

Association of Intraocular Cataract Lens Replacement With Circadian Rhythms, Cognitive Function, and Sleep in Older Adults

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IMPORTANCE Cataract is associated with a progressive decline in light transmission due to the clouding and yellowing of the natural crystalline lens. While the downstream effects of aging lenses include long-term disruption of circadian rhythms, cognitive function, and sleep regulation, it remains unknown whether there is an association of intraocular cataract lens (IOLs) replacement with circadian rhythms, cognition, and sleep.

OBJECTIVE To test whether IOL replacement (blue blocking [BB] or ultraviolet [UV] only blocking) in older patients with previous cataract is associated with the beneficial light effects on the circadian system, cognition, and sleep regulation.

DESIGN, SETTING, AND PARTICIPANTS Cross-sectional study at the Centre for Chronobiology, University of Basel in Switzerland from February 2012 to April 2014, analyzed between June 2012 and September 2018. Sixteen healthy older controls and 13 patients with previous cataract and IOL replacement participated without medication and no medical and sleep comorbidities.

EXPOSURES Three and a half hours of prior light control (dim-dark adaptation), followed by 2 hours of evening blue-enriched (6500 K) or non-blue-enriched light exposure (3000 K and 2500 K), 30 minutes in dim post-light exposure, 8 hours of sleep opportunity, and 2 hours of morning dim light following sleep.

MAIN OUTCOMES AND MEASURES Salivary melatonin, cognitive tests, and sleep structure and electroencephalographic activity to test the association of IOLs with markers of circadian rhythmicity, cognitive performance, and sleep regulation, respectively.

RESULTS The participants included 16 healthy older controls with a mean (standard error of the mean [SEM]) of 63.6 (5.6) years; 8 women and 13 patients with previous cataract (mean [SEM] age, 69.9 [5.2] years; 10 women); 5 patients had UV IOLs and 8 had BB IOLs. Patients with previous cataract and IOLs had an attenuated increase in melatonin levels during light exposure (mean [SEM] increase in the BB group: 23.3% [2.6%] and in the UV lens group: 19.1% [2.1%]) than controls (mean [SEM] increase, 48.8% [5.2%]) (difference between means, 27.7; 95% CI, 15.4%-41.7%; $P < .001$). Cognitive function, indexed by sustained attention performance, was improved in patients with UV lens (mean [SEM], 276.9 [11.1] milliseconds) compared with patients with BB lens (mean [SEM], 348.3 [17.8] milliseconds) (difference between means, 71.4; 95% CI, 29.5%-113.1%; $P = .002$) during light exposure and in the morning after sleep. Patients with UV lens had increased slow-wave sleep (mean [SEM] increase, 13% [3.4%]) compared with controls (mean [SEM] increase, 5.2% [0.8%]) (percentage of total sleep time; difference between means, 7.9; 95% CI, 2.4%-13.4%; $P = .02$) and frontal non-rapid eye movement slow-wave activity (0.75-4.5 Hz) during the first sleep cycle (mean [SEM], 79.9 [13.6] $\mu\text{V}^2/\text{Hz}$) compared with patients with BB lens (mean [SEM], 53.2 [10.7] $\mu\text{V}^2/\text{Hz}$) (difference between means, 26.7; 95% CI, 9.2-48.9; $P = .03$).

CONCLUSIONS AND RELEVANCE These in-laboratory empirical findings suggest that optimizing the spectral lens transmission in patients with previous cataract may minimize the adverse age-related effects on circadian rhythms, cognition, and sleep.

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Cataract is the most common source of vision loss in older adults and is the major worldwide cause of blindness in the general population.¹ Age-related cataract is associated with a progressive decline in light transmission due to the clouding and yellowing of the natural crystalline lens,² particularly in the shorter blue light wavelength.³ The downstream effects of aging lens include reduced photic input to the circadian clock, with subsequent long-term disruption of circadian rhythms, cognitive brain function, and sleep regulation.⁴⁻⁶ However, it remains unknown whether modifying the photic input to the circadian clock, by optimizing the spectral characteristics of crystalline lens after cataract surgery, improves circadian, sleep, and cognitive symptoms in older adults. Here, we investigated whether there is an association between intraocular cataract lens replacement (intraocular blue blocking [BB] or ultraviolet [UV] only blocking) with hallmarks of the circadian system, cognitive function, and sleep regulation.

Methods

Participants

The protocol, advertisements, screening questionnaires, and consent form were approved by the local ethical committee (EKBB/Ethikkommission beider Basel, Switzerland) and agreed with the Declaration of Helsinki.⁷ All participants provided written consent.

Our study sample included an extensive list of inclusion criteria: age, 55 to 80 years; body mass index (calculated as weight in kilograms divided by height in meters squared), 18 to 28 for women and 19 to 29 for men; bilateral cataract surgery for age-related cataract (4-8 weeks after intraocular lens [IOL] replacement of the second eye); new lens, 18 to 26 diopters; willing and able to give informed consent; stable medication for past 2 months and throughout the study duration (exception: medication in exclusion criteria); compliance with regular sleep-wake schedules (see Study Design section); no coexisting ocular pathologies, medical, or psychiatric conditions based on clinical history, biochemical blood screening tests and physical examination (eMethods in the Supplement). Owing to our stringently controlled inclusion/exclusion criteria list, approximately 1200 patients with previous cataract were assessed to recruit 60 patients. Of these 60 patients, 44 were excluded owing to (1) inability to follow the mandatory regular sleep-wake schedule throughout the 3 weeks of the study duration; (2) inadequate sleep quality, as indexed by a Pittsburgh sleep quality index score more than 5⁸; and (3) extreme morning or evening chronotype ratings.⁹ The control group was enrolled using the same inclusion/exclusion criteria (except for the cataract-related study requirements). Sixteen participants were enrolled of approximately 60 participants (similar dropout rate for the ambulatory segment as for the postcataract surgery patients).

Study Design

The study, including all experimental setups, ophthalmological examinations, participant enrollment, and study proto-

Key Points

Question What is the association of intraocular cataract lens replacement with circadian rhythms, cognitive function, and sleep?

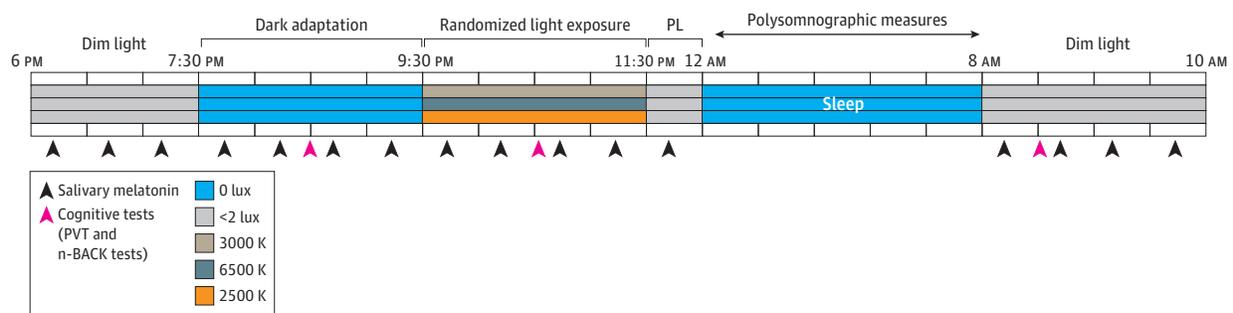
Findings In this cross-sectional study of 13 patients with previous cataract and 16 healthy controls, intraocular cataract lens replacement significantly increased melatonin sensitivity to light by approximately 45%, ultraviolet lens improved cognitive function by approximately 70%, and sleep function by approximately 50% compared with blue-blocking lens.

Meaning These in-laboratory empirical findings suggest that optimizing the spectral lens transmission in patients with cataract may be associated with better circadian, cognitive, and sleep function.

cols, was conducted from February 2012 to April 2014. Analysis began in June 2012 and ended in September 2018. The ambulatory segment of the study consisted of approximately 3 weeks of sleep-wake cycle regularity (from the week before the first in-laboratory protocol until the third in-laboratory protocol). Participants were instructed to keep a regular sleep-wake schedule (bed times and wake-up times within 30 minutes of self-selected target). Compliance was verified by wrist actigraphy (actiwatch L; Cambridge Neurotechnology). The 3 groups did not significantly differ in their ambulatory sleep and wake-up times, nor their sleep duration. No sleep assessment was performed prior to the bilateral post-cataract lens replacement surgery owing to potential sleep disorders and sleep complaints associated with cataract, which would have been deemed as exclusion criteria in our study protocol.

The in-laboratory protocol consisted of a within-participant cross-sectional observational design with 3 in-laboratory segments, separated by a 1-week intervening period (Figure 1). Based on each participant's ambulatory habitual sleep and wake-up times, each of the 3 study protocols started approximately 10 hours after usual wake-up time in the early evening (eg, 6 PM for a participant whose wake-up time was 8 AM) and ended the next day, 2 hours after usual wake-up time (eg, 10 AM). On arrival, participants remained in an individual laboratory room during each laboratory protocol to ensure stringent environmental condition control (ie, no windows to avoid external environmental light). Participants underwent 1.5 hours of dim light (<8 lux), followed by 2 hours of dark adaptation (0 lux). The 3.5 hours of controlled prior light history exposure allowed us to adequately assess the 2 hours of evening light exposure thereafter, as non-image-forming effects of light crucially rely on its specific properties, including photic history.¹⁰ Subsequently, light exposure was initiated for the next 2 hours. During this 2-hour episode, participants received light from either compact fluorescent light source with 6500 K or 2500 K or incandescent light source at 3000 K (eMethods and eFigure 1 in the Supplement). Light exposure was timed to occur during the evening given its well-established effects on all our primary and secondary outcome measures during that time of day.¹¹⁻¹³ Afterwards, participants remained awake for a 30-minute episode under

Figure 1. Study Design



Within-participant cross-sectional observational study design. The study protocol comprised 3 in-laboratory light segments, separated by a 1-week intervening period (eg, 6 PM for a participant whose wake-up time was

habitually 8 AM; for detailed explanation, see the Methods section). PL indicates post-light exposure (dim light, <8 lux); PVT, psychomotor vigilance task.

dim light conditions (<8 lux) before an 8-hour sleep opportunity timed to occur at each participant's habitual sleep time (based on their ambulatory sleep-wake timings). The time in bed lasted 8 hours, and participants remained in complete darkness and on the bed throughout. On habitual wake-up time on the subsequent day, each participant remained in their individual room for 2 hours under dim light (<8 lux) to perform 4 assessments of their endogenous melatonin levels and 1 cognitive test battery. Each study protocol was performed 1 week apart, and the entire study protocol was identical, except for the 2-hour evening light setting that was either 6500 K, 3000 K, or 2500 K per study protocol. The treatment order (6500 K vs 2500 K vs 3000 K) was randomized before the first study protocol for each participant, and the treatment order was counterbalanced to avoid possible order effects of the light treatment with outcomes.

Primary and Secondary Outcome Measures

Our primary outcome measures were endogenous melatonin levels, a well-established marker of the circadian system¹⁴ and sleep structure (slow-wave sleep), and non-rapid eye movement (NREM) sleep slow-wave electroencephalographic (EEG) activity, which are hallmarks of sleep homeostatic regulation.¹⁵ Our secondary outcome measure was cognitive performance, as indexed by sustained attention and working memory, which are cognitive domains exquisitely sensitive to the effects of sleep loss and circadian phase.^{11,16,17} Salivary melatonin collections were scheduled during wakefulness every 30 minutes throughout each study protocol. Sleep EEG activity was recorded throughout the scheduled sleep opportunity with the Vitaport Ambulatory system (Vitaport-3 digital recorder TEMEC Instruments BV). Sleep stages were visually scored per 20-second epochs (Vitaport Paperless Sleep Scoring Software).¹⁸ Spectral analysis was conducted using fast Fourier transformation (10% cosine 4-second window), which yielded a 0.25-Hz bin resolution. Electroencephalographic power spectra were calculated during NREM sleep and rapid eye movement (REM) sleep in the frequency range 0 Hz to 32 Hz. Here, we assessed frontal NREM slow-wave activity (0.75-4.5 Hz), a classic hallmark of sleep homeostatic process¹⁵ and the deri-

vation most sensitive to light effects¹² (eMethods in the Supplement). The psychomotor vigilance task and the 0-back task, both of which related to attentional resources, and the 2-back, a working memory task, were administered during dark adaptation, light exposure, and the morning after sleep (approximately 1 hour after the start of dark, light, and wake-up time).

Statistical Analyses

Statistical analyses were performed with SAS, version 9.4 (SAS Institute). Melatonin and cognitive data were assessed with mixed-model analyses of variance (PROC MIXED) using within-participant factors light condition (6500 K, 3000 K, and 2500 K) and time and between-participant factor group (healthy controls, patients with UV lens, and patients with BB lens), as well as the 2-way interaction of light condition vs group, time vs group, and their 3-way interaction. Visually scored sleep stages were expressed as percentages of total sleep time and analyzed with mixed-model analyses of variance (PROC MIXED) using within-participant factors light condition and group, and their interaction. Electroencephalographic power density in NREM sleep was analyzed for the frontal derivation (most sensitive to light¹² and sleep homeostatic process effects¹⁵). For the dynamics of frontal slow-wave activity across sleep episodes, NREM-REM sleep cycles were defined according to Feinberg et al.¹⁹ Thereafter, each sleep cycle was subdivided into 10 time intervals (percentiles) of equal length during NREM sleep and 4 time intervals during REM sleep. Data from the first NREM-REM sleep cycle were used for the mixed-model analysis of variance (PROC MIXED), using within-participant factors light condition and percentiles and between-participant factor group, as well as the 2-way interaction of light condition vs group, time vs group, and their 3-way interaction. As the interaction of light condition with group was not significant for the primary and secondary outcome measures, we report the results of main effect group and interaction of group and time. All *P* values were based on Kenward-Rogers corrected *df* (significance level, 2-sided *P* < .05). Least squares means statement was used for post hoc comparisons, and the Tukey-Kramer test was used for post hoc corrections.²⁰

Results

The study sample comprised 16 healthy older controls (age range, 55-80 years; mean [standard error of the mean (SEM)] age, 63.6 [5.6] years; 8 women) and 13 patients with previous cataract (age range, 55-80 years; mean [SEM] age, 69.9 [5.2] years; 10 women), whereby 5 patients had UV-only lens replacement (mean [SEM] age, 70.8 [4] years; 4 women) and 8 patients had BB lens replacement (mean [SEM] age, 69.8 [6.2] years; 7 women) (Table). We first assessed whether there was an association of intraocular cataract lens replacement with circadian rhythms, as indexed by the acute suppression of endogenous melatonin levels by light exposure (primary outcome measure). Compared with healthy older individuals, patients with previous cataract and lens replacement had an attenuated increase in melatonin levels during light exposure (mean [SEM] BB: 23.3% [2.6%] and UV lens: 19.1% [2.1%]) compared with controls (mean [SEM], 48.8% [5.2%]) (percentage of change in melatonin levels from baseline levels; interaction time vs group; difference between means, 27.7; 95% CI, 15.4%-41.7%; $P < .001$) (Figure 2A).

We then tested whether there was an association of intraocular cataract lens replacement with cognitive function (secondary outcome measure). Cognitive function, as indexed by tasks tapping onto attentional resources (psychomotor vigilance task slowest reaction times), significantly improved sustained attention performance across time (interaction of time

vs group; difference between means, 71.4; 95% CI, 29.5%-113.1%; $P = .002$). Accordingly, patients with UV lens had faster reaction times during light exposure (mean [SEM], 276.9 [11.1] milliseconds) and in the morning after sleep (mean [SEM], 279.3 [8.9] milliseconds) compared with patients with BB lens replacement (mean [SEM], 348.3 [17.8] milliseconds and 353 [18.8] milliseconds, respectively) (Figure 2B). Furthermore, we observed a significant improvement in performance to a 0-back task, which is a type of reaction-time task (main factor group; difference between means, 9.1; 95% CI, 0.2%-18%; $P = .03$) (eFigure 2A in the Supplement), such that patients with UV lens showed increased percentage of correct responses (mean [SEM], 98.1% [1.3%]), compared with those with BB lens (mean [SEM], 88.9% [3.3%]). Conversely, no significant effects were observed for the 2-back task, which is a more demanding working memory task (eFigure 2B in the Supplement).

Lastly, we investigated whether there was an association of intraocular cataract lens replacement with sleep function, as indexed by NREM slow-wave sleep and frontal NREM sleep slow-wave activity. We observed that in the sleep opportunity after evening light exposure, patients with UV lens had increased slow-wave sleep (mean [SEM], 13% [3.4%]), compared with controls (mean [SEM], 5.2% [0.8%]) (percentage of total sleep time; main effect, group; difference between means, 7.9; 95% CI, 2.4%-13.4%; $P = .02$ multiple comparison correction with Tukey-Kramer test) (Figure 3A and eTable in the Supplement). Furthermore, NREM slow-wave sleep associations were consistent among participants: 80%

Table. Participants Demographics, Sleep and Wake Times, and Ocular Characteristics

Characteristic	Healthy Older Controls (n = 16)	Patients With Previous Cataract and BB Lens (n = 8)	Patients With Previous Cataract and UV-Only Lens (n = 5)
Age, mean (SD), y ^a	63.6 (5.6)	69.8 (6.2)	70.8 (4)
Men, No. (%) ^b	8 (50)	4 (50)	1 (20)
Women, No. (%) ^b	8 (50)	4 (50)	4 (80)
Body mass index, mean (SD) ^c	23.4 (1.7)	24.8 (2.6)	24.3 (2.5)
White, No. (%)	16 (100)	8 (100)	5 (100)
Sleep times, mean (SEM, min)	11:19 PM (6)	11:04 PM (12)	10:57 PM (8)
Wake times, mean (SEM, min)	7:11 AM (10)	7:22 AM (12)	7:12 AM (7)
Sleep duration, h:min, (SEM, min)	6:55 (11)	6:58 (11)	7:05 (12)
Intraocular pressure, mean (SD) [range], mm Hg			
Right eye	15.1 (2.1) [11-19]	14.3 (2.1) [10-17]	15.5 (2.4) [13-20]
Left eye	15.5 (2.2) [11-19]	14.3 (2.5) [10-17]	15.5 (3.1) [13-20]
LOCIII grade			
Right eye	NO = 2	NO = 4	NO = 4
	NC = 2	NC = 4	NC = 4
	CC = 0	CC = 1	CC = 1
	PSC = 0	PSC = 1	PSC = 1
Left eye	NO = 2	NO = 4	NO = 4
	NC = 2	NC = 4	NC = 4
	CC = 0	CC = 1	CC = 1
	PSC = 0	PSC = 2	PSC = 2
BCVA, mean (SD), [range], logMAR			
Right eye	0.93 (0.1) [0.6-1.0]	0.86 (0.2) [0.63-1.0]	0.92 (0.2) [0.63-1.0]
Left eye	0.94 (0.2) [0.6-1.0]	0.94 (0.1) [0.8-1.0]	0.96 (0.1) [0.8-1.0]

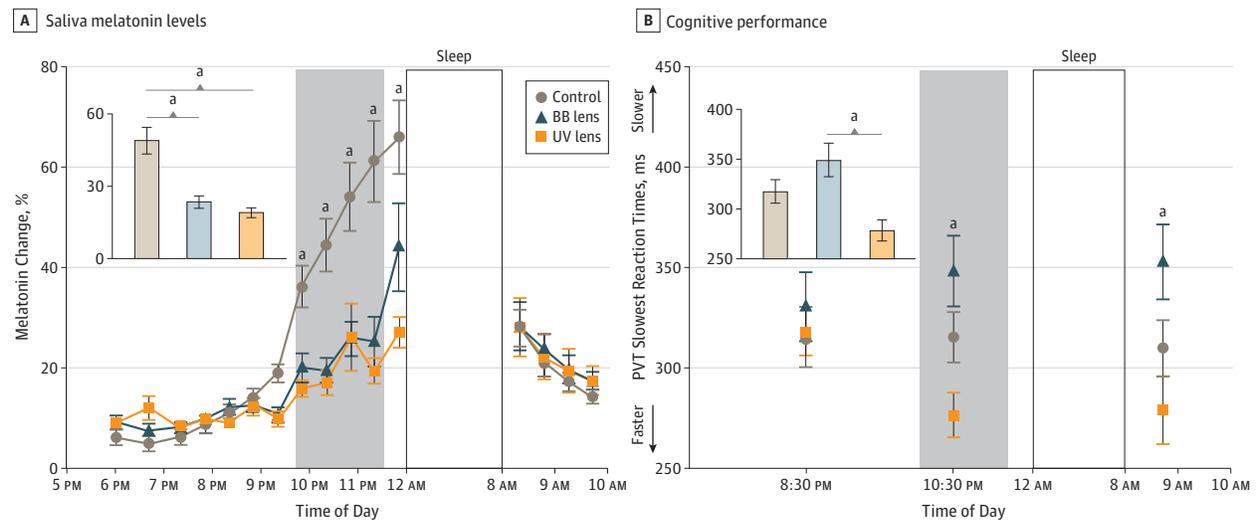
Abbreviations: BB, blue-blocking; BCVA, best-corrected visual acuity; CC, cortical cataract; LOCIII, Lens Opacities Classification System III; NC, nuclear color; NO, nuclear opalescence; PSC, posterior subcapsular cataract (mean values); SEM, standard error of the mean; UV, ultraviolet.

^a Analysis of variance: $P = .04$.

^b Analysis of variance: $P = .03$.

^c Calculated as weight in kilograms divided by height in meters squared.

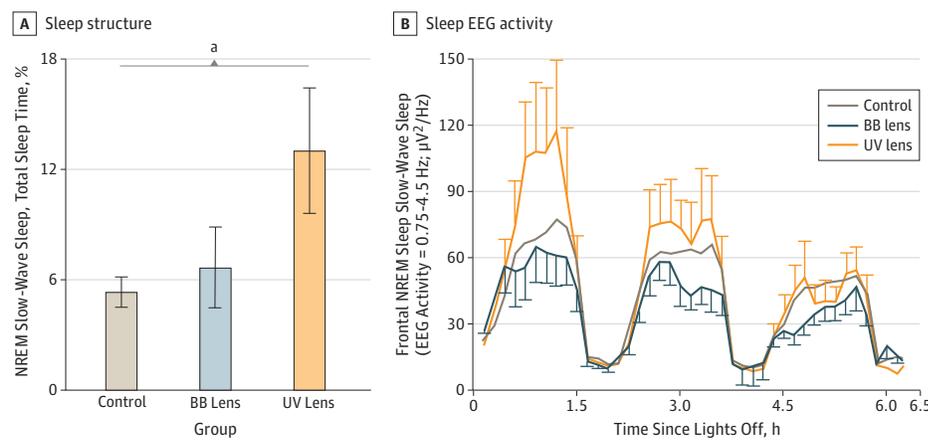
Figure 2. Melatonin Rhythms and Cognitive Performance



Association of intraocular cataract lens replacement with circadian photosensitivity by saliva melatonin levels (O indicates prelight levels) (A) and cognitive performance (psychomotor vigilance task performance) (B). Data are reported as mean (standard error of the mean). BB indicates blue blocking;

PVT, psychomotor vigilance task; UV, ultraviolet.
^a $P < .05$ (see Results section for more information).

Figure 3. Sleep Structure and Sleep Electroencephalographic (EEG) Activity



Association of intraocular cataract lens replacement with sleep structure (slow-wave sleep) (A) and sleep EEG activity (slow-wave activity) (B). B, EEG activity = 0.75 Hz to 4.5 Hz; $\mu V^2/Hz$. Data are reported as mean (standard error of the mean). BB indicates blue blocking; NREM, non-rapid eye movement; UV, ultraviolet.

^a $P < .05$ (see Results section for more information).

(4 of 5) of patients with UV lens, 12.5% (1 of 8) of patients with BB lens, and only 6.25% (1 of 16) controls had increased NREM slow-wave sleep (threshold set as >10% of increase in NREM slow-wave sleep; $\chi^2 = 11.4$, $P = .007$; eFigure 3 in the Supplement). Furthermore, the dynamics of frontal NREM sleep slow-wave activity (0.75-4.5 Hz), a functional index of homeostatic sleep pressure,¹⁵ was higher during the first NREM-REM sleep cycle in patients with UV lens (mean [SEM], 79.9 [13.6] $\mu V^2/Hz$) compared with patients with BB lens (mean [SEM], 53.2 [10.7] $\mu V^2/Hz$) (analyses on first NREM-REM sleep cycle; interaction, time vs group; difference between means, 26.7; 95% CI, 9.2-48.9; $P = .03$; contrasts of interest: percentiles 5-8) (Figure 3B).

Discussion

Our in-laboratory empirical findings suggest an association of intraocular cataract lens replacement with key aspects of circadian rhythms, cognitive performance, and sleep regulation. By using a cross-sectional observational study, we observed that replacing natural lenses with IOLs normalizes melatonin response to light, regardless of whether they were UV-only or BB lens, while UV lens improved sustained attention performance and sleep function compared with BB lens.

Our participants' demographics indicate that the healthy older controls were significantly younger (ie, approximately 5

years) than patients with BB and UV lens. Nonetheless, they had comparatively lower circadian photosensitivity and NREM sleep slow-wave sleep and frontal NREM slow-wave activity. Furthermore, the 50%:50% men:women distribution in healthy controls and patients with BB lens was not observed in patients with UV lens (25%:75%). Although we were not powered to test for sex-dependent effects on light sensitivity, previous data indicate that men may show higher light sensitivity than women for cognitive performance and hallmarks of sleep regulation (slow-wave sleep and slow-wave activity).²¹ Importantly, no ocular pathologies were observed across the groups (apart from the cataract in the clinical groups).

Circadian photoentrainment is predominantly initiated by stimulation of intrinsically photosensitive retinal ganglion cells containing the photopigment melanopsin by light, particularly in the blue range (450-490 nm).²² With aging, the natural lens of the eye acquires a yellow-brownish discoloration because of accumulation of chromophores that absorb preferentially the short wavelength region of visible spectrum. Consequently, decreased stimulation of melanopsin is expected with age, whereby not only the amount of light reaching the retina is dramatically reduced to about one-tenth that of younger adults,²³ but the spectrum of light transmission into the eye is also altered. This scenario is posited to worsen even further in patients with previous cataract and may impair their ability to entrain the circadian clock, with subsequent long-term disruption of the circadian system. Here, we show that optimizing the spectral lens transmission in patients after cataract lens replacement can restore circadian photosensitivity, as indexed by their increased acute melatonin suppression to evening light exposure.

We then showed an association between lens replacement in patients with previous cataract and cognitive performance, such that, during acute light exposure and in the morning subsequent to sleep, sustained attention performance is improved in patients with UV lens only. Healthy aging is accompanied by a decline in cognitive fitness, due to a combination of different factors, such as morphological age-related brain differences, and reduced non-image-forming responses to light.⁴ Cataract and cognitive impairment are common age-related ailments, and surgical intervention in patients with cataract may improve some aspects of cognitive function, including reaction time tasks.²⁴ While increasing ambient light levels for 1 week may improve cognitive impairment in older patients with dementia,²⁵ similar effects in patients with previous cataract remain largely unknown. Here, we observed that IOL replacement in patients with previous cataract may enhance the beneficial light effects on cognitive tasks associated with attentional resources. Recent functional magnetic resonance imaging data suggest a plasticity to light sensitivity in aging, such that after approximately 4 years of surgery, lens replacement did not significantly affect daytime light impact on cognitive brain function (associated with 0-back and 2-back task performance).²⁶ These results suggest that some aspects of cognitive brain function may adapt to the progressive decrease in daytime light exposure in aging. Importantly, sleep ailments are common in older patients with cataract, who subjectively report difficulties initiating and/or maintaining sleep, and impoverished subjective sleep quality, which can be alleviated after IOL replacement cataract.²⁷ While different lens re-

placements exist, there is a scarcity of knowledge on how these different treatment strategies translate to objective hallmarks of sleep function. Currently, most evidence builds on epidemiological data using subjective sleep questionnaires and/or ambulatory actigraphy measures,^{27,28} thus devoid of objective in-laboratory sleep measures. To our knowledge, no in-laboratory studies have been carried out to assess the association of cataract lens replacement with sleep physiology. Here, we show that slow-wave sleep and frontal NREM slow-wave activity, a functional index of homeostatic sleep pressure,¹⁵ was higher in patients with replacement UV lens, suggesting a beneficial effect on their sleep physiology. Age-related changes in sleep²⁹ include reduced total sleep time, slow-wave sleep, and frontal NREM slow-wave activity. Our data indicate that these age-related effects on homeostatic sleep regulation might be mitigated in patients with previous cataract and UV lens.

It is important to consider the potential visual and nonvisual benefits of different IOLs for patients with cataract. The development of BB IOLs was driven by concerns about blue light hazard^{30,31} and for correcting the cyanopsia reported with early IOLs.³² Furthermore, BB and UV lens may show similar contrast sensitivity, visual and glare acuity, and color perception under photopic conditions,^{33,34} even after 5 years of surgery.³⁵ However, evidence also suggests that, while BB and UV lens have similar postoperative visual function, color perception may be improved in patients with UV lens compared with BB lens after 1, 3, and 6 months of surgery.³⁶ Taken together, while our study shows that UV IOLs may benefit nonvisual function, the associations with visual function must also be considered.³⁷

Strengths and Limitations

The key strengths of our study include stringently controlled in-laboratory study protocols that allow us to reliably assess the association of IOL cataract lens replacement with well-established objective hallmarks of circadian photosensitivity, cognitive function, and sleep regulation. Furthermore, because we used stringent exclusion criteria to minimize medical conditions, which might add variability to our outcome measures, we could reliably test our study hypotheses. Thus, our empirical evidence provides a demonstration of a measurable change in nonvisual function following an increasingly routine clinical intervention.

Despite the stringency of our inclusion/exclusion criteria and study protocols, ours is a laboratory empirical study with a limited sample size. Our results suggest the value of larger and longer-term clinical and observational studies to better understand the circadian, cognitive and sleep-related outcomes that might differ by light transmission properties of IOLs. Therefore, caution should be made in extrapolating our findings to larger cataract populations.

Conclusions

Collectively, our stringently controlled laboratory data provide evidence for an association of intraocular cataract lens replacement with the beneficial effects of light on the circadian photosensitivity (ie, greater melatonin suppression), cogni-

tive performance (sustained attention), and sleep stages (ie, slow-wave sleep) and EEG hallmarks (ie, EEG slow-wave activity) of homeostatic sleep regulation. Our data suggest that

optimizing the spectral lens transmission in cataract patients may mitigate some of the adverse circadian, cognitive, and sleep effects associated with aging cataract lens.

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Concept and design: Chellappa, Bromundt, Frey, Schlote, Goldblum, Cajochen.

Acquisition, analysis, or interpretation of data: All authors.

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