

## Modulation of fMRI Assessed Brain Responses to Blue and Green Light by Sleep Homeostasis, Circadian Phase and *PER3* Polymorphism

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Light elicits numerous physiological and behavioural non-visual responses, such as acute effects on attention and arousal, and long term regulation of sleep/wake cycles. These responses are mediated by the recently discovered melanopsin-dependent and the classical photoreception systems. We have previously investigated non-visual effects of light on various brain functions as assessed by fMRI and PET and identified some of the areas and pathways mediating these effects during either the day or night. Recent data in nocturnal rodents suggest that the non-visual effects of light on sleep propensity are modulated by both circadian phase and homeostatic sleep pressure. We used a genetic marker (VNTR polymorphism in *PER3*) for inter-individual differences in the build up of homeostatic sleep pressure and the negative effects of sleep loss on performance and brain activity to further investigate these interactions in humans.

Fifteen *PER3*<sup>4/4</sup> (7F; 24.13 ± 0.95 y.o.) and 12 *PER3*<sup>5/5</sup> (5F; 24.17 ± 1.17 y.o.) healthy individuals were recruited solely on the basis of their *PER3* genotype. Brain responses to an auditory 3-back working memory task were recorded in 4 fMRI sessions during 2 separate visits. In each visit, they were recorded in the evening and the following morning. In one visit subjects slept in the laboratory between both sessions, while in the other, they remained awake (25.5h sleep deprivation). Sleep deprivation (SD) and sleep visits were counterbalanced within and between genotypes. In each session, participants were exposed to alternating 60s blue (473nm) and green (527nm) monochromatic light exposures. Irradiance levels of half of the illuminations were set at 7x10<sup>12</sup> ph/cm<sup>2</sup>/s, the other half at 3x10<sup>13</sup> ph/cm<sup>2</sup>/s. Orders of irradiances and wavelengths were counter-balanced.

In *PER3*<sup>4/4</sup> individuals, non-visual (i.e. blue > green light) modulation of brain activity by light in the morning declined from after sleep to after SD in the bilateral parietal cortex, and in two right prefrontal cortex areas involved in contextual and episodic control of behavior. This decline was already detected in the right parietal cortex in the evening before SD. In *PER3*<sup>5/5</sup> no significant changes in non-visual modulation of brain activity by light was detected.

The data suggest that non-visual responses to light are modulated by sleep homeostasis, circadian phase and *PER3* polymorphism.

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*Key terms:* fMRI – non-visual responses to light - sleep and circadian