Received: 30 May 2019 | Revised: 25 July 2019 | Accepted: 25 July 2019

DOI: 10.1111/jpi.12602

COMMENTARY

Journal of Pineal Research
Molecular, Biological, Physiological and Clinical Aspects of Melatonin

WILEY

Binocular facilitation in light-mediated melatonin suppression?

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Funding information
Wellcome Trust, Grant/Award Number: 204686/Z/16/Z

Abstract

In humans, the production of melatonin is suppressed by light exposure. This effect is mediated by a retinal pathway involving the melanopsin-containing intrinsincally photosensitive retinal ganglion cells (ipRGCs), which exhibit maximum sensitivity to short-wavelength light. Here, based on extant and published data, we examine how signals from the two eyes are integrated in driving the suppression of melatonin by light. We find that melatonin suppression by light exposure to two eyes corresponds to a sensitivity shift by about 1.2 log units (factor ~17.4).

KEYWORDS

binocular integration, binocular summation, light, melanospin, melatonin suppression, non-image forming function

Astronomers and pilots have known for a long time that closing one eye can preserve vision in that eye while going from dark to light and back. Recently, it was reported that viewing a smartphone monocularly in an otherwise dark room can lead to transient, but strong reductions in retinal sensitivity in that eye.[1] But seeing and perceiving the visual environment is not the only function by the retina. Here, we address the question whether light exposure to one eye only (monocular) has tangible effects on the suppression of melatonin by light, relative to both eyes open (binocular).

The visual fields of our two forward-facing eyes overlap by some 120°. Due to the eyes being at different locations in space, each eye has a different vantage point on objects in the world, thereby allowing depth from binocular stereopsis.[2] But in addition to these "classical" visual functions, the retina in our eyes mediates a parallel function: the synchronization of physiological rhythms to the external illumination conditions and the acute suppression of the hormone melatonin by light exposure. What is the role of binocular vision in these physiological responses to light?

To answer this question, we first obtained a canonical intensity-response function relating light to the amount of melatonin suppression as a starting point. Recently, Prayag et al[3] reanalysed extant data on the spectral sensitivity of melatonin suppression and fitting a four-parameter logistic function which relates the melanopic irradiance of a light to the amount of melatonin suppression (Figure 1).

With this canonical dose-response curve in mind, we interrogated two previous studies that examined the effect of binocular versus monocular stimulation on melatonin suppression: Brainard et al[4] examined melatonin suppression to 630 lux light between 02:00 and 03:30 at night under binocular and monocular viewing conditions. With a similar protocol and in the same laboratory, Wang et al[5] examined melatonin suppression in response to 100 and 200 lux light under binocular and monocular viewing conditions during the same time window. We are not aware of other studies examining melatonin suppression evoked by appropriately matched pairs of binocular vs monocular stimuli.

Both studies reported more melatonin suppression under binocular viewing compared to monocular viewing conditions. After converting the reported illuminance to melanopic irradiance, we found that the monocular effect can be accounted for by simply displacing the sensitivity curve for binocular suppression by a little more than one order of magnitude (Figure 2A). We realized this sensitivity shift by

keeping all parameters fixed in the four-parameter logistic function except for the saturation constant. Thus, we reduced the fitting problem to one degree of freedom (the horizontal shift) and applied the least-squares best fit. We found that the saturation constants for binocular and monocular melatonin suppression are 70.21 and 1224.8 mW/m^2, respectively. This corresponds to a factor of ~17.4 or 1.2 log units.

According to this surprising result, viewing with both eyes requires only requires approximately 1/10 of light when compared to monocular viewing. Consistent with these data, Hull et al[6] found attenuated light-induced melatonin suppression in a patient with one eye enucleated, providing converging evidence that there is binocular facilitation in non-image-forming visual function.

We entertained a competing hypothesis explaining the difference in monocular and binocular melatonin suppression. We probed whether the binocular data could be explained by simply doubling the monocular data (Figure 2B), and whether the monocular data could be explained by simply halving the binocular data (Figure 2C). While the data points at the highest intensity could be explained using this strategy, it did not adequately predict the data for the lower two intensities.

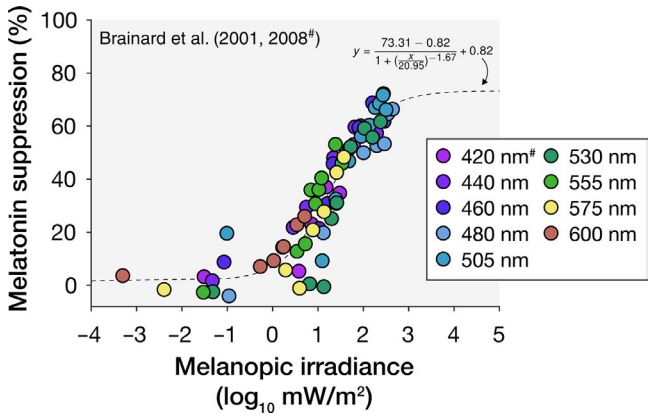

FIGURE 1 Melatonin suppression to monochromatic lights[25,26]; fitted intensity-response curve from Prayag et al[3]

Melatonin suppression is not the only retinal function that displays binocular facilitation. In the control of the pupil size, monocular viewing produces a reduced attenuation by a factor 10 compared to binocular viewing.[7-10] In a study on the dazzle reflex, that is the aversive response to bright light, the authors note that "the light intensity to produce extreme dazzle under monocular conditions has to be an order of magnitude greater than under binocular conditions",[11] corroborating earlier reports of binocular facilitation in discomfort to light.[12,13] In vision, binocular summation has been investigated thoroughly for detecting faint lights.[14] For stimuli that are easily detectable, an otherwise unarticulated field when viewed with both eyes appears twice as bright as a field seen by one eye.[15] It seems likely that different visual tasks integrate information from the two eyes differently.

In primates, including humans,[16,17] the suprachiasmatic nucleus (SCN) receives bilateral input, with the predominant input from the ipsilateral eye.[18] Functional measurements of the photic inputs into human SCN, or suprachiasmatic area (SCA), have recently been reported using fMRI,[19] though a careful characterization of how signals are integrated into these structures is still outstanding. In mouse SCN, it was recently demonstrated that cells that integrate binocular information respond to fast temporal features such as those elicited by drastic changes in illumination.[20] Most studies examining human circadian responses have used long-duration continuous light exposures. It is conceivable that temporally

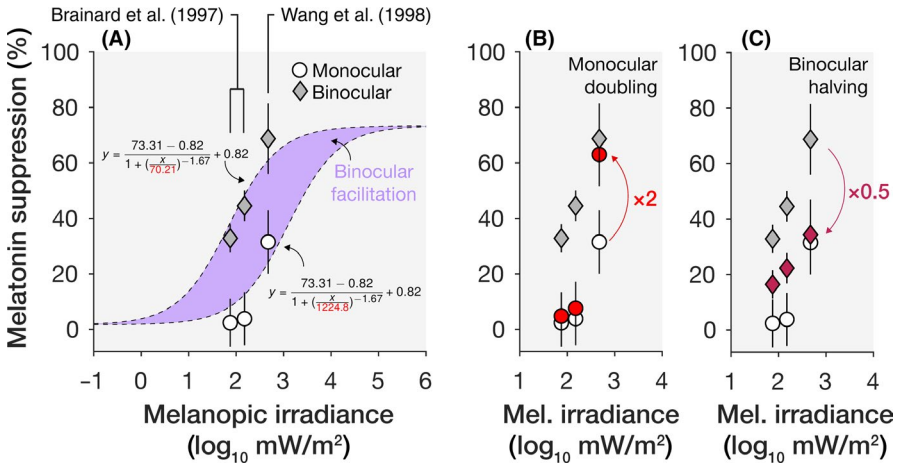

FIGURE 2 Binocular advantage in melatonin suppression. A, Data from Brainard et al[4] and Wang et al[5] were extracted from published plots using WebPlotDigitizer (https://automeris.io/WebPlotDigitizer/). Photopic illuminance was converted to approximate melanopic irradiance using a 0.75 conversion factor from photopic illuminance (lux) to melanopic irradiance (mW/m^2). The intensity-response curve for the binocular and monocular conditions was derived by simply allowing for a horizontal displacement (highlighted in red in equations). B, Comparison between binocular data and doubled monocular data (in red). C, Comparison between monocular data and halved binocular data (in dark red)

patterned stimuli,[21,22] in addition to also involving cones and rods, may also bias the system towards binocular responses.

Here, we have examined the evidence that monocular viewing might reduce the melatonin-suppressing effects of light at night. It is important to note that while an effect under monocular viewing conditions was not detectable at 100-200 lx,[5] a higher light intensity led to an appreciable effect.[4] This has direct implications for experimental design: a null effect measured at one intensity might simply be due to being in the "wrong" region of the dose-response curve. Of note, it was reported that light exposure in the lower visual field (superior retina; at 200 lux) has no appreciable effects on melatonin suppression.[23] This result has been translated in the popular science literature (eg Zielinska-Dabkowska[24]) as the superior retina being a "zone of no biological influence". Presumably, however, it is possible to find melatonin suppression in response to a sufficiently bright light when only the superior retina is illuminated.

Here, using digital data extraction techniques, we aggregated existing data from the only two studies on binocular integration in melatonin suppression in humans. More research is necessary to fully understand how signals from the two eyes are integrated into non-image-forming function. Our synthesis has the tangible conclusion that if light exposure at night is necessary and binocular stereopsis is unnecessary: keep one eye closed.

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How to cite this article: Spitschan M, Cajochen C. Binocular facilitation in light-mediated melatonin suppression? *J Pineal Res*. 2019;67:e12602. https://doi.org/10.1111/jpi.12602