Ocular input for human melatonin regulation

George C. Brainard (1), Robert Levin (2)

(1) Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA; (2) OSRAM SYLVANIA, Salem, MA, USA; E-mail: George.Brainard@mail.tju.edu

It has been hypothesized that increased risk of breast cancer in industrialized countries is partially due to increased exposure to light at night which reduces melatonin production (Stevens and Rea, 2001). To assess this hypothesis, it is important to understand how the human eye transduces light stimuli for melatonin regulation. In both animals and humans, more light is required to activate the circadian and neuroendocrine systems than to stimulate the visual system. Initially, it was thought that light of at least 2500 lux was needed to regulate melatonin secretion from the human pineal gland. When exposure is carefully controlled, however, illuminances as low as 1.3 lux of monochromatic blue light at 460 nm or 100 lux of broadband white light can significantly ($p<0.01$) suppress melatonin in humans (Brainard et al., 1997; 2001). Similarly, a white light illuminance of 119 lux or lower can phase shift the human melatonin rhythm (Zeitzer et al., 2000). To understand how these lower illuminances can regulate melatonin in humans, it is necessary to examine the relevant ocular physiology that mediates this photic effect. These ocular elements include: 1) gaze behavior, 2) ocular lens age, 3) pupillary dilation, 4) photopigment and photoreceptor sensitivity, 5) photoreceptor location within the retina, 6) photoreceptor adaptation and 7) the ability of the circadian system to integrate photic stimuli spatially and temporally. Recent findings suggest that a novel, nonvisual photopigment located in the ganglion cell layer of the retina is the primary regulator of melatonin and circadian rhythms (Provencio et al., 2000; Brainard et al., 2001; Berson et al., 2002; Hattar et al., 2002). Given the increasing exposure of citizens to light during the night in industrialized countries, it is useful from both a scientific as well as a clinical perspective to elucidate the photosensory physiology in the eye for melatonin regulation.

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Berson, Dunn, Takao 2002 Science 295:1070-1073.
Brainard, Rollag, Hanifin 1997. J. Biol. Rhythms 12:537-546.
Brainard, Hanifin, Greeson, Byrne, Glickman, Gerner, Rollag 2001 J. Neurosci., 21:6405-6412.
Hattar, Liao, Takao, Berson, Yau 2002 Science 295: 1065-1070.
Provencio, Rodriquez, Jiang, Hayes, Moreira, Rollag 2000 J. Neurosci. 20: 600-605.
Stevens, Rea, 2001 Cancer, Causes, Control 12: 279-287.
Zeitzer, Dijk, Kronauer, Brown, Ceiszler 2000 J. Physiol (Lond) 526:695-702.