

Supplemental Materials and Methods

All methods were performed in accordance with the relevant guidelines and regulations. Data collected and used in this study is available upon request.

Miniature, programmable, and portable ganzfeld design

Modified safety goggles were fitted with diffusers and LED illumination to provide the light stimuli (Figure S1). LEDs and LED driver circuitry were mounted to curved plastic-corrugated aluminum bands, which were, in turn, mounted to the goggles by metal standoffs (Figure S1). A spectrally flat transmissive diffuser (Lee filters, LEElux #400RW) replaced the original lens of the goggles. Three sets of four high-powered LEDs (Luxeon CZ line by Lumileds) were mounted in each goggle stimulator: L1CU-VLT1 with a peak at 427 nm, L1CU-BLU1 with a peak at 476 nm, L1CU-LME1 with a peak at 544 nm, and L1CU-RED1 with a peak at 637 nm. Each had a maximum continuous forward DC current rating of 350 mA, but driver circuitry was set to drive each LED at 150 mA to increase longevity and a 120-degree emission angle. Three pads for each of the four different LEDs were placed at regular intervals across the curved aluminum band, with the middle pad positioned at the center of the goggles. This arrangement provided diffuse homogenous full-field illumination (Figure S1), covering approximately 130 degrees of visual angle.

The goggles' illumination was controlled by custom-made electronic constant current Pulse Width Modulation (PWM) control driver circuitry. This device was configured to allow LED settings to be stored on an EEPROM. These devices were calibrated and programmed in the laboratory and sent home with individual subjects. The absolute radiance in Watts of the different light conditions was taken at the pupil plane using a UDT Model 247 flat response radiometric sensor (Gamma Scientific). The spectral characteristics of the light reaching the eyes were measured using a CS-2000A spectroradiometer (Konica Minolta). The stimulus characteristics of the three lighting conditions in CIE α -opic EDI (lux) (Table S1) were calculated using the CIE S 026 α -opic toolbox (CIE, 2020) (Schlangen and Price, 2021). We equated each of the conditions for the quantal catch by melanopsin using a photopigment template curve corrected for preretinal absorption by the lens using the van Norren and van da Kraats (2007) large angle age-dependent lens estimate. These assumptions differ slightly from those used inside the CIE S 026 α -opic toolbox. However, we feel they are most appropriate for our subjects' ages and experimental conditions. The differences in assumptions have only a minor effect, and melanopsin effectiveness is also similar across the three conditions with the α -opic toolbox assumptions (Table S1).

Table S1 α -opic EDI (lux)

Light Condition	L-cone	M-cone	S-cone	Rhodopsin	Melanopsin
Equal Energy White	165.43	140.29	166.76	177.72	203.48
Blue	174.35	76.87	42.16	163.46	208.65
S- Modulated White	439.84	254.30	339.37	201.23	185.77

The two spectrums that were alternated temporally to drive high S-cone modulation were calculated theoretically using retinal sensitivities for S-, melanopsin, M-, and L-retinal sensitivities given by a photopigment template (Carroll et al., 2000) with peaks set at 419 nm, 480 nm, 530 nm, and 559 nm, respectively, corrected for absorption by the lens (Van De Kraats and Van Norren, 2007). For the S-cone modulating light, the ratio of S-cone activation between the temporally alternated spectrums was 100:1, while L- and M-cone activations were held constant between the two temporal phases. The alternating spectrums were programmed onto the goggles and modulated at 19 Hz, presented as a square wave with a 50% duty cycle. The radiance of these lights measured at the back of the goggles was 150.5 $\mu\text{W}/\text{cm}^2$. The alternation of the two spectrums produced approximately 500 lux at the subject's pupil plane as measured with a lux meter (Digital Light Meter, LX 1330B). The two other conditions, the static white light spectrum (Figure 1A), which produces a radiance measured at the back of the goggles of 72.9 $\mu\text{W}/\text{cm}^2$, and the static blue spectrum from the 476 nm LED (Figure 1B), which produce a radiance measured at the back of the goggles of 31.6 $\mu\text{W}/\text{cm}^2$, were adjusted in intensity to produce the same time-averaged melanopsin activation as the S-cone modulated light.

Human subjects

The Institutional Review Board at the University of Washington approved the human subject's research. Research involving human subjects was performed in accordance with local and federal regulations. Human subjects research adhered to the principles embodied in the Declaration of Helsinki. Informed consent was obtained from all participants. The subjects were adult volunteers from the University of Washington community in Seattle.

Nine healthy adult (3 male and six female) subjects (mean age = 30; range 23-43) continued with their daily academic lives during the fall and winter months (December - February) in Seattle, WA, over the course of the experiments. During this season, there is less than 9 hours of sunlight daily. The sky is typically overcast, leading to an average exposure to light of 430-500-lux illuminance and a significantly delayed sleep phase (Dunster et al., 2022). The experiments aimed to determine the effects on circadian phase of three different lighting paradigms, which were viewed for two hours centered 10.5 hours after their individual DLMO. Lights administered at this time should produce the maximum circadian phase advance (Figure 1F). Circadian phase was determined from the rise in evening melatonin levels assayed from saliva samples. To measure phase accurately, it was important to identify subjects with a robust, reliable evening rise in salivary melatonin. In addition, our participants must be stably entrained to the 24-hour environmental cycle even though we expect most University of Washington community members to suffer from some phase delay. Recruits collected baseline evening salivary melatonin samples every hour between 6 pm and 2 am. While saliva samples were collected, subjects were instructed to keep illumination levels measured by an illuminometer below 10 lux. When necessary, short periods of higher illumination were allowed but were always kept below 30 lux. Subjects also confirmed that they were keeping a regular sleep-wake schedule in the days surrounding the experiment. After the first baseline salivary melatonin measurement, the only participants who continued the experiment were those who showed a robust rise in salivary melatonin between 6 pm and 2 am.

Of the nine subjects who met the inclusion criteria, all were involved in (or familiar with) studies related to circadian rhythms. As such, they were all very motivated to adhere to the grueling demands of the protocol. These included adhering to the strict dim evening lighting regimen, collecting saliva on a strict

schedule, proper handling of the saliva samples, and viewing the lights at the times and for the durations specified. We believe that having motivated, compliant participants was key to obtaining precise and reliable results. However, this means that the highly compliant participants were not blind to the conditions or hypotheses. Salivary melatonin measurements are objective, so the fact that participants were not naïve could not bias the results. In addition, we took extensive measures to ensure the subjects' knowledge could not bias the results. The subjects received a box of tubes pre-labeled with the times they were to provide samples, two tubes for each hour. The subjects used timers to keep them on the precise schedule of taking samples each hour and storing them on dry ice. All the samples from a given evening were collected and processed according to the Salimetrics protocol, and an automated colorimeter system read the resulting 96 well plate. An automated procedure was used to fit an integrated Gaussian (error function) by minimizing the sum of least squares. The goggles were pre-programmed for each lighting condition such that subjects could not control the spectral or temporal properties of the light or its intensity. The subjects followed a strict protocol dictating when and for how long to view each light condition. Phase advances in circadian phase are notoriously difficult to produce, so it is unlikely that subjects' knowledge of a particular light condition could be responsible for the large phase advances observed in these studies.

Paired t-tests were used to compare baseline and experimental results within a condition. Three of the subjects in the steady white light condition participated in the other two conditions, but the steady white light condition also used three subjects who did not participate in the other experiments. Thus, a statistical comparison between the steady white light, the blue light, and the 19-Hz S-cone modulated condition was unpaired. The comparison was made with a one-way analysis of variance, which was highly significant ($F = 9.8$, $p = 0.0019$) across the three conditions. This was followed by a multiple comparison post-test with a Bonferroni correction to compare the effect sizes of the different conditions.

Experimental protocol for viewing light stimuli

The experiment was conducted during the COVID-19 pandemic. Safety protocols prevented participants from coming to the laboratory for experimental procedures; thus, all experiment procedures were performed in participants' homes. The subjects collected saliva samples at one-hour intervals and placed on dry ice immediately after collection. Two saliva samples were collected at each time point, which were analyzed separately and averaged to minimize noise for each time point. Since the experiments were done in the winter in Seattle, saliva collection was done well after sunset, so there was no possibility of exposure to sunlight during saliva collection, and subjects stayed in their homes with the illumination generally kept below 10 lux and always below 30 lux. Circadian timing was measured by the dim light salivary melatonin onset (DLMO, Salimetrics melatonin ELISA). DLMO20% was calculated as the time point at which melatonin levels reached 20% of the fitted peak-to-trough amplitude of each person's data. The data was fitted to an integrated Gaussian (error function) by minimizing the sum of least squares. Maximum phase advances were assumed to occur 10.5 hours after DLMO20%. Administrations of a 2-hour light pulse of the therapeutic lights were centered around 10.5 hours after DLMO20%. Thus, a person whose DLMO20% was 8:00 pm started the next morning's light treatment at 6:30 am. Lights were administered in the subjects' homes the morning after the baseline internal circadian timing was measured. Baseline DLMO was measured separately for each of the three conditions. To determine the phase advance caused by each light, circadian timing was remeasured the

evening of the day the light was administered. Phase advances were calculated as the difference between DLMO20% after light administration and baseline DLMO20%.

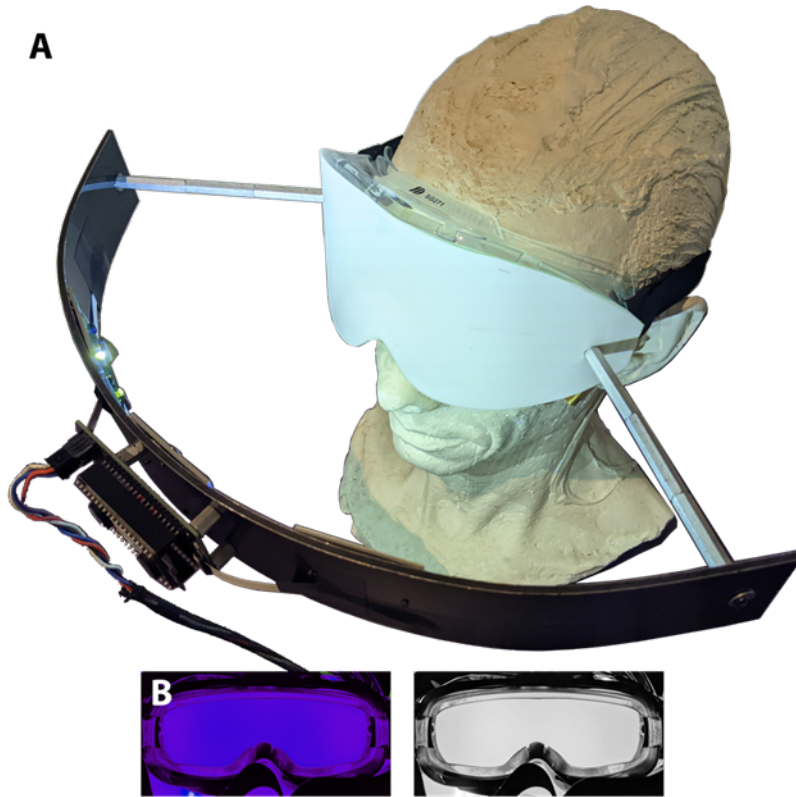


Figure S1. **A.** Battery-powered portable "ganzfeld" light stimulator with self-contained uniform four-color LED illumination programmable in intensity, temporal, and spectral characteristics. **B.** The front diffuser of the illumination system goggles was uniformly illuminated by the 476 nm LEDs (left) and static white (right).

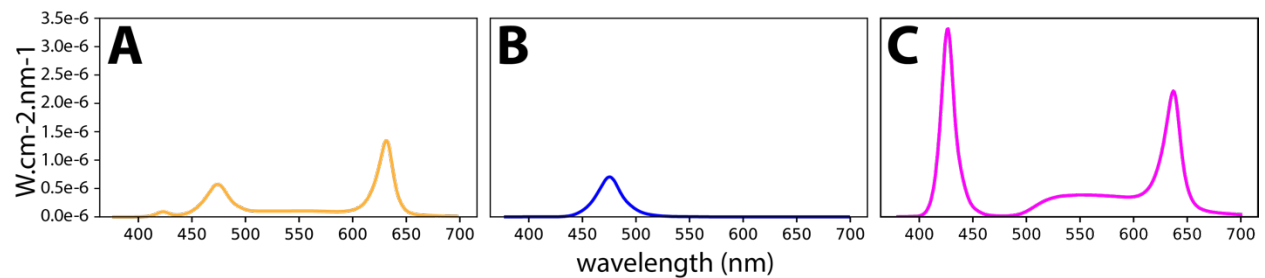


Figure S2. Spectral power distributions for the three light paradigms viewed by subjects in this experiment. **A.** The equal energy static white light spectrum, **B.** the blue LED spectrum, and **C.** the time-average S-cone modulating spectrum.