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Research paper

Exposure to blue wavelength light modulates anterior cingulate cortex activation in response to 'uncertain' versus 'certain' anticipation of positive stimuli

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HIGHLIGHTS

- We compared the effects of thirty minutes of blue versus amber light exposure.
- Participants completed an emotional anticipation task after the light exposure.
- 'Uncertain event' > 'certain reward' led to lower activation for blue vs. amber.
- Blue light may improve adaptive learning-related synaptic processing within the ACC.

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ABSTRACT

Blue wavelength light has been used as an effective treatment for some types of mood disorders and circadian rhythm related sleep problems. We hypothesized that acute exposure to blue wavelength light would directly affect the functioning of neurocircuity implicated in emotion regulation (i.e., ventromedial prefrontal cortex, amygdala, insula, and anterior cingulate cortex [ACC]) during 'certain' and 'uncertain' anticipation of negative and positive stimuli. Thirty-five healthy adults were randomized to receive a thirty-minute exposure to either blue (active) or amber (placebo) light, immediately followed by an emotional anticipation task during functional magnetic resonance imaging (fMRI). In contrast to placebo, participants in the blue light group showed significantly reduced activation within the rostral ACC during 'uncertain' anticipation (i.e., uncertainty regarding whether a positive or negative stimulus would be shown) in comparison to 'certain' anticipation of a positive stimulus. These findings may be explicable in terms of interactions between blue light exposure and the influence of specific neuromodulators on ACC-mediated decision-making mechanisms.

1. Introduction

Daily exposure to bright blue wavelength (≈480 nm) light has been used as a successful treatment for individuals with depression and seasonal affective disorder (SAD) [1]. The mechanisms underlying this effect of blue light on cognition/emotion remain poorly understood but likely include the well known indirect effects of light on the regulation of sleep and circadian rhythms, as well as more direct effects on neurological and neuroendocrine systems [2]. Considerable evidence suggests that the retina contains unique melanopsin photosensitive receptors that respond specifically to the blue wavelengths of light and that these neurons project predominantly to the suprachiasmatic nucleus of the hypothalamus, the primary regulator of circadian rhythms in the brain [3]. However, in addition to the circadian effects of light, some preliminary evidence suggests that light exposure may produce direct and immediate changes in the functioning of neural systems implicated in emotion-related functions. For example, it has been shown that direct exposure to a single dose of blue wavelength light for two hours not only led to improvements in alertness and cognitive performance, but also to increases in subjective wellbeing [4]. This may be explained by the fact that the melanopsin photosensitive ganglion cells also project to brain regions other than the hypothalamus. For example, blue light exposure has been shown to activate

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the locus coeruleus (LC), which in turn releases norephinephrine throughout the cerebral cortex and influences a variety of brain functions as a result [5,6]. Several functional MRI studies have also suggested that blue light has an effect on emotion-related brain regions. For example, a 3-week daily white light intervention with peaks in the blue spectrum was associated with brain activation changes during perception of angry and fearful faces, including decreased activation within the amygdala and medial prefrontal cortex (mPFC), brain areas critical for the regulation of emotional responses [7]. Another study instead showed that short alternating periods of exposure (i.e., forty seconds) of blue versus green wavelength light were associated with increased activation within the temporal cortex and hippocampus during exposure to threatening versus neutral auditory stimuli [8], and such alternating light exposure produced greater activation within the hypothalamus in patients with SAD in comparison to healthy controls [9]. The inconsistencies in prior research require further exploration but may be due to differences in exposure time, the specific wavelengths used, the visual versus auditory nature of the tasks, differences in the populations or spatial location of the brain regions under investigation. Specifically, it is possible that prolonged daily exposure to blue light has distinct effects on functional brain responses when compared to short bursts of blue light exposure acutely during fMRI scanning, and that blue light has a differential effect in different regions of the brain, as well as in healthy versus clinical populations. However, the limited data on the effects of blue light on functional brain responses currently makes it impossible to draw firm conclusions and further research is necessary to clarify the effects of acute blue light exposure on emotional task responses.

The goal of the present study was to examine the effects of acute exposure to blue wavelength light on immediate post-exposure responses within neural systems implicated in affective regulation. Such systems, which include the amygdala, insula, anterior cingulate cortex (ACC) and ventromedial prefrontal cortex (vmPFC), among others, have been shown to be dysregulated in individuals with depression and anxiety, particularly when perceiving threatening stimuli [10,11] and when anticipating aversive stimuli [12–14]. For most people, uncertainty and unpredictability about the affective nature of future events is aversive, and has been shown to lead to hyperactivation of the insula, amygdala, and ACC relative to expectations about events with high certainty or predictability [15,16]. The ACC in particular appears to play an important regulatory role in decision-making within affective situations; recent models suggest that it does so by integrating information about uncertainty and reward expectations (in part, via dopaminergic reward prediction-error signals it receives from the ventral tegmental area [VTA]), and predicted cost/effort associated with perceptual cues and potential actions [17,18]. These decision-making functions also appear to be optimized via reward prediction-error based learning mechanisms. For example, it has been shown that in anticipation of reward, firing of neurons within the ACC increases as reward approaches [19]; interestingly, depressed individuals show reduced activation of the ACC during reward anticipation [20], and this resolves with successful treatment [21]. Further, synaptic plasticity within the ACC (which may underlie the learning rate within the aforementioned decision-making functions) appears to be facilitated by greater norepinephrine release under conditions of 'certain reward' anticipation [18,22,23]; as blue light is known to increase norepinephrine release from the LC (which itself has extensive projections to the ACC), this suggests that, under such conditions, blue light should increase the synaptic activation within the ACC associated with the integration of reward prediction-error and related learning mechanisms [5,6].

Considering that abnormalities in the processing of reward and uncertainty are implicated in multiple emotion-related psychiatric disorders, and that one major source of unpleasant emotion is uncertainty with respect to affectively significant future outcomes, the aim of this study was to investigate whether the effects of blue wavelength light discussed above might have a modulatory influence on brain responses during the anticipation of 'uncertain events' (i.e., a positive or a negative stimulus) versus 'certain threat' or 'certain reward' events. Specifically, we measured functional brain responses during three conditions of anticipation ('certain threat' cues, 'certain reward' cues, or 'uncertain event' cues) in healthy adults following a single dose of thirty minutes of blue wavelength versus an equal exposure to an amber wavelength light condition. We aimed to explore how exposure to thirty minutes of blue wavelength light would lead to functional brain changes within the amygdala, insula, ACC and mPFC during anticipation of 'certain threat', 'certain reward' and 'uncertain event' stimuli, in comparison to an equal dose of placebo (amber) light.

2. Methods

2.1. Participants

Thirty-five healthy adults who were free from psychiatric, neurological or substance use disorders, and reported a regular sleep schedule of going to bed between 10pm and 1am and waking between 6am and 9am participated in the study. Participants reported sleeping on average 7.2 h (SD = 0.93) per night, and obtained 6.8 (SD = 0.89) h of sleep the night before the assessment. Seventeen participants were randomized to receive thirty minutes of blue wavelength light exposure and eighteen participants were randomized to receive thirty minutes of placebo light exposure (see below). Groups did not differ regarding age, sex, BDI-II scores, number of hours slept on weeknights, and number of hours slept the night prior to assessment (see Table 1). All participants provided written informed consent. The research protocol was reviewed and approved by the Institutional Review Board of the University of Arizona and the U.S. Army Human Research Protections Office.

2.2. Materials

2.2.1. Light exposure

Participants were randomized to receive either thirty minutes of blue wavelength light or placebo amber wavelength light while sitting a darkened room. Blue light was administered by four commercially available Philips goLITE BLU® Energy Light devices (Model HF3321/60; Philips Electronics, Stamford, CT), mounted on a desk at a distance of 80 cm, with each light centered at a 45° angle from midline. Each device consisted of a plastic table-mounted device with a 10 × 6 array of light emitting diodes (LEDs), encased in 1 × 1 cm cubical projection elements and a translucent plastic window cover. The goLITE BLU is commercially available and has a narrow bandwidth (peaking at λ = 469 nm, at 214 Lux, and panel irradiance (mW/cm^2) = 1.23 at 20 cm). The amber placebo devices were provided by the manufacturer for research purposes and were essentially identical to the goLite BLU devices, with the exception that they were fitted with amber LEDs (peaking at λ = 578 nm, at 188 Lux, and total irradiance (mW/cm^2) = 0.35).

2.2.2. Emotional anticipation task

The Emotional Anticipation Task (EAT) was designed to evaluate the brain activation associated with anticipating a positive, negative, or uncertain stimulus. The task was adapted from Aupperle et al.'s [24] study design and lasted a total of 460 s. Participants completed the task in the MRI scanner by viewing images on a translucent projection screen and viewed through the mirror mounted on the head coil. For each trial, participants were presented with a grey background with a black arrow that alternated