

Short-Wavelength Sensitivity for Activating Effects of Light: An Ascent to the Arcane?

Comment on: Lockley SW; Evans EE; Scheer FAJL et al. Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. *SLEEP* 2006; 29(2):161-168.

Scott S. Campbell, PhD

Director, Laboratory of Human Chronobiology, Department of Psychiatry, Weill Medical College of Cornell University, White Plains, NY

NATURAL AND ARTIFICIAL LIGHT EXPOSURE CAN INFLUENCE HUMAN PHYSIOLOGY AND BEHAVIOR IN A MULTITUDE OF WAYS. IN THE AREAS OF HUMAN sleep and biological rhythms research, light's entraining and circadian rhythm phase-shifting capacity has been a primary research focus since discovery of the phenomenon over two decades ago.¹ Literally thousands of studies and millions of research dollars have been dedicated to characterizing light's effects on the circadian timing system, detailing the mechanisms underlying these effects and testing and implementing interventions using light exposure for sleep and other disorders (e.g. DSPS, SAD) thought to have circadian etiologies.

In contrast to this very extensive and remarkably intensive examination of the effects of light on the human circadian system, relatively little attention has been paid to another influence of light on the human brain — its alerting and activating effects. As of 1995, only a handful of studies had directly, or indirectly, examined the immediate activating effects of light on alertness, performance and/or mood² and little has changed in that regard in the past decade.

Why the apparent discrepancy in research interest? Well, the finding of light-induced phase-shifting was, to some extent, a surprise. Until the early 1980s, it was generally accepted that the human circadian system was insensitive to the influence of light (see reference 3 for example). So, there was a “wow factor” there. In contrast, the notion that light exposure can cause us to feel more alert and activated (especially at night) is nothing short of a truism. After all, isn't that why we turn the lights off to sleep? Adding to the “wow factor” of light-induced phase shifting was its relative mystery. For many, the concept of a phase response curve (PRC) is counter-intuitive and for others, just plain difficult to understand. The terminology is confusing and arcane. Implementation of light treatments using circadian principles requires a white-coated expert, well versed in the abstruse art. In contrast, anyone can crank up the office rheostat.

Or can they? In this issue of *Sleep*, a paper by Lockley et al suggests that we may still have a great deal to learn about the alerting/activating effects of bright light. In a carefully-conducted study comparing 6.5 hours exposure to two monochromatic light

sources (460nm vs 555nm) of equal photon density, the authors report that subjective alertness, auditory vigilance, waking EEG activity and melatonin levels were more significantly influenced by exposure to the shorter, than to the longer, wavelength. The authors conclude that, as with circadian effects, alerting/activating effects of light are “blue-shifted” -- that our brains have a differential sensitivity to light transduced primarily via a non-visual photoreceptor system, since the maximum wavelength sensitivities of both rods and cones are substantially greater than 460nm. The authors acknowledge that such effects may be mediated through the cone photoreceptor system, as well, but to a substantially lesser extent.

Based on these findings, and on the tenor and focus of the authors' discussion, it would be easy to come away from this paper with the distinct impression that light-induced improvements in alertness and performance are mediated almost exclusively by wavelengths in the 460nm range. This conclusion would be inaccurate, on several counts. First, despite the authors' repeated use of the term, it appears that neither performance nor alertness were actually “improved” by exposure to either light source. Rather, the typical circadian dip in those measures appears to have been attenuated more so by exposure to 460nm than by exposure to 555nm. Yet, comparisons to other wavelengths, combinations thereof, a broad-spectrum, 460nm “knockout” light source, or some other appropriate control were not made. As such, the only conclusion that can be drawn from this study is that we are more sensitive to monochromatic blue light than we are to monochromatic yellow light. Moreover, because the study did not include a control condition, and because the authors did not analyze each condition relative to a circadian phase-equivalent baseline, it is impossible to assess the degree to which alertness and performance were actually affected by exposure to either wavelength.

Another methodological problem involves the fact that timing of light exposure was scheduled to occur during an interval that can also result in significant circadian phase delays (6.5 hours, ending 15 minutes prior to the presumed nadir of body temperature). It is impossible, therefore, to effectively differentiate between possible circadian effects on alertness and performance and those attributed by the authors solely to acute activating effects. This confound is particularly problematic when trying to interpret the finding that subjective sleepiness remained relatively low for up to an hour after exposure to the short-wavelength light was terminated. While the authors conclude that this likely reflects a carry-over effect of the direct activating effects of light, the alternative interpretation that it was the result of a differential phase-delay induced by exposure to 460nm cannot be ruled out.

Another conclusion that needs to be considered with caution

Disclosure Statement

Dr. Campbell has indicated no financial conflict of interest.

Address correspondence to: Scott Campbell, PhD, Laboratory of Human Chronobiology, New York Presbyterian Hospital, 21 Bloomingdale Road, White Plains, New York 10605; Tel: (914) 997-5924; E-mail: sscampb@med.cornell.edu

involves the authors' statement that "...routine tasks that require sustained vigilance are most likely to be enhanced by exposure to short-wavelength-enriched light, for example, prolonged driving or extended safety monitoring". Because the study used only an auditory vigilance task to examine performance, there is little basis for this conclusion and, in fact, there is some evidence to the contrary. Other studies, using broad-spectrum white light have reported enhanced performance on a variety of tasks, including those thought to require higher-level cognitive processing.⁴⁻⁷ Whether exposure to short-wavelength light influences performance on such cognitive tasks, or whether it has, as the authors suggest, a more selective effect on tasks that require sustained vigilance remains an empirical question.

Notwithstanding such methodological and interpretational difficulties, the current report is noteworthy in that it adds to the debate concerning the possible mechanism(s) underlying the acute alerting/activating effects of light. Most previous studies have concluded that these effects are the indirect consequence of light's capacity to suppress melatonin: Melatonin is soporific; thus, suppressing melatonin should make you more alert. Correlational data have generally (but not always; see reference 8) supported this conclusion. In the current study, as well, the authors observed significant correlations between the degree of melatonin suppression and several measures of enhanced brain activation, certainly suggesting that melatonin suppression may have been a factor.

Yet, citing neuroanatomical and neurophysiological findings from animal studies, and recent work by Phipps-Nelson and co-workers⁹ showing that light exposure can enhance alertness and performance even during the daytime hours, when circulating melatonin levels are virtually undetectable, Lockley, et al raise an interesting alternative hypothesis, recently proposed by others, as well.⁸ This hypothesis states that light-induced brain activation is governed, primarily, not by levels of circulating melatonin, but rather, by neural circuitry involved in the regulation of sleep/wake states.

The retinal ganglion cells from which such circuitry originates have direct projections not only to brain areas implicated in regulation of arousal levels, but also to brain areas implicated in other non-visual responses such as circadian phase-shifting (i.e. the SCN). There are also indirect projections from the SCN to those same arousal-regulating brain areas. With such information in hand, several questions arise: Before all is said and done, is it possible that we will see a phase response curve for the activating effects of light? What about a wavelength response curve? Is it possible that the processes underlying the activating effects of light are as arcane and complex as those underlying the circadian effects? Is lighting up the room to improve alertness and performance actually more complicated than simply hitting the switch? Might there be a "wow factor" here, after all? It seems increasingly clear that the more we learn the less we know about the nature and underpinnings of what has been viewed, heretofore, as the more pedestrian effect of light exposure on the human brain.

REFERENCES

1. Campbell SS, Eastman CI, Terman M, Lewy AJ, Boulos Z, Dijk DJ. Light treatment for sleep disorders: consensus report. I. Chronology of seminal studies in humans. *J Biol Rhythms*, 1995. 10: 105-9.
2. Campbell SS, Dijk DJ, Boulos Z, Eastman CI, Lewy AJ, Terman M. Light treatment for sleep disorders: consensus report. III. Alerting and activating effects. *J Biol Rhythms*, 1995. 10: 129-32.

3. Wever RA. The Circadian System of Man: Results of Experiments Under Temporal Isolation. *Topics in Environmental Physiology and Medicine*, ed. K.E. Schaefer. 1979, New York: Springer-Verlag. 276.
4. Badia P et al. Psychophysiological and behavioral effects of bright and dim light. *Sleep Research*, 1990. 19: 387.
5. Badia P, Myers B, Boecker M, Culpepper J, Harsh JR. Bright light effects on body temperature, alertness, EEG and behavior. *Physiol Behav*, 1991. 50: 583-8.
6. Campbell SS, Dawson D. Enhancement of nighttime alertness and performance with bright ambient light. *Physiol Behav*, 1990. 48: 317-20.
7. French J, Hannon JP, Brainard GC. Effects of bright illuminance on human performance and body temperature. *Ann Rev Chronopharmacol*, 1990. 7: 37-40.
8. Ruge M, Gordijn MC, Beersma DG, de Vries B, Daan S. Weak relationships between suppression of melatonin and suppression of sleepiness/fatigue in response to light exposure. *J Sleep Res*, 2005. 14: 221-7.
9. Phipps-Nelson J, Redman JR, Dijk DJ, Rajaratnam SM. Daytime exposure to bright light, as compared to dim light, decreases sleepiness and improves psychomotor vigilance performance. *Sleep*, 2003. 26: 695-700.