BLUE LIGHT RAPIDLY MODULATES COGNITIVE BRAIN ACTIVITY IN SOME BLIND INDIVIDUALS

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INTRODUCTION

Light regulates multiple 'non-image-forming' or 'non-visual' circadian, neuroendocrine and neurobehavioral functions in humans including direct enhancement of alertness and cognition. The relative contributions of inputs from visual (rod/cone) and intrinsically photosensitive retinal ganglion cell (ipRGC) photoreception to the stimulant effect of light and the brain mechanisms involved remain unclear, however. A small percentage of blind individuals with complete loss of sight retain circadian responses to light and offer a unique opportunity to investigate the impact of light on cognitive brain functions, in the absence of a functional outer retina and presumably via melanopsin-expressing ipRGCs.

OBJECTIVES

- We used fMRI to test whether exposure to high intensity blue light for 55s modulates cognitive brain responses to an auditory task in blind participants who retain non-imaging-forming responses to light.
- We used EEG to investigate whether 0,5s or 2s exposure to high intensity blue light modifies auditory evoked potentials in these individuals.
- We wanted to test the presence of light 'awareness' using a two alternative forced choice paradigm

METHODS

- ***PARTICIPANTS.*** Three participants with complete loss of sight for at least 10 years and confirmed light induced melatonin suppression took part to the study (9 such individuals have been identified so far, worldwide).

Participants followed a regular sleep-wake schedule 7 day prior to and during their stay in Montreal.
Absence of visually evoked potential was verified using 800 flashes of high intensity blue light.

- ***FMRI.*** One hour after habitual sleep time, participants performed twenty 55s blocks of an auditory 2-back task alternatively in complete darkness or while exposed to high intensity blue light for 55s (480nm; 1.95 x 10^{14} photons/cm^2/s). This task requires updating, maintenance and comparing of information in working memory, in addition to attention and auditory processing.

Structural and functional data were acquired using a 3T MR scanner. Data were analyzed using SPM8. A fixed effect analyzes compared task blocks performed in darkness or under blue light exposure accross the 3 subjects. Significance level was fixed at $p<0.05$ after correction for multiple comparisons over the entire brain volume.

- ***EEG.*** In the afternoon, participants performed an auditory psychovigilance task while exposed to 0.5 or 2s pulses of high intensity blue light (465nm; 9.7 x 10^{14} photons/cm^2/s). The task probes the ability to maintain sustained attention. Light exposures and sounds were administered either alone or simultaneously (300 trials per condition), in which case auditory stimuli were produced during the last 150ms of the light exposure so that lights off and the termination of the sound coincided.

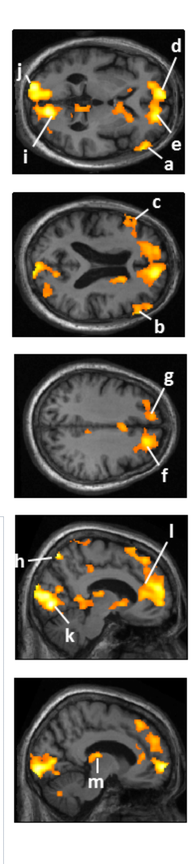
EEG time were edited off-line using BrainVision Analyzer and analyzed in Matlab 7.1. Event Related Potentials (ERP) from the auditory-alone and visual-alone conditions were summed for nonparametric permutation test for statistical comparison with the ERP response to the simultaneous audiovisual condition. Significance level was fixed at $p<0.05$ (probability of difference > 0.95) over at least 10 continuous time points.

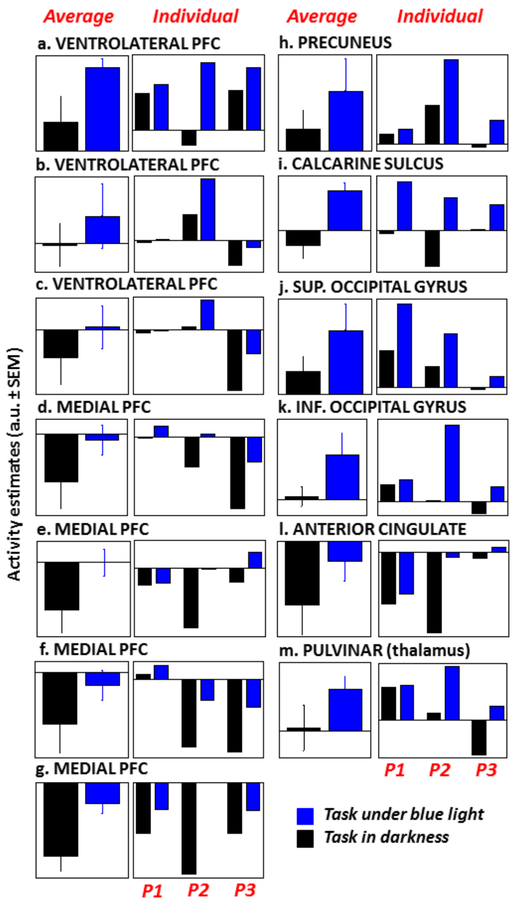
- ***LIGHT AWARENESS.*** In the afternoon, participants had to report on the presence of high intensity blue light (465nm; 9.7 x 10^{14} photons/cm^2/s) in a two-alternative forced-choice task. In 3 separate sessions, they were given forty 4s, 10s and 20s trials (one trial duration per session) randomized for whether the first of second half of the test included blue light exposure, the other half consisting of darkness.

The 4s and 10s sessions were conducted on the same day; the 20s session was conducted the preceding or following day. Cumulative binomial statistics on discrimination were carried out to determine whether responses were significantly different from random choices ($p < 0.05$).

RESULTS

Figure 1. Light increases brain activity during an auditory cognitive task in fMRI

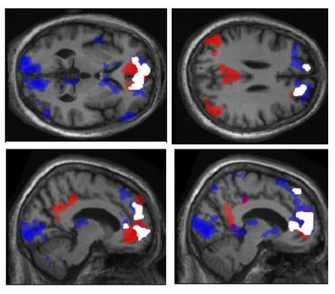




Brain areas showing significant activity increases during 55s exposure to blue light, while performing a 2-back task, as compared to darkness.
Graphs. Activity estimates (arbitrary unit – a.u. ± SEM) in these areas. Average activity estimates of the 3 participants (left) are plotted together with the individual activity estimates (right) to show the inter-individual variability.
PFC: Prefrontal cortex

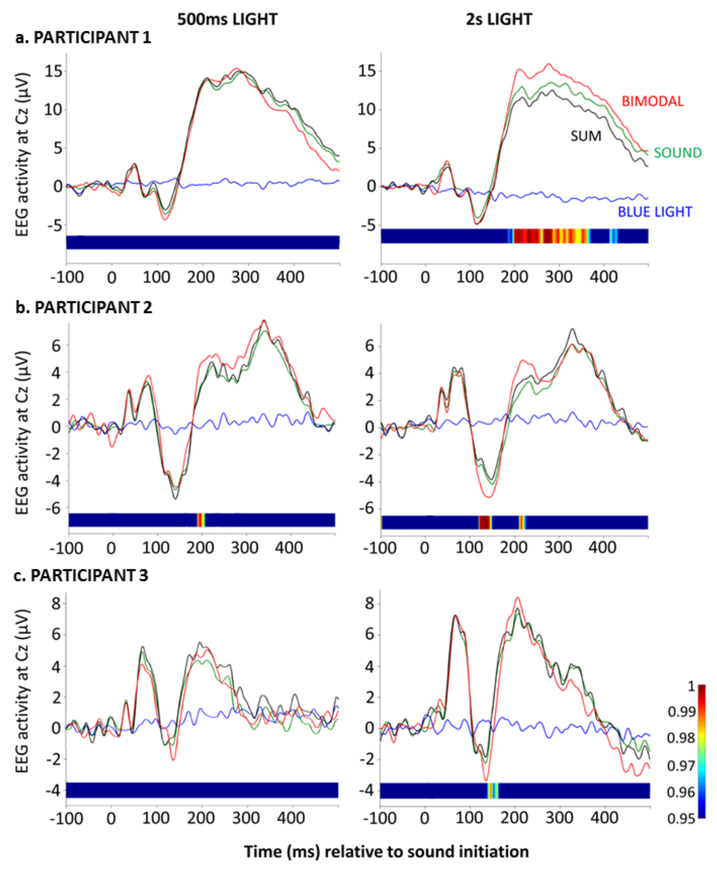
Significant differences were observed in the ventrolateral and medial prefrontal cortex, in the anterior cingulate, precunues and thalamus pulvinar as well as in the occipital cortex (calcarine sulcus, and superior and inferior occipital gyri).

Figure 2. Light prevents decreased activation in medial prefrontal areas of the default mode network



Red. areas showing significant decrease in activation in response to the task when performed in darkness. The areas correspond to the default mode network
Blue. Areas of figure 1.
White. Overlaps in the medial prefrontal cortex and anterior cingulate, i.e. significant increase in brain activity due to blue light exposure in areas deactivated in response to the task in darkness

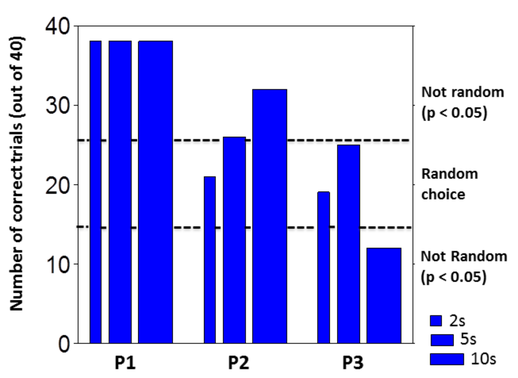
Figure 3. Two seconds of light modulates EEG activity if administered simultaneously to auditory stimulation, but not if administered alone



EEG activity evoked at the Cz location by an auditory stimuli alone (**green**), by blue light exposure alone (**blue**), or light and sound simultaneously (bimodal, **red**).
We compared the bimodal trials to the mathematical sum of both the auditory and light alone trials (**black** line). Horizontal bars correspond to results of the permutation statistics between the bimodal trials and sum of both trials alone.
In the 500ms condition (*left panels*), each auditory stimulus was preceded by 350ms of light, while in the 2s condition (*right panels*), each auditory stimulus was preceded by 1850ms of light.

In the 2s condition, all 3 participants show significant differences, while in the 500ms condition only participant 2 presented marginal (but significant) differences.

Figure 4. Light awareness is present in at least two subjects



Participants chose whether the light was on or off during the first or second half of a 4, 10 or 20s epoch.

Participant 1 had high accuracy (95%) irrespective of trial duration.
Participant 2 exhibited a duration-dependent behavior with a linear increase in accuracy from 52.5% (2s), to 65% (5s) and 80% (10s).
Participant 3 showed a duration-dependent behavior with 47.5% (2s), 62.5% (5s) and 30% (10s) selection accuracies. The latter value indicates that participant 3 stated the incorrect option on 70% of occasions, which is a non-random behavior.

SUMMARY/CONCLUSIONS

In the absence of a functional outer retina, but when non-image-forming photoreception is retained,

i. exposure to light for less than a minute modulates cognitive brain activity in prefrontal areas involved in higher cognitive functions, in the occipital cortex, and in the pulvinar, which is implicated in arousal regulation;
ii. light prevent decreased activation in medial prefrontal areas of the default mode network;
iii. as little as 2 seconds of light modulates EEG brain activity, but only when the brain is actively processing the acoustic stimulations;
iv. awareness' of light can occur

Our results indicate that melanopsin ipRGC signaling can rapidly affect brain activity and fundamental cerebral organization, so that it could potentially participate in the regulation of numerous aspects of human brain function, in addition to the recruitment of supplemental brain areas to perform an ongoing cognitive process.

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