## Melanopsin bistability impinges on higher order cognitive brain function

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## ABSTRACT

**Introduction:** Light strongly stimulates human alertness and cognition, presumably through intrinsically-photosensitive retinal ganglion cells (ipRGCs) that express melanopsin. However, direct evidence for the involvement of ipRGCs in stimulating cognition in normal individuals has not yet been reported. Recent *in vitro* and *in vivo* studies suggest that melanopsin is bistable and that light sensitivity is modulated by prior light exposure. According to this hypothesis, pre-exposure to longer but not shorter wavelength light increase photics responsiveness of melanopsin. Here we tested whether immediate prior light history modulates the subsequent impact of light on cognitive brain function, and whether this modulation is consistent with melanopsin bistability properties.

**Methods:** Sixteen participants underwent 3 consecutive fMRI sessions during which they were exposed to monochromatic green light (511nm) while performing auditory working memory 3-back and 0-back tasks. One hour prior to each session, participants were exposed to 10min of orange (589nm), green (511nm) or blue (461nm) monochromatic light. We computed the difference between 3-back and 0-back tasks to isolate executive responses and compared the influence of light on these responses between sessions.

**Results:** Prior exposure to orange, as compared to blue light, increased executive responses bilaterally in the superior frontal gyrus and dorsolateral prefrontal cortex and in the right ventrolateral prefrontal cortex. Furthermore, prior exposure to green, as compared to blue light, increased executive responses in the left ventrolateral prefrontal cortex. The remaining comparisons (orange>green; green>orange; blue>orange; blue>green) led to no significant prefrontal response changes.

**Conclusion:** Although participants performed the same auditory task under the same monochromatic light condition, prior light exposure influenced the impact of light on responses of prefrontal areas in agreement with hypotheses on melanopsin bistability. Our data favor a significant role for melanopsin-expressing ipRGCs in stimulating cognitive brain responses. Melanopsin bistability may therefore confer a "photic memory" that modulates human cognition.

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