



Theoretical Review

Lifetime changes in the biological effects of light on non-visual brain functions

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ABSTRACT

Biological effects of light go beyond vision and influence non-image forming (NIF) brain functions such as sleep, circadian regulation, mood and cognition. These effects are primarily driven by the third class of photoreceptors (called ipRGCs), which are maximally sensitive to blue wavelength light and confer a maximal effectiveness to shorter wavelength light on NIF functions. Despite the growing recognition of the importance of light's NIF effects, most research has focused on young, healthy adults, while the impact of light may change during the early development and aging of the brain. This narrative review describes how the NIF effects of light change across the lifespan from foetus development and childhood (when data is available) through adolescence, adulthood and into older age. We begin by discussing how age impacts ocular structure, particularly the changes in photoreceptors. Our main focus is on cognitive brain functions which we define as the brain activity sustaining cognition as well as performance as the output of this activity. We highlight that evidence remains fragmented and unevenly distributed, particularly over the pre-adult trajectory, and that quantification of the lifespan changes is mostly not available. We further consider pupil and melatonin responses to light and circadian entrainment to allow approaching quantitative differences between age groups. We conclude by proposing future directions to reach the quantitative estimates needed by researchers, clinicians, policymakers, and designers to reach light interventions geared to a specific age group.

1. Introduction

Light not only allows vision, but it is also an essential cue for many biological functions that are not directly related to vision. These functions of light are often referred to as non-visual or non-image-forming (NIF) [1]. Exposure to light is the main time giver or zeitgeber of the circadian system which organizes physiology in time over the 24h rest-activity cycle [2]. Light therapy for a few weeks can improve affective state and treat mood disorders [3]. Light exposure can also trigger acute effects on physiology, including on cognition, alertness and sleep [1,4].

Since most of our daily activities happen indoors, artificial lighting has a major influence on how light affects our bodies. This matters because artificial and natural light often differ in their blue light content, which is the most effective at triggering non-image-forming (NIF) effects. While inappropriate lighting may contribute to cognitive deficits,

daytime sleepiness, poor sleep, and mood disturbances, well-designed lighting can enhance brain function, prevent cognitive decline, improve sleep, well-being and overall health [1,5–8].

To develop effective interventions, a comprehensive understanding of light's effects on brain function and their variability is essential. Currently, most research on light's impact on the human brain focuses on young, healthy adults. However, maturation and aging of the brain influence its function. Additionally, age-related changes in the eye can modify light input to the brain, ultimately affecting NIF effects. We currently lack comprehensive comparative reviews across different age groups that would clearly depict the current understanding. This narrative review aims to summarize findings across the lifespan to shed light on how sensitivity to light and its effects on brain function may change throughout the lifespan, from infancy to old age. We highlight that evidence remains fragmented and unevenly distributed, particularly over the pre-adult trajectory for which research data is most often not jointly available for infants, children and teenagers when these are

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Abbreviation list

AUC	area under the curve
BLT	bright light therapy
BST	bed nucleus of stria terminalis
CCT	correlated colour temperature
dLGN	dorsal lateral geniculate nucleus
fMRI	functional magnetic resonance imaging
IGL	intergeniculate leaflet
K	kelvin
LC	locus coeruleus
LED	light emitting diode
LH	lateral hypothalamus
MRI	magnetic resonance imaging
NIF	non-image forming
ipRGCs	intrinsically photosensitive retinal ganglion cells

OPN	olivary pretectal nucleus
PAG	periaqueductal gray
PET	positron emission tomography
PHb	perihabenular nucleus
PIPR	post illumination pupillary response
PLR	pupil light reflex
PRC	phase response curve
PVT	psychomotor vigilance task
RHT	retinohypothalamic tract
SC	superior colliculus
SCN	suprachiasmatic nucleus
SRET	self-referential encoding task
T	tesla
vLGN	ventral lateral geniculate nucleus
vmPFC	ventromedial prefrontal cortex
VPO	ventrolateral preoptic nucleus

very different populations from a physiological point of view.

We first consider the changes that are known to occur at the level of the eye across age groups. We then examine how the age-related changes in NIF responses may affect cognitive brain functions, which is our main focus and which we define as the brain activity sustaining cognition and the resulting behavioral performance. Given the scarcity of the data, we show that quantification of the lifespan changes is mostly not available, speaking for more research on the topic. We further consider pupil and melatonin responses to light and circadian entrainment to allow approaching quantitative differences between age groups. We conclude by proposing future directions to reach the quantitative estimates needed by researchers, clinicians, policymakers, and designers to reach light interventions geared to a specific age group.

2. NIF photosensitivity

The first evidence suggesting the existence of a distinct NIF photoreceptor system was provided by Keeler in 1927, when he observed a pupil constriction in response to light exposure in blind mice [9]. Much later, the spectrum of the light best affecting the circadian entrainment of locomotor activity in rodents was reported to mismatch the characteristic of the known retinal photopigments [10]. Suppression of melatonin secretion by light was subsequently reported in rare blind human individuals devoid of functional rods and cones [11]. It is only at the turns of the 21st century that the development of genetically engineered mice models allowed to prove that Keeler's prediction was to be true: mice lacking functional rods and cones still showed melatonin suppression, pupil reflex and circadian entrainment with light, with special affinity towards short wavelengths for a more extensive review see Ref. [1]. This led to the discovery of a new class of photoreceptors—intrinsically photosensitive retinal ganglion cells (ipRGCs)—which express the photopigment melanopsin [12]. Today we know that ipRGCs make up ~5% of retinal ganglion cells in rodents and ~1% in humans in the inner layer of the retina [13]. While it is broadly accepted that melanopsin is maximally sensitive to blue light (~480 nm), recent comparative work [14] has identified subtle but significant interspecies differences. Specifically, human melanopsin exhibits a peak sensitivity of ~479 nm, whereas the mouse photopigment is slightly shifted to ~484 nm. Although these differences are small, they are accompanied by substantial divergence in lens transmission for shorter wavelengths. Consequently, adopting species-specific α -opic metrology is essential for accurate light modelling and the development of age-specific interventions, as even minor shifts in peak sensitivity can influence the predicted biological impact of light across different life stages. Furthermore, ipRGCs constitute the main (if not the only) channel through which light affects NIF biological functions and combine their

intrinsic melanopsin-dependent photosensitivity with inputs from rods and cones to shape their response to light, which implies that their spectral sensitivity output varies with the illuminance [13].

IpRGCs can effectively signal the capture of single photons, but their scarcity makes them less sensitive to light compared to rods [15]. While rods respond to very low light levels, ipRGCs require a higher photon flux to respond, though still lower than that required by cones [13]. Additionally, ipRGCs have relatively slow response dynamics, taking up to a few seconds at low light levels and a few hundred milliseconds at higher levels [12]. In contrast to rods and cones, ipRGCs continue firing even after light extinction, influencing pupil size during subsequent darkness [16]. This persistent response depends, however, also on inputs from rods and cones [17]. In contrast to rhodopsin and cone opsins, the melanopsin photopigment is characterized by its ability to regenerate photochemically without the immediate need for the visual cycle. While human melanopsin is currently thought to be bistable—toggling between an inactive 11-*cis* state and an active signaling *all-trans* state [18, 19]—evidence in rodent models suggests a more complex tristable mechanism—with one signaling state and two inactive states, one tuned to cyan wavelengths and another to violet. This photochemical arrangement would allow rodent ipRGCs to maintain a high reservoir of available pigment, preventing “bleaching” and enabling the broader spectral sensitivity and exceptionally sustained firing required for long-duration NIF processing [20]. Clarifying these species-specific photochemical differences is critical, as the robust tristability of the rodent system may not fully translate to the human NIF system, potentially influencing how light sensitivity and NIF processing vary across the lifespan and between species.

It is important to recognize that there is a diversity among ipRGCs with up to 6 subtypes that were reported to contribute differently to the biological NIF responses to light in animal studies [1]. On the other hand, **human data remains scarce**, with histological studies predominantly restricted to identifying the M1 and M2 populations due to the low melanopsin expression in other putative subtypes [21,22] and there is no data regarding ipRGCs subtypes and lifetime changes. A detailed focus on ipRGC subtypes goes therefore beyond the scope of this review.

The discovery of melanopsin and of ipRGCs renewed the research interest towards light's impact in basic as well as in clinical neuroscience. New lighting technologies taking into account light intensity, spectrum and timing to fulfil our biological needs in addition to visual considerations have the potential to improve cognition, mood and sleep. There is, however, no one-solution-fits-all and lifetime changes are among the most prominent factors to integrate.

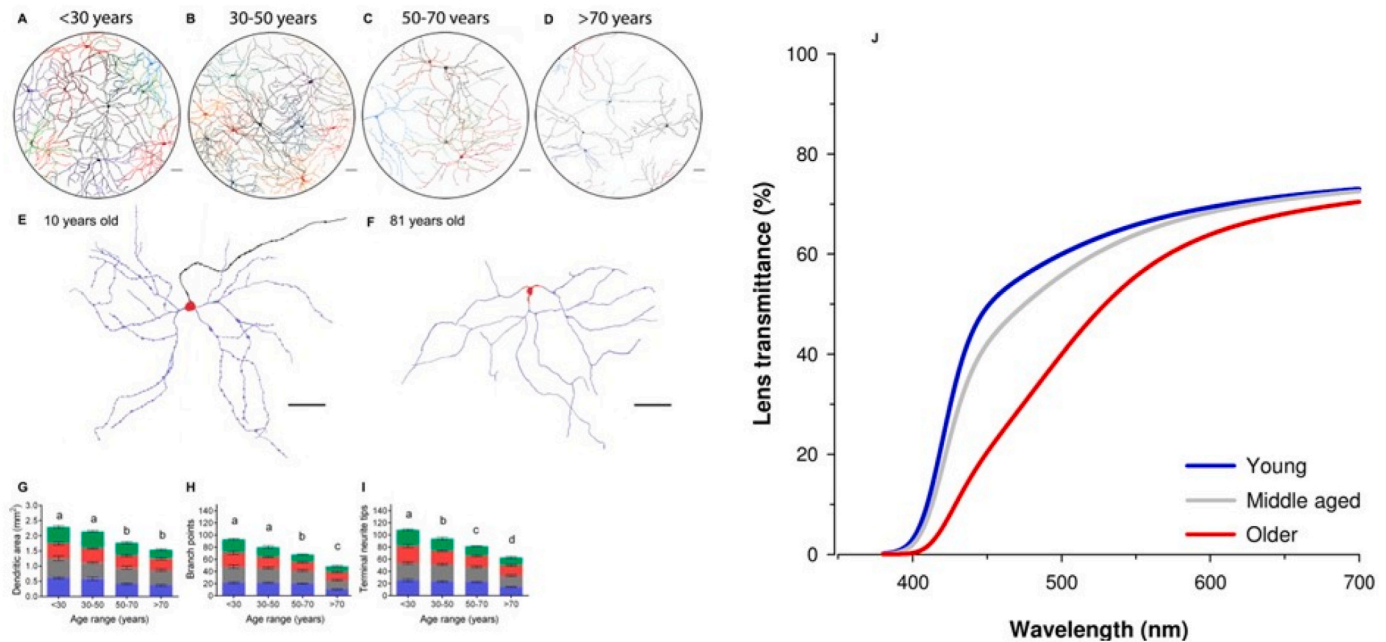


Fig. 1. Impact of aging on the mRGC morphological and arborization patterns in human retinas and crystalline lens transmission.

(A–D) Digital reconstructions illustrating the cell bodies and entire dendritic spread of mRGCs sourced from the central superior-nasal human retinal region. Panels display samples from donors aged 10 (A), 46 (B), 53 (C), and 89 (D) years, representing the age brackets: <30, 30–50, 50–70, and >70 years.

(E,F) Comparative dendritic profiles of M1 cells from human retinas at 10 (E) and 81 (F) years of age. Dendritic structures within stratum S1 are rendered in blue, while somas located in the GCL are shown in red. The axon is illustrated in black.

(G–J) Quantitative analysis of average dendritic field size (G), branching point frequency (H), total terminal neurite tips per cell (I), and Sholl area (J) Human lens spectral transmission profiles. The elderly group (red) displays a marked decrease in both the area under the curve (AUC) and total visible light transmission relative to the young (blue, –16.3% variance) and middle-aged (gray, –13.1% variance) cohorts. This attenuation is most pronounced at shorter wavelengths (400–500 nm, –53% reduction) compared to medium (–16.9%) and long (–5.1%) wavebands. No significant variation in AUC was detected between young and middle-aged subjects.

A–I: Reproduced from Ref. [36]; J: Reproduced from [37] (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3. Retinal light exposure modifications through the lifespan

We can intuit the retina undergoes profound modifications over the lifespan. Since ipRGCs combine their intrinsic photoreception with signals received from rods and cones, we will focus first on rod and cone lifetime changes prior to turning to ipRGCs.

Overall, the human cone mosaic undergoes two distinct stages: developmental packing and maturation during youth, followed by a gradual decline in several structural and functional aspects during adulthood. Maturation of the cone outer segments, particularly within the fovea, is a continuous process spanning childhood and adolescence. This development occurs partly through centripetal cone migration, which significantly thickens the outer retinal layer. For example, cone outer segments at 15 months are only half their adult length; even by 45 months, they have not yet reached maturity. Consequently, foveal cone density increases from birth until maturity; a newborn's central cone density is reported to be approximately half that of a 37-year-old adult [23]. In contrast, the literature regarding cone density changes after reaching maturity remains inconsistent. While some studies report relative stability [24,25], others documenting a wide age range have found a progressive decline in density during adulthood [23,26]. This annual loss is estimated at 0.2% to 0.4% [26] or approximately 104–116 cells/mm² [27]. Evidence suggests this loss is non-linear, characterized by an initial plateau in early adulthood followed by a subsequent decline in later years [27]. Furthermore, some studies indicate that cones may show considerable resistance to aging-related cell death, though they still undergo structural changes such as the shortening of outer segments [28]. Ultimately, photopic sensitivity is affected by aging through several mechanisms, including declines in photon absorption rate, colour acuity, contrast sensitivity (CS), and

flicker sensitivity [29–31]. In fact, recent evidence clarifies that the age-related decline in CS is primarily driven by reduced crystalline lens transmittance rather than by chronological age or pupil size alone [32].

Beyond changes in the cone mosaic, aging is associated with a preferential and significant loss of rod photoreceptors, particularly within the macular region. With aging, we can also observe a notable decline in rod photoreceptors in the human retina, especially within the macula. The number of rods in the macula may diminish by up to 30% in aging, with the most pronounced decline happening in the parafoveal area, 1–3 mm from the fovea. This reduction can lead to decreased scotopic sensitivity and a deterioration in rod function [24,33].

Unlike rods and cones, intrinsically photosensitive retinal ganglion cells (ipRGCs) serve as the primary source of photoreception during early development, maintaining structural stability throughout mid-adulthood before declining significantly in late senescence. Investigations of lifetime changes of ipRGCs are relatively scarce in humans, but animal studies showed that ipRGCs are photoreceptive in newborn and early postnatal mice, before the development of rods and cones, such that ipRGCs would provide the initial photoreception [34, 35]. One study indicates that NIF functions in early neonatal mice are exclusively mediated by ipRGCs. As the eyes open and rods and cones develop, ipRGCs begin to integrate signals from these photoreceptors, resulting in a larger and faster onset of ipRGC depolarization, quicker offset, increased sensitivity, and a slight shift in peak sensitivity from 480 nm to 490 nm [34]. A *postmortem* study of human specimens reported that the structural integrity of ipRGCs remains relatively constant until the age of 50 [36] (Fig. 1A–D). Beyond the age of 70, the complexity and density of ipRGCs begin to exhibit significant declines: the number of ipRGCs can fall by up to 44% compared to younger retinas and by 31% compared to those of 30–50 year-old donors. Additionally,

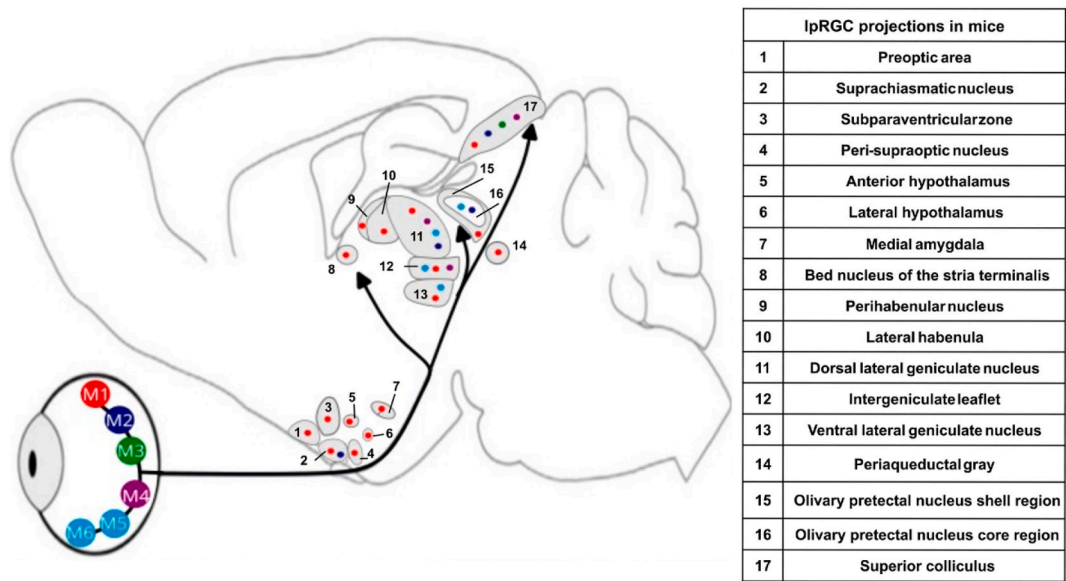


Fig. 2. Anatomical arrangement of primary ipRGC pathways in the mouse brain. This diagram provides a schematic overview of the principal central circuits originating from murine ipRGCs. Numerical labels integrated within the graphic correspond to the anatomical regions specified in the associated table. Coloured markers denote the specific innervation patterns and target sites for the range of established rodent ipRGC subtypes (M1–M6). Reproduced from Ref. [1]. See Ref. [1] for more details on ipRGC subtypes.

dendritic complexity decreases markedly, especially when comparing individuals aged 50-70 to those over 70, as well as the dendritic profiles of the cells from 10- and 80-year-old retinas [36]. These observations appear consistent with animal studies where significant decline in ipRGCs occurs only in advanced aging stages [38] while evidence gathered across species also estimated 35-40% decline in all-type RGCs over the adult lifespan [39].

Together with the changes in rod and cone function, IpRGC loss or reduced arborization in aging may result in a reduced NIF photosensitivity as suggested, for instance, in an elderly donor (over 70) [36]. In addition, several studies suggest the development of compensatory mechanisms to increase the sensitivity and firing rate of ipRGCs which further complicates change quantification [40]. The relatively late commencement of notable alterations in ipRGCs supports a high resistance of ipRGCs to injury and to aging with respect to other RGCs, possibly because of the expanding dendritic fields of ipRGCs as suggested in rodents [41,42]. The loss of ipRGCs and alteration in their morphology, including altered dendritic arborization, smaller cell bodies, and a patchier distribution of melanopsin, appears to accelerate in certain neurodegenerative conditions in humans, such as Alzheimer's and Parkinson's diseases (AD and PD) [43,44]. IpRGCs may, however, be resistant to RGC neurodegeneration in Leber's Hereditary Optic Neuropathy which has been used as human models to investigate the NIF effects of light [45,46].

Despite all this evidence, precise quantification of the contribution of each age-related retinal changes to the overall photosensitivity of ipRGCs is lacking. Quantification of age-related modification of ipRGCs output and how it contributes to the age-related changes detailed in the next section is also not available, calling for more investigations.

Besides photoreceptor changes, pupil size decreases over the healthy adulthood due to senile myosis, with some authors reporting a linear reduction of 0.015 to 0.043 mm per year in human pupil diameter, because of factors like sphincter muscle atrophy, iridal rigidity, altered autonomic tone, and chronic fatigue [47]. The accumulation of crystalline aggregates and yellow chromophores in the lens, commonly known as “lens yellowing”, also accompany human aging. This process causes increased lens density and reduces light transmission, particularly for blue light, and results in a relative “blue blindness” in older

individuals. Attempts to quantify this reduction reveal significant decreases in transmittance: transmittance for short-wavelength light would be reduced by 53% between 20 and 35y young adults and 55-70y older people, and by 45% between 36 and 55y middle-aged and older people. For long-wavelength light, there would be a 17% decreased transmittance between 20 and 35y young adults and 55-70y older people, and a 5% decrease between 36 and 55y middle-aged and 55-70y older people [37] (Fig. 1J).

However, whether lens yellowing and senile myosis affect the NIF biological impacts of light or whether compensatory mechanisms take place remains debated (see below). IpRGCs may indeed be able to enhance their sensitivity to offset the reduced photon absorption caused by lens-yellowing, such as increasing the presence of the 11-cis form of melanopsin as reported in rodents [48,49].

4. Projections of ipRGCs to the brain

Due to methodological limitations in human research, the brain pathways of ipRGCs have been largely studied in animal models [13]. The present section will summarize these animal findings (Fig. 2). IpRGCs innervate 70% of approximately 46 RGCs' brain targets [50]. These projections encompass areas related to both image-forming and NIF functions. Broadly classifying the target regions based on their roles in physiology and behavior, we can categorize the main projections in 7 groups.

- 1 **Circadian entrainment.** The suprachiasmatic nucleus (SCN) is a primary target for ipRGCs and receives dense direct inputs from these cells via the retinohypothalamic tract (RHT) [51]. IpRGCs also reach the thalamus in intergeniculate leaflet (IGL) which is a necessary nucleus for circadian entrainment since it sends inputs to the SCN [52]. The IGL is considered to correspond to the pre-geniculate nucleus of the thalamus in primates including humans. As in rodents, the pregeniculate nucleus projects to the SCN [53].
- 2 **Sleep-wake regulation.** IpRGCs project to various hypothalamic nuclei, not limited to the SCN, including the ventrolateral preoptic nucleus (VLPO) and lateral hypothalamus (LH) [50] that both play a key role in sleep-wake regulation [54].

- 3 **Pupillary light reflex:** The olivary pretectal nucleus (OPN), located in the midbrain, is another target for ipRGCs. OPN shell (sOPN) plays a crucial role in the pupillary light reflex (PLR) pathway [55,56].
- 4 **Affective state:** Light can influence brain areas associated with mood regulation either directly or indirectly through pathways that pass through the SCN, ventral lateral geniculate nucleus (vLGN), and IGL. ipRGCs directly project to the amygdala (medial amygdaloid nucleus) and perihabenular nucleus (PHb) of the thalamus [57]. Indirect pathways involve the ventral tegmental and raphe areas receiving innervation from the SCN, as well as the lateral habenula (LHb) being innervated by the vLGN and IGL that receive input from ipRGCs [58]. ipRGC projections to bed nucleus of the stria terminalis (BST) and periaqueductal gray (PAG), involved in mood and behavioral state have also been reported [59].
- 5 **Attention/alertness:** Projections of ipRGCs go to the brainstem in the superior colliculus (SC), that is involved in attention and eye movement coordination, as well as the pulvinar, a central hub in the thalamus interconnecting cognition, attention, and alertness [50,51, 60,61]. A notable indirect pathway involves the locus coeruleus receiving indirect innervation from the SCN [62].
- 6 **Memory and learning:** The hippocampus, a key area associated with learning and memory, also indirectly receives light signals from ipRGCs through the SCN [63].
- 7 **Vision:** As previously mentioned, ipRGCs contribute to image forming functions through their projections to visual processing areas, including the dLGN and visual layers of SC [61].

The majority of these projections were uncovered in nocturnal laboratory animals. Translation to diurnal humans, where the later maturation of the cortex allows for complex cognitive processing [64], remains limited. There are notable exceptions, however. In both diurnal rodents and non-human primates, ipRGC projections have been reported to several key regions. These include the SCN, IGL (pregeniculate nucleus in primates), OPN, LGN, and SC [22,65,66]. While it seems that a diurnal rodent had overall similar ipRGCs projections, specificities were reported. Specifically, the vLGN, dLGN and the OPN receive less innervation from ipRGCs in grass rats compared to reports in nocturnal rodents [66].

All the structures mentioned above undergo changes over the lifespan and covering them goes beyond the scope of this review. Research on age-related changes in ipRGCs projections, their density for instance, is almost nonexistent. One notable exception is the fact that ipRGCs present functional connections with the suprachiasmatic nucleus at birth, implying that the NIF pathways become functional much earlier in development than the image-forming pathways [67]. When ipRGCs projections to other brain targets take place during development is not known.

5. Impact of light on cognitive brain function

5.1. Functional impact of light on ipRGC targets in animals

The functional impact of ipRGCs on their direct anatomical projections has been predominantly investigated in nocturnal rodents. A seminal paper used conditional activation of ipRGCs and reported evoked circadian phase resetting and pupil constriction as well as c-Fos induction – a marker of neural activation – in almost all the areas mentioned in the previous section, including multiple nuclei in the hypothalamus, thalamus, and limbic system [68]. As an example, we highlight the densest, and probably most documented, projections of ipRGCs to the SCN, site of the principal circadian clock, emphasizing the key role of ipRGCs in circadian entrainment and regulation of sleep and wakefulness. The SCN shows increased c-Fos expression in response to light. The effect in nocturnal rodents is phase-dependent, with light increasing c-Fos expression at night/dark phase and having less or little effect during daytime/light phase [69]. It also appears that it is through

the projection of ipRGCs to the SCN that light affects learning [62,70]; an observation that is in line with the need for a functional SCN for hippocampus-dependent learning [63]. As another example and still in rodents, ipRGCs projections to the central and medial nuclei of the amygdala are reported to mediate at least part of anxiety-related behaviors following acute light exposure, likely totally independent of the SCN [71]. These findings highlight the diverse and intricate role of ipRGCs' projections in modulating various behaviors in rodents.

The investigation of the NIF impact of light beyond the initial synapses of ipRGCs remains scarce in rodents. A notable exception, however, is the involvement of ipRGCs in controlling the activity of the ventromedial prefrontal cortex (vmPFC), a crucial region for regulating emotional and social behaviors. This regulatory function, which operates independently of circadian and mood changes, is facilitated through an ipRGC-thalamic-corticolimbic pathway [72]. In addition, the impact of light on mood-related measures was associated with ipRGCs' projections to the PHb, a key region of the regulation of affective state, which would in turn pass on light signal to the nucleus accumbens or to the vmPFC [70].

Overall, animal data provide evidence that ipRGCs' signals have a functional impact on most of (if not all) their projections. They further indicate that light can affect learning and memory retrieval as well as affective state (attention and executive functions are more difficult to probe in rodents).

5.2. Biological impact of light on the human brain

Neuroimaging techniques applied to humans provide the advantage of collecting data over the entire brain. Several studies reported light-induced increases in activity in cortical regions involved in the ongoing cognitive processes (attentional, executive, emotional domains), both at night and during the day [1]. Investigation of the impact of light on memory function is scarce in humans, likely given the complexity of covering all the aspects of memory (encoding, consolidation, retrieval; declarative vs. non-declarative memory).

When light exposure lasts less than a minute, significant effects are more often seen in subcortical areas than in the cortex, suggesting that light's impact on NIF function is mainly mediated by subcortical structures [73]. The thalamus, particularly a region corresponding to the pulvinar, may act as a relay between these subcortical areas involved in alertness and the cortex [74,75]. The only positron emission tomography (PET) study that focused on the NIF impact of light found that during the biological night, exposure to light decreased the activity of the anterior hypothalamus in an area encompassing notably the SCN during the darkness period immediately following the exposure [76]. This early observation was recently confirmed by 2 fMRI investigations, which used high-resolution 7 T MRI [77,78]. Interestingly, a concomitant increase in activity was also found over the posterior part of the hypothalamus suggesting an anterior-posterior difference in the functional impact of light on the hypothalamus [78]. Hypothalamus nuclei, such as the lateral hypothalamus or the SCN are therefore likely to receive ipRGC signaling and mediating in part the impact of light on NIF brain functions, possibly through a relay in the pulvinar. Another relay may be found in the locus coeruleus (LC) in the brainstem which may be affected by light onset in a fMRI study involved an executive task, though the resolution of the 3T MRI apparatus only allows speculative localization [73]. Indirect support for the involvement of the LC was recently gained through analyses of transient changes in pupil size in responses to auditory stimulations as well as when considering the variability in pupil size during a light exposure of stable illuminance, warranting further high-resolution imaging focused on the LC [79,80]. Light is likely also influencing activity in the amygdala, though both increased and decreased activity were reported [81,82], potentially because of insufficient resolution (using 3T MRI) to distinguish different responses across amygdala nuclei.

Human data indicate therefore that light can affect the activity of at

least some of the targets of ipRGCs in a cognitive context. The inherent limitations of human research make it, however, difficult to ascertain that ipRGCs are mediating these effects. Light impact on ipRGCs targets were detected comparing polychromatic white light to darkness, but also using blue monochromatic light compared to other monochromatic longer wavelength light [1]. Additional support for a role of ipRGCs comes from an investigation in visually blind individuals with intact non-image-forming photoreception (and very likely ipRGC), which showed increased brain responses to auditory tasks in the thalamus while exposed to blue light [83,84] and from a study showing that manipulating light history triggered change in the impact of light on thalamus activity that could be explained through a theoretical change in ipRGCs' sensitivity [19].

5.2.1. Attention and executive functions

Light was most consistently reported to affect attention (and alertness) with improved reaction times under high illuminance polychromatic light (vs. lower illuminance/darkness) or under blue or blue enriched light (vs. longer wavelength or blue depleted light) [85]. Executive functions including working memory, decision-making, inhibitory control and cognitive flexibility (task switching) were also reported to be positively affected by exposure to light [86–88]. Several studies reported significant improvements in performance and productivity (self-reported performance, verbal and spatial tasks performance) through exposure to blue-enriched white light or high correlated colour temperature (CCT) lighting [89]. Likewise, using the EEG while wearing glasses filtering a range between 380 and 570 nm (encompassing violet to green light) showed that filtering lenses reduced beta activity (linked to alertness), while alpha and theta activity remained unchanged [90]. Importantly, while the impact of light was consistently detected when administered at night, significant performance changes were not always observed during the day indicating that light impact may depend on the context of its administration (e.g. prior sleep loss, baseline light level, etc.) [4]. The effects of light on cognitive performance were in many instances accompanied by electrophysiological recordings which, in general, indicated that behavioral effects were mirrored by impact of light on brain functioning [91–93] (for more information on the behavioral effect of light on performance and electrophysiology see Refs. [1,94]).

More precise location of light impact within the brain was provided by MRI investigations. Light increased the activity within the prefrontal and parietal cortices during auditory tasks, in areas involved in the ongoing executive and attentional processes (respectively probed via auditory n-back and oddball tasks) [75,95,96]. Areas of other cortices, within the insular, occipital or temporal lobes were also affected by light depending on the ongoing task [73,75,96,97]. Visually blind individuals with intact non-image-forming photoreception showed increased brain responses to the n-back task auditory tasks in the prefrontal cortex while exposed to blue light [83,84]. Manipulating light history also modulated the activity of the prefrontal cortex in line with ipRGCs change in sensitivity [19]. The effects of light on executive brain responses were further found to vary depending on circadian phases and sleep homeostasis, with light impact relatively lower in the evening and relatively larger following sleep deprivation [97].

5.2.2. Emotional functions

Behavioral measures of the impact of light on emotion/affective state mainly pertain to the positive impact of light therapy on affective state scales, with the benefits of the therapy being detected within 2 to 4 weeks of intervention (depending on the control condition and light characteristics). Prolonged light therapy in humans increased amygdala connectivity to the prefrontal cortex likely therefore contributing to the positive impact of the intervention [98]. The production of serotonin and dopamine are also known to be induced by exposure to light and to undergo seasonal variation [99,100]. Light can also trigger acute (or immediate) responses that can modulate emotional processing [81].

Ambient blue light was reported to lower blood pressure and reduce anger (as measured by facial electromyography) indicating improved emotional responses in high-stress operational environments [101]. Using self-perception through a self-referential encoding task (SRET), blue light was found to accurately reduce negative self-thoughts [102]. The daily repetition of these acute responses is plausibly contributing to the long-term impact of light on affective states. The impact of light on emotional responses may act via a brain pathway in part different from attention, executive functions and alertness. While the posterior and anterior hypothalamus are affected by light in an emotional context [78], light is also likely directly influencing regional activity in the amygdala [81,82], mostly within medial and superior nuclei which are also showing seasonal variation in activity and seasonal changes in the acute impact of light [103]. Light may also enhance the activity in the anterior cingulate cortex in an emotional context related to anticipation and decision-making [95].

5.3. Impact of light on cognition in infants, children and adolescence

Few studies on the impact of light dealt with cognition prior to adulthood - infant, children or teenagers - while no PET or fMRI studies were conducted on pre-adult populations, except for a few recent investigations in late-adolescence [104,105], such that the changes occurring at the level of the brain over this lifetime period are not established.

In infants (6–12 weeks), higher light intensity in the early afternoon has been associated with more consolidated nighttime sleep, though no correlation was found between daily light exposure and crying [106]. As children reach toddlerhood (2y), reduced outdoor light exposure during winter has been linked to increased sadness, as reported by teachers, while levels of frustration and aggression remained unchanged [107]. In preschool-aged children (3–6y), later and shorter light exposures were linked to delayed sleep onset and offset, although no relationship was found between affective state and weather conditions [108,109]. Within this same age group (4.5–5.5y), exposure to higher correlated color temperature (CCT) lighting (5000K vs. 3500K) has been shown to enhance task-switching performance [110]. Regarding school-aged children (4–12y), studies investigating room light and cognitive outcomes have yielded mixed results; some suggest that higher CCT lighting benefits concentration and on-task behavior [111–113], while others found no overall improvement in standardized cognitive tests [110,114]. Overall, research on the impact of light on children's emotions has yielded mixed results (More details regarding the broader impact of light in children can be found in a recent review [115]).

These observations likely reflect the high transparency of the young crystalline lens and the ongoing maturation of the circadian system. Mechanistically, these developmental stages may be more sensitive to short-wavelength light (blue-enriched), which modulates frontal lobe activity (e.g., increased beta power [116]) to improve task-switching and attention. However, the lack of direct comparisons with teenagers or adult cohorts leaves it unclear whether these cognitive gains are unique to the developing brain's plasticity or simply more pronounced due to greater light transmission to the retina.

Studies indicate that appropriate light exposure is beneficial for teenagers. Specifically, a significant association was uncovered between the duration of bright light therapy (BLT) device use and increased beta power in the frontal regions, alongside improvements in math performance and attention tests among adolescents aged 13–18y [116]. Similarly, teenagers aged 16–19y exhibited faster cognitive processing speeds and improved concentration under blue-enriched white lighting compared to standard lighting. However, this lighting did not affect short-term memory encoding or retrieval, suggesting its impact is primarily limited to basic information processing [117]. Currently, inconsistencies in exposure periods, testing protocols, and mixed evidence limit the comparability with findings in adults. While it is reasonable to assume that children and adolescents may exhibit different sensitivities

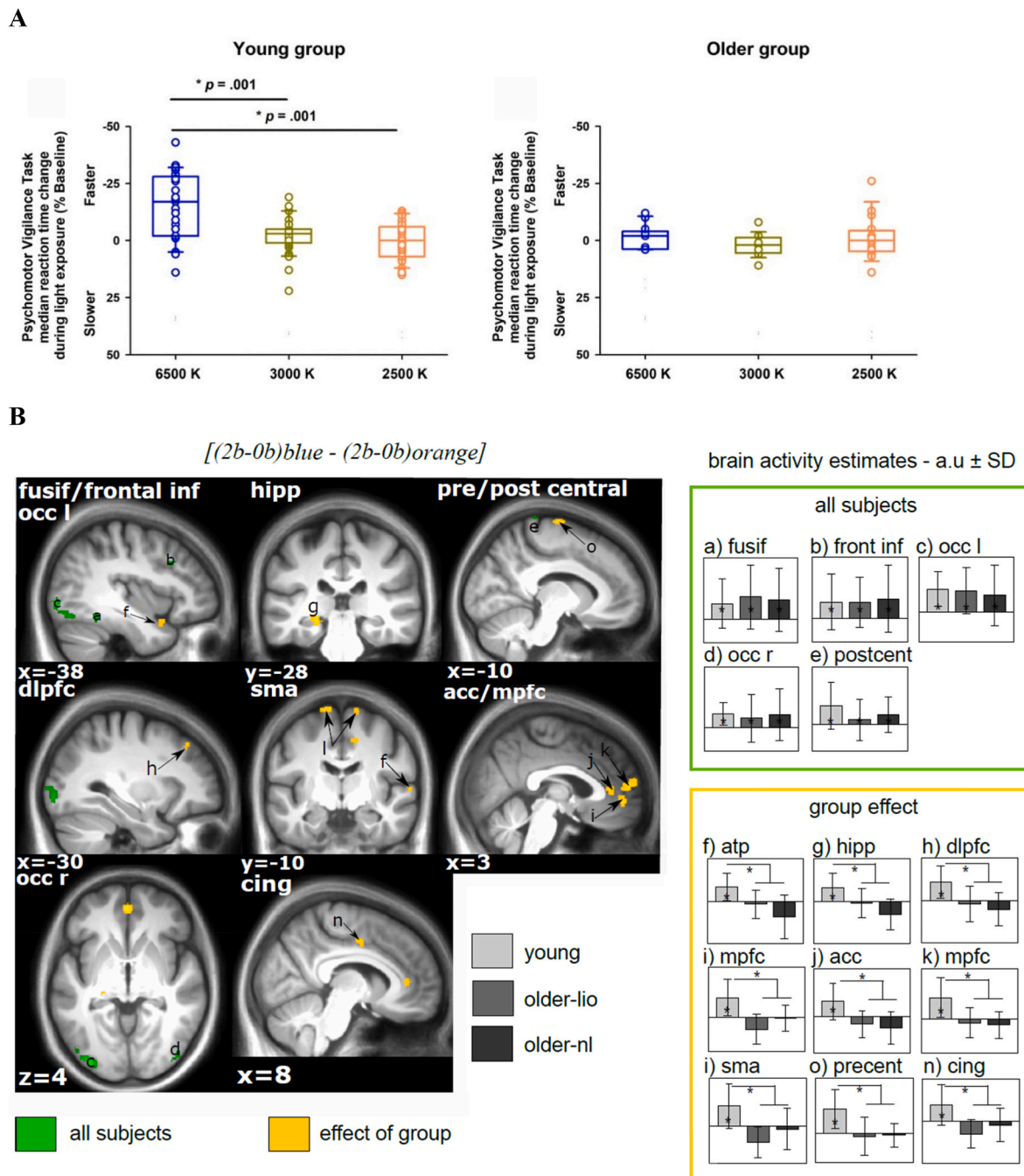


Fig. 3. Influence of aging on light-driven cognitive processes.

A. Age-related effects of light exposure on sustained attention, evaluated via the Psychomotor Vigilance Task (PVT). In the younger group, blue-enriched light (6500 K, blue circles) markedly improved performance, as demonstrated by reduced reaction times (RT) relative to non-blue-enriched spectra (3000 K, dark yellow circles; 2500 K, orange circles). In contrast, the older cohort showed no significant shifts in sustained attention regardless of the spectral composition. Reproduced from Ref. [117].

Panel B. Impact of light on executive functions across different ages and ocular conditions. Brain activity was quantified during executive tasks under monochromatic blue light (480 nm, 3×10^{13} photons/cm²/s) compared to a monochromatic orange control (620 nm; matched photon flux). The study evaluated healthy young adults, older adults with natural lenses (older NL), and older adults with intraocular lens replacements (older IOL).

Cortical regions where the light effect remained uniform across all three cohorts are marked in green. Areas exhibiting significant group differences are indicated in yellow. The right-hand panels display activity estimates (mean $\pm$ SEM) for the respective brain regions. As indicated in the green box, blue light effectively modulates local neural activity independently of age or lens type. Conversely, the yellow box highlights that the young group exhibits a significantly stronger neural response to blue light than both older groups, whose responses were comparable.

Anatomical Abbreviations: fusif: fusiform gyrus; front inf: inferior prefrontal cortex; occ l/r: left/right occipital cortex; postcent: postcentral gyrus; atp: anterior temporal pole; hipp: hippocampus; dlpfc: dorsolateral prefrontal cortex; mpfc: middle prefrontal cortex; acc: anterior cingulate cortex; sma: supplementary motor area; precent: precentral gyrus; cing: middle cingulate cortex.

Reproduced from [121] (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1

Close-to-quantitative lifetime changes in pupil light reflex, post-illumination pupillary response, melatonin suppression and circadian entrainment.

Age Group	PLR & PIPR	Melatonin Suppression	Circadian Entrainment	Refs
Gestation	- PLR under blue light with 32 weeks gestation			[127]
Infants (Newborns–2 Years)	-Pupil size increases and peaks in adolescence, maybe until the age of 20y (from 5.5 to ~7.5 mm); -Pupil constriction increase; -Decreasing PLR latency until childhood (9y)			[127–130]
Children (3–10y)	-PIPR qualitatively similar to adults (5y old); -Gradual maturation of PLR.	-Up to 70% suppression with low-intensity (5–40 lx) light (3–5y); -Suppression about 2x more than adults (8–10 y).	-high sensitivity to low evening light (5–40 lx), could delay 50 min the circadian clock; -variability in bedtimes set by the parents.	[131–134]
Adolescents (11–18 Y)	-PIPR qualitatively similar to adults; -PIPR starts to decrease.	-Suppression starts decreasing, but still higher than adults (~10% difference between early and post puberty); -Potential faster recovery of melatonin post-light exposure levels (compared to adults).	-become late chronotypes; -PRC is symmetrical, phase advance and delay are similar in magnitude to adults.	[131, 135–141]
Young Adults (18–35 Y)	-PIPR decreases with age. -Sustained pupil constriction starts to decrease (age 26y); -Lens transmission starts to decrease from 30y (1% loss per year); -Pupil size starts decreasing at 30y (.05 mm per y).		-PRC asymmetrical, phase advance is smaller than delay.	[135,142,143]
Middle-Aged Adults (36–50 Y)	-Reduced sustained pupil constriction; -Reduction in PIPR; -Smaller pupil compared to younger adults.			[143]
Older Adults (50y+)	-Reduced PIPR; -Decreased lens transmittance (40%, 1% decrease per y from 30 to 60) -Smaller pupil size compared to younger adults (could be up to 40%; 0.05 mm decrease each year).	-Reduced suppression for low and intermediate illuminance; -Shift in peak sensitivity.	-Become earlier chronotypes; -Impaired capacity to accommodate light/dark cycles; -Light phase-shift less effective; -reduced light phase-shifts for low-moderate light levels.	[48,119,120, 143–150]

to light stimuli (cf. previous sections), none of these studies directly compared these younger age groups with adults, calling for more research on the topic including group comparisons. Recent studies tried to resolve the issue in teenagers. In an fMRI study including participants aged 15–18 and 18–30 years, evening exposure to blue-enriched light modulated thalamo-cortical connectivity during a memory task, with adolescents showing a stronger increase in connectivity between the thalamus and the parietal cortex than young adults [104]. In addition, adolescents showed larger response amplitudes at higher light levels, including more pronounced deactivation in the superior-anterior and inferior-tubular hypothalamus [105]. Both studies suggest an impact of light on areas or on the crosstalk between areas that may underlie a stronger effect of light on attention and/or on sleep and alertness and that are sensitive. In contrast, a study using Transcranial Magnetic Stimulation (TMS) did report an impact of light on cortical excitability in young adults but not in adolescents [118], indicating that difference between developmental ages may be more complex than anticipated and warranting further investigations.

5.4. Impact of light on cognition in aging

There is, in contrast, more insight available at the other end of a lifetime. Reduced impact of monochromatic blue light in 65-year-old adults – relative to 23-year-old – has been reported for some acute responses such as subjective alertness, sleepiness and mood [119]. Polychromatic light conditions varying from non-blue enriched light (2500K) to blue-enriched light (6500K) at low light levels (as in typical indoor settings) were used to assess the link between aging and light sensitivity. While young adults (18–30y) showed improved subjective sleepiness and psychomotor vigilance task (PVT) performance under 6500K, older individuals (55–80y) did not show any difference in those indices across light conditions [120] (Fig. 3A). In contrast both non-blue

enriched white light (2800K) and blue enriched white light (9000K) were found to trigger an alertness response (measured by subjective sleepiness) in both young ($25y \pm 0.9$) and old groups ($64y \pm 1.3$), although only the younger participants showed melatonin suppression in the evening [122].

Similarly to young adults ($23y \pm 4.1y$), exposure to blue light was found to increase cortical and thalamus cognitive activity in healthy older individuals aged $>55y$ [123]. Yet, compared to younger adults, older participants were less affected by light in several brain regions including the pulvinar, part of the prefrontal cortex, as well as possibly in ventral tegmental area (VTA), which is an important source of dopamine [124]. These findings were later confirmed, and it was found that the reduced impact of light on cognitive brain activity (still using auditory tasks) was not solely explained by senile myosis or lens yellowing, as controlling for pupil size and including individual with novel lenses, following cataract surgery, did not abolish age-related differences [121] (Fig. 3B). This latter finding may arise in part from the relatively long gap between lens replacement and brain measurement (~4-years). Investigating light impact on diverse physiological responses to light closer to cataract surgery (~4–8 weeks) indeed found improvement in several responses to light including in sleep and cognitive function [125]. Likewise, cataract patients demonstrated significantly faster reaction times closely (5–18days) following surgery, supporting the idea that increased exposure to blue light, previously reduced by the yellowing of the lens, may contribute to improved cognitive processing [126]. The brain may therefore adapt to the gradual ocular changes associated with aging, as well as to lens replacement.

Overall, it seems that light exposure may have to be stronger as we age to reach the same level of cognitive stimulation as in younger adults. Despite the availability of data with group comparisons attesting of a reduction of the impact of light in aging, no quantification of the

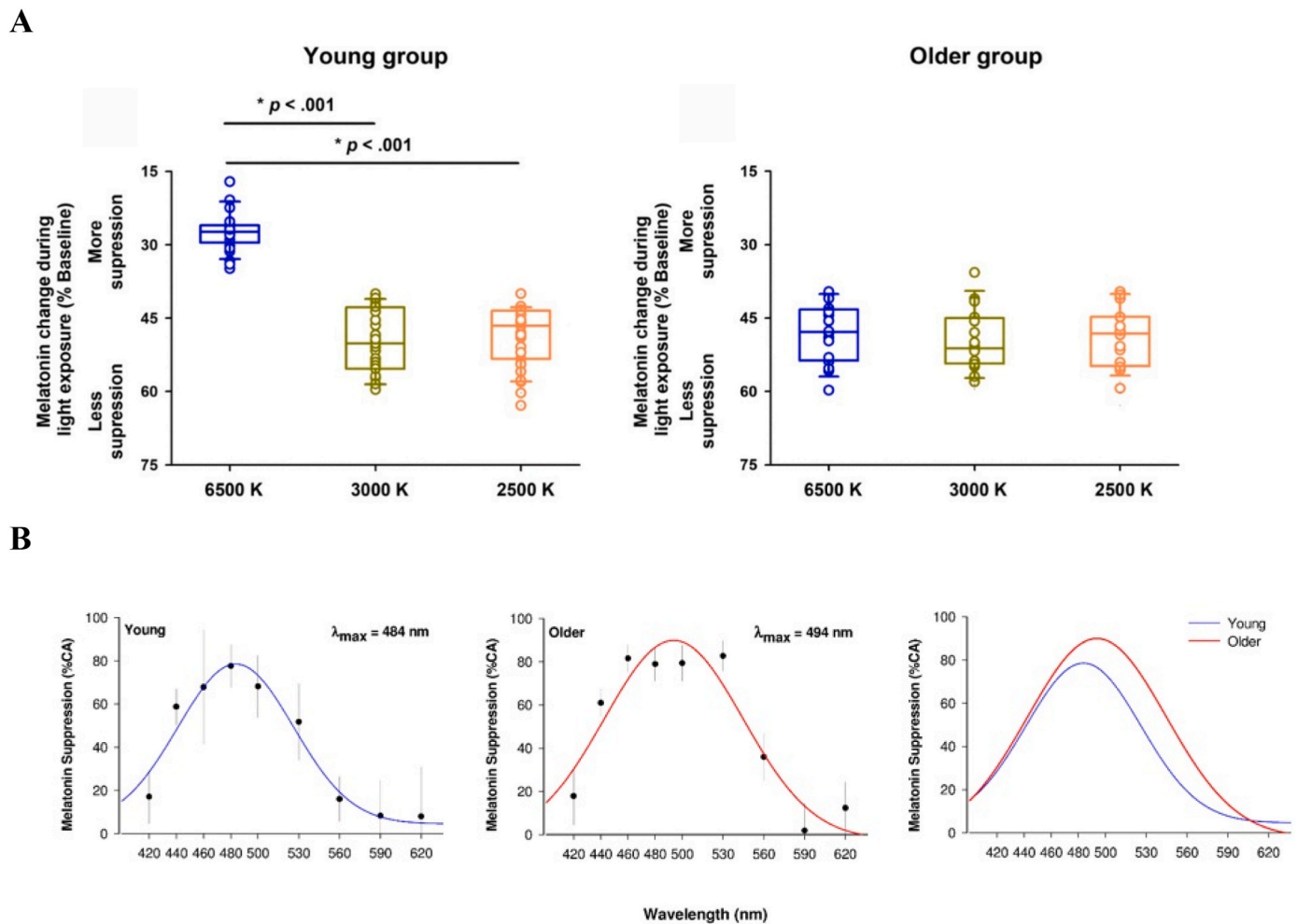


Fig. 4. Age-related alterations in the melatonin-suppressing effect of light.

A. In younger subjects, exposure to blue-enriched light (6500 K, blue circles) produced a marked inhibition of the evening rise in endogenous melatonin relative to non-blue-enriched conditions (3000 K, dark yellow circles; 2500 K, orange circles). In contrast, the older cohort displayed no significant variation in melatonin levels across the various light spectra. Reproduced from Ref. [117].

B. Melatonin suppression magnitudes for younger ($n = 5$; left panel) and older participants ($n = 8$; middle panel), expressed as Percentage Control Adjusted (%CA). Both age groups exhibited negligible suppression at near-UV (420 nm) and long (>560 nm) wavelengths. Peak sensitivity was observed at 484 nm for the younger group (blue curve), whereas it shifted to 494 nm in older individuals (red curve). The right-hand panel provides a direct comparison of these spectral sensitivity curves between the two groups. Reproduced from Ref. [48]. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

reduction is available.

6. Pupil, melatonin, circadian entrainment in aging

Considering pupil and melatonin responses to light and circadian entrainment allows approaching quantitative difference between age groups. We provide an overview of the findings in the next section and summarize them in Table 1.

6.1. Pupil light reflex and post-illumination pupil response

Focusing on the pupil provides an easy read-out of the impact of light on brain function. It is therefore not surprising that it received a substantial scientific interest with respect to lifetime changes in the impact of light. Although the impact of light on pupil size depends on input from all retinal photoreceptors, the overall picture is that rods and cones mainly contribute to the acute pupil constriction ($< \sim 10$ s) while ipRGCs intrinsic sensitivity is responsible for the sustained pupil constriction over longer exposure [151]. IpRGCs also trigger a lasting relative pupil constriction after light exposure, known as the post-illumination pupil

response (PIPR). This response consists of a partial constriction of the pupil following its dilation at light off, most likely because of the continued firing of ipRGCs [152].

Evidence from studies on newborns and children up to two years of age suggests that pupil size begins to increase during the early stages of life, with this growth trend continuing into adolescence, when the pupil reaches its peak size [127,128,153]. From infancy through adolescence, the pupillary light reflex (PLR) matures from an initial ipRGC-dominated response to a more integrated system involving rods and cones. This transition begins as early as the 32 nd week of gestation, where premature infants demonstrate a PLR in response to blue light—but not red—confirming that early developmental stages are primarily mediated by ipRGCs. As children age from 6 months to 9 years, pupil constriction increases and response latency decreases, likely suggesting the progressive recruitment of rod and cone inputs [128,129,153]. While the post-illumination pupillary response (PIPR) in 5- to 15-year-olds is qualitatively similar to adults [131], recent research identifies significant differences in both tonic pupil size and PIPR between children and adolescents, suggesting that ipRGC-driven circuits continue to refine their physiological output throughout puberty [154].

Beyond this peak, PIPR strength begins to decrease between ages 16 and 35, a decline that correlates with delayed sleep timing and suggests that intrinsic ipRGC sensitivity is a key determinant of circadian alignment in young adulthood [142]. Ultimately, the developmental maturation of pupillary dynamics—transitioning from neonatal ipRGC dominance to peak sensitivity in adolescence, followed by gradual decline—likely determines the strength of the photic signal reaching the brain and, consequently, the individual's overall sensitivity to light.

The literature suggests that pupil reaction to light may decline with age during later adulthood, though the findings are sometimes contradictory. A correlation between age and reduction in the sustained constriction during the light exposure was reported in participants between 26 and 68y [143]. PLR was, however, not different between healthy older individuals aged 50 to 70y and younger individuals aged 18–30y in several studies [155]. Although these studies led to different conclusion – potentially because of differences in the age of the recorded participants and in the variety of light conditions administered (monochromatic blue, green, red and polychromatic light) – they both reported that the older participants consistently exhibited smaller pupil sizes across all light conditions, this was especially true in the later study particularly at low irradiances (7×10^{12} photons/cm²/s; total photon flux). A positive correlation between PIPR and baseline pupil size was further detected in a sample of 19–80y old participants, but no significant relationship between PIPR and aging was found [152]. In contrast, the early part of the early poststimulus area under the curve (AUC) [131] following blue light exposure was reported to be increased in older individuals and the findings were not accounted by rod- or cone-induced rapid redilation after light off, potentially implying an alteration in ipRGC intrinsic response [143]. Interestingly also, decreased lens transmission was associated with reduced early PIPR, although lens transmissions - which is correlated with age - appeared less associated than age itself [143]. Overall, while PLR may or may not be reduced in aging, it seems that PIPR, mainly driven by ipRGCs, is altered in aging though it may be due to the decrease in lens transmittance.

6.2. Melatonin secretion

Light suppresses melatonin secretion by the pineal gland - in the evening/at night, i.e. when it is produced, and it is the aspect probably most considered to investigate the NIF biological impacts of light [120, 156]. This is likely because melatonin metabolites can be routinely assayed in the saliva, such that, as for the pupil, it is a relatively accessible parameter of an important NIF function of the brain.

Children were found to be more sensitive to light-induced melatonin suppression than adults. For example, in preschoolers aged 3 to 5y, even low-intensity light exposure before bedtime can reduce melatonin production by up to 70% and provoke sustained melatonin suppression after light offset [132]. In older children, such as those aged 8 to 10y, melatonin suppression can be up to twice as large as in adults [133]. This heightened sensitivity is likely due to children's larger pupils and clearer lenses. The sensitivity to light seems to decrease afterwards and there is a report that melatonin suppression is reduced between early and mid-puberty teenagers [135], even though adolescents still show higher melatonin suppression than adults [136,137]. This could mean that evening light could be especially disruptive for children and teenager sleep, which may be a problem considering the increasing presence of artificial light through portable screen devices. Using blue blocking lenses in the evening may provide a response to this issue. The use of such blue blocking lenses for one week in the evening decreased melatonin suppression in teenagers while it increased and decreased subjective sleepiness and alertness respectively (while objective measures related to sleep did not change) [138]. Importantly, however, melatonin secretion in teenagers may recover faster, i.e. return to normal dim-light level quicker than adults following an exposure, suggesting that the disruptive effect of light on circadian rhythm (and sleep) may be reduced in teenagers and warranting further research [139].

At the other end of the lifetime spectrum, several studies reported that, as adults get older, they undergo less melatonin suppression when exposed to light in comparison to their younger counterparts, especially when they are exposed to short wavelength light, suggesting lens yellowing as the underlying cause [120,144,145,157] (Fig. 4A). One study found, however, no strong dose-response relationship between melatonin suppression and illuminance [146]. Some authors report a shift in the peak sensitivity of melatonin suppression [48], claiming the neural integration of photoreceptor signals also shifts across the lifespan. Specifically, the relative contributions of rods, cones, and ipRGCs to the initial and sustained phases of melatonin suppression differ significantly between young and older adults. This could suggest that aging alters the functional weighting of retinal inputs within the NIF system, providing a neural mechanism for reduced light sensitivity that persists even when accounting for reduced retinal illuminance [48,158] (Fig. 4B). It should be noted that difference in melatonin suppression between young and older adults may only be present for low and intermediate illuminances while suppression saturation under high illuminance, which has been less actively tested, may remain unchanged [159,160]. Although one study looking at low to moderate levels of illuminance did not find differences in melatonin suppression between teenagers and adults [146], the limited number of studies suggests that more research is needed to draw definitive conclusions.

One way light can affect cognition and sleep-wake regulation is through melatonin suppression. In children and teenagers, heightened melatonin suppression from evening light exposure (e.g., from screens) directly delays sleep onset, and this can curtail sleep and lead to daytime cognitive deficits in attention and executive function. Conversely, in older adults, the reduced suppression—caused by both lens yellowing and neural integration shifts—weakens the “circadian signal”. This reduction in the biological contrast between day and night can lead to fragmented sleep and diminished alertness during cognitive tasks, suggesting that older populations may require higher light intensities to achieve the same cognitive “boost” as younger cohorts.

6.3. Circadian entrainment

The ability of light to shift the clock is critical to adapt to different rest-activity schedule (shift work, jetlag) and depends on the timing of the exposure as captured in phase response curves (PRC). In essence, morning light exposure advances the circadian clock, while evening and late-night exposures delay it [161]. Although circadian rhythmicity is present in many aspects of brain function, the circadian secretion of melatonin, is almost the only parameter considered when it comes to PRC; and this is also true when it comes to PRC and aging [162]. Appropriate circadian entrainment is critical to brain functions, including those sustaining cognition and performance, as it will dictate sleep timing and sleep quality and will also set our entire physiology in phase with the light-dark cycle (to which our social constraints are rooted to).

There is no published PRC in infants or children. On average parents set their children's bedtimes about 48 min after melatonin onset [163]. There is, however, a great variability which can lead to later bedtime relative to melatonin onset and complicate studies on circadian entrainment and light-induced phase shift in children. A recent study reported that children's circadian clock (i.e. melatonin secretion) may be shifted by even low levels of evening light [134]. This may contribute to some of the sleep problems found in children, which seem to peak around preschool. To address these challenges, future longitudinal studies could help account for individual variability.

Teenagers tend to become later chronotype, which may be prone to a phase delay by evening light. A shallower build-up of sleep pressure may push them to stay awake later when light is available, curtailing their already insufficient sleep [140]. This may again constitute an issue as teens are high consumers of screen devices, including in the evening. A PRC compiled in teenagers found, however, that circadian rhythms do

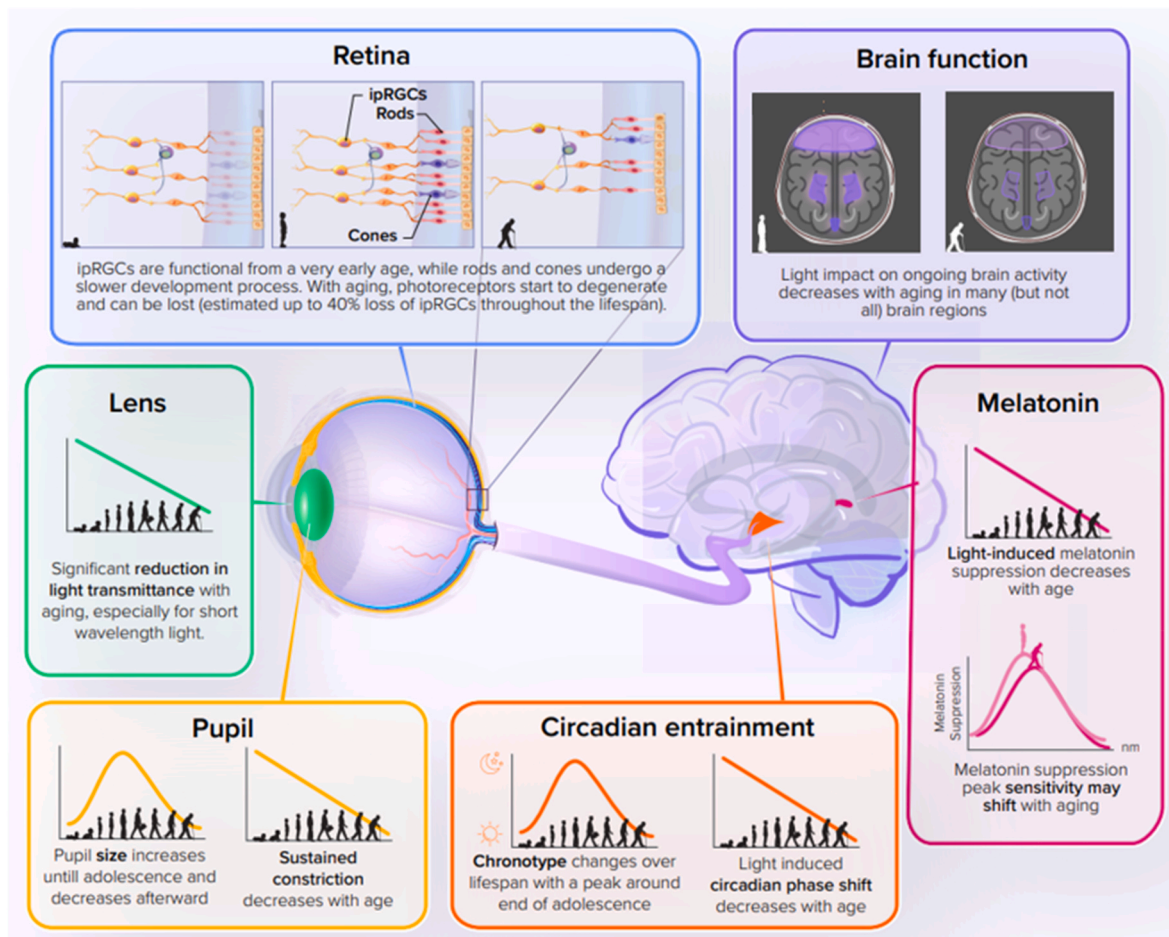


Fig. 5. Conceptual illustration of lifetime changes in the biological impact of light non-image-forming brain function. This figure provides a synthesis of empirical findings regarding age-related shifts in NIF sensitivity. Panels reflect: **Lens:** Illustrating the reduction in short-wavelength (blue) light transmission due to crystalline lens yellowing [37]. **Retina:** Representing the age-related decline in retinal photoreceptor density, including the 30–40% loss of ipRGCs and reduced dendritic complexity in late senescence [36]. **Brain Function:** Summarizing the reduced light-induced activation in subcortical relays like the pulvinar and cortical regions like the prefrontal cortex, which underpins observed declines in acute alertness and executive processing speed in older adults [121,123]. **Melatonin:** Depicting the overall reduction in absolute suppression amplitude across the lifespan when exposed to shorter wavelength light - found by several but not all studies in older individuals [140,135,144,146] - and the spectral shift in peak sensitivity reported by the only two studies that completed a full action spectrum of the response in five to eight older individuals (~484 nm to 500 nm) [48,158]. **Circadian Entrainment:** Summarizing the developmental stabilization of rhythms and the maximal evening shift in chronotype observed on average in late adolescence, followed by a shift toward phase advancement (morningness) in older age [140,148,168]. **Pupil:** Illustrating the increase in pupil size until adolescence, alongside the decline in baseline pupil size (senile myosis) and sustained constriction [127,128,143,153]. *Note: Curves represent qualitative tendencies based on the reviewed literature; refer to main text and Table 1 for quantitative details and for full reference list. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)*

not respond differently to light during adolescence as compared to young adults [141]. It seems, however, that the PRC may be symmetrical in teenagers – while in adults the phase advance portion of the PRC is smaller than the phase delay portion.

Older adults tend to become earlier chronotype as they age and, concomitantly, the ability of their circadian clock to accommodate light/dark schedule changes may be impaired [147,148]. Several investigations indicate that the shift in the rhythmicity of melatonin secretion might be reduced in aging, both in the phase delay and phase advance portion of the PRC [119,149]. Part of the changes in the impact of light on circadian rhythmicity may come from a change in the position of the sleep episode over the circadian cycle (phase angle between sleep and circadian phase). Older individuals may have their sleep episodes earlier with respect to their melatonin secretion profiles, masking therefore part of the phase delay portion of their PRC and reducing thereby the ability of evening light to phase-delay the circadian cycle [149]. The ability of light to delay the circadian phase was also found to be reduced in older subjects exposed to low-moderate illuminance (50–1000 lux) and they needed higher non-saturating illuminance to

experience the same phase shift as the younger group [146].

7. Conclusions and future directions

Recent developments have shifted indoor lighting from incandescent bulbs, which are poor in short-wavelength blue light, to LEDs that are often enriched in these wavelengths compared to natural light. [1]. This increases the likelihood of inappropriate light stimulating cognition or suppressing melatonin at the wrong time and/or contributing to poorer sleep and circadian entrainment. Given LEDs flexibility this also opens new possibilities in designing light interventions to promote well-being and health and particularly for cognition and performance. Several studies investigated how to rebalance individual light exposure profiles [164–166]. Dynamic white lighting systems allow adjusting colour temperature throughout the day and have proven beneficial [167]. Exposure to cool blue – enriched white light (5000 – 6500K) in the morning to mimic natural daylight and increase alertness, followed by a gradual shift to lower colour temperatures (2700K), which promotes melatonin release and lower alertness.

Practice Points:

1. Retinal photoreceptors (rods, cones, and ipRGCs) undergo changes across the lifespan. These changes may influence NIF signalling.
2. Light influences brain function through both direct and indirect projections of ipRGCs to various brain regions, allowing light to regulate a range of physiological and cognitive functions, including sleep, alertness, mood, and hormonal rhythms.
3. With aging, NIF effects of light, such as cognitive performance, circadian regulation, melatonin secretion, and pupil responses tend to decline. This reduction may result from age-related changes in both the eye (e.g., lens yellowing) and neural circuits mediating light responses.
4. Although larger pupil size and greater lens transparency in childhood and adolescence may increase light sensitivity, potentially enhancing NIF effects such as melatonin suppression, NIF influences on cognitive function in these age groups remain less well understood.

Research Agenda:

1. Comparative studies to assess how findings from diurnal rodent models translate to humans, acknowledging that while they offer the most viable route for species translation, key differences in ipRGC projections and brain targets still require careful validation.
2. Comparative investigations including infants, children, adolescents, adults, and older adults using harmonized protocols to map developmental and aging trajectories of NIF effects.
3. Longitudinal studies to track individual variability in light sensitivity and NIF brain responses from infancy to old age.
4. Quantification of the reduction in light-induced cognitive and physiological responses from infancy to older age to inform intensity and spectral adjustments for personalized effective interventions.
5. Functional imaging and behavioral studies to map how NIF light affects brain regions related to cognition, mood, and circadian timing across all age groups, with a focus on underrepresented pre-adult populations.
6. Quantitative *in vivo* studies to characterize age-related ocular changes and their impact on ipRGC-mediated photosensitivity across the human lifespan.
7. Large-scale field studies using connected wearable devices to assess real-world individual variability in light exposure as well as effectiveness of light interventions trials across different settings (e.g., schools, hospitals, workplaces, care facilities).
8. Expansion of current lighting guidelines into personalized, context-specific recommendations informed by large, ecologically valid datasets.
9. Evaluation of light sensitivity markers (e.g., pupil size and constriction dynamics, PIPR, brain responses) as potential indicators of neurodegenerative disease progression.

There is, however, a large inter-individual variability in the sensitivity to light and its impact on biological NIF functions. Here we stress that age, from birth to late life, is a major source of variability. Fig. 5 provides a conceptual summary of the changes we reviewed. While the figure is not meant to be precise and quantitative, it underscores the complexity of light's impact on the brain across the lifespan and, most often, the insufficient amount of data to draw firm conclusions, particularly at younger ages. While teenagers and children are receiving increasing attention, studies in newborns and toddlers remain scarce and even nonexistent for some aspects of the biological impact of light on brain function. Likewise, data in middle-aged individuals aged ~40y is rare and one can only infer based on younger or older individuals. Similarly, longitudinal studies monitoring several physiological aspects would allow better causal insights into the main factors underlying lifetime changes and, more generally, inter-individual differences in the NIF impact of light.

An increasing number of wearable devices collect physiological data with movement, ambient light, body temperature, heart rate within reach of most of them (for an open access light wearable device design see e.g. Ref. [169]). These devices should be included in all light studies and could quickly increase our understanding of the lifetime changes in light impacts. These data should be collected prior to controlled in-lab experiment which should be standardized in terms of the reporting of the light characteristics and experimental condition (as recommended in Ref. [170]), comply to the FAIR principles, ensuring data is Findable, Accessible, Interoperable, and Reusable, and OPEN principles, promoting transparency through open-access designs and data sharing [171, 172]. Building on the promises of AI and machine learning these data could be used to develop dynamic, age-tuned lighting control systems

capable of real-time optimization based on the specific biological needs of different age groups. These *in silico* developments can only be achieved if scientists collect enough data to feed algorithms. In the meantime, light intervention for cognitive brain function could be designed based on data available at other levels of physiology (cf. Table 1).

Field studies already bring promises for the effectiveness of light interventions – in schools, hospitals, at work, patient institutions [164–166,173]. These studies often suffer from limited sample size and statistical power. Larger samples are now within easier reach given the availability of connected wearable devices. These studies are indispensable to extend the current guidelines [5] to more personalized recommendations that policymakers, architects, and designers need to further support real-world translation. In addition, response to light may be used as a marker for a disease trajectory (e.g. pupil size, PIPR and pupil constriction in Alzheimer's and Parkinson's diseases [174,175]). Likewise, light administration can also be considered a simple means to disturb/affect the brain. It can therefore provide insights about novel ecological means to improve the quality of brain function at different ages.

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