (2-back) when exposed to blue light compared to red light, which is consistent with previous studies [3, 11, 12]. However, no difference was observed to the GO/NO-GO inhibition task while Chellappa et al. observed faster reaction times under 6500k light compared to a 2500K light exposure to this task [10].

On the contrary, old individuals responded faster to the inhibition tasks under red light compared to blue light and the same trend was observed for the attention and working memory task and no differences were seen for attention and working memory tasks. This is not in line with the results of Daneault et al [3]. that showed that blue light enhanced cognitive performance in both young and older adults, even though the effect was smaller in older individuals. Several experimental reasons might explain this discrepancy. Firstly, control light differed in the two studies. Daneault et al. selected amber light (620nm) as equidistant from the peak sensitivity of the photopic visual system (550nm) while blue light coincided with the peak sensitivity of ipRGCs (480nm) and equalized photon densities of the two lights. We designed the control light in order to equalize both photon densities and illuminance that correlates with how human perceives brightness of a light (Fig. 1). Secondly, because ipRGCs are known to have sustained effects on non-visual functions, we chose to expose the participants to only one light on the same day in our study and to avoid sustained stimulation of melanopsin before the experiment with low pass blue cut filter glasses provided to the participants (1-500nm), while Daneault et al. exposed participants to both lights on the same day in a counterbalanced order. However this unlikely explains the observed discrepancy; indeed it would have rather increased working memory performances under amber but not blue light exposure. Thirdly, the 16 old participants included in our study ( $75.3 \pm 3.1$  y) were older than the two groups of old participants in Daneault et al. study – 12 participants with natural lenses ( $66.7 \pm 5$  y) and 12 participants with intra-ocular lenses ( $69.6 \pm 5$ y) – and none of them had performed a cataract surgery. This might have led to less amount of blue light reaching the retina of our participants as the age and cataract surgery impact lens transmission of short wavelengths. Moreover, Daneault et al. found

no difference between older participants with natural lenses and those who had undergone cataract surgery. This suggested that aged ocular media has a low impact on the effect of light on working memory. They proposed that brain plasticity would allow adaptation to reduced light transmission over time. On the contrary, our study rather suggests that aged related changes in ocular media such as lens yellowing (which partially blocks short-wavelength light from reaching the retina), reduced pupil size, decreased number of retinal ganglion cells play a primary role in the way light impacts working memory. This is further supported by a more recent studies that showed that a blue-enriched white light compared to a non-enriched white light has an effect on melatonin level, subjective sleepiness and sustained attention in young but not in old participants [13] and that lens replacement in old adults leads to improved cognitive function and sleep quality, particularly with ultraviolet lens compared to blue-blocking lens [7].

Moreover, the newly developed visual working memory task enabled us to investigate more closely the effect of light on the different phases of working memory. Young individuals needed less time to encode the presented stimulus when exposed to blue light vs red light, but surprisingly they presented longer inter-stimulus threshold time when exposed to blue light compared to red light. As for cognitive auditory tasks, old individuals performed better under red vs. blue light exposure and showed longer encoding threshold times when exposed to blue light compared to red light. This result suggests that light, through the activation of ipRGCs, has a specific effect on the encoding phase of working memory in both young and old participants, and that ipRGCs may impact more strongly encoding phase than other working memory phases. This is supported by another study that investigated the effect of light on cortical oscillatory activity using magnetoencephalography during working task and showed that event-related synchronization was greater under blue light than green light event though no behavioural differences were observed between the two lights [14].

Interestingly, subjective perception of light, sleepiness and electrodermal activity come to support these behavioural results. Young participants – who performed better under blue light exposure – perceived blue light as more stimulating than red light and were less sleepy after blue vs. red light exposure but presented the same level of electrodermal activity under both light exposures. However, old participants – who performed better under red light exposure – did not subjectively perceived difference between the two lights but presented a lower electrodermal activity under blue light exposure compared to red light. We suggest that this age difference in electrodermal activity behaviour and in subjective sleepiness and perception of light may be primarily due to ocular media changes with aging. Indeed, additional activation of ipRGCs at the same level of retinal illuminance and photon irradiance has led to more subjective arousal in young participants but did not have an impact on their electrodermal activity. However, a lower retinal illuminance and photon irradiance in old participants due to ocular media changes leading to a lower transmission of short wavelengths of light compared to long wavelengths led to lower level of electrodermal activity but not in subjective arousal. Consequently, the retinal illuminance, ie the brightness perceived at the level of the retina, might globally impact arousal and thus electrodermal activity, while activation of ipRGCs may act as a central arousal offset. Finally, brightness and activation of ipRGCs may play a role in respectively global and central arousal level and are both positively correlated with behavioural performances in cognitive tasks. Bright light has already been correlated with higher level of subjective and physiological arousal [15, 16], and better performances at difficult working memory task [16], while ipRGCs are well known to be associated with higher level of arousal and lower subjective sleepiness [17]. Nonetheless, given the low number of participants whose electrodermal activity could be analysed, this result should be replicated

In sum, blue vs red light increased cognitive performances of young individuals while it decreased cognitive performances of old individuals and it had a specific effect on the encoding phase of working memory. Subjective sleepiness, perception of light and physiological responses support these behavioural suggest that aged related changes in ocular media such as lens yellowing (which partially blocks short-wavelength light from reaching the retina), reduced pupil size, decreased number of retinal ganglion cells play a primary role in the way light impacts cognition. Thus, one interesting avenue would be to further explore and confirm if aged ocular media, in particular lens yellowing, plays a primary role in the modulation of light effect on cognition with aging.

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