Changes in Spectral Sensitivity of the Human Circadian System

by

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ABSTRACT

The human eye is commonly only thought of as important for vision but evidence suggests that light sensed by the eye is the most influential stimulus to regulate the human circadian cycle (Dijk et al. 1995). It has been shown that the quantity, spectrum, distribution and timing (Rea et al 2002) play important roles in this response. Currently a combination of photoreceptors (rods, cones, and the ipRGC) are well accepted to be involved in the circadian response (Hattar et al. 2003, Panda et al. 2002, Rea et al. 2005, Ruby et al. 2002). A model for human circadian phototransduction based on the neurophysiology and neuroanatomy of the retina was developed by Rea and colleagues (Rea et al., 2005).

A study by Figueiro (2004) suggest an increase in sensitivity to short wavelengths towards the end of the night compared to the beginning of the night, suggesting a change in spectral sensitivity of the circadian system over the course of the night. Based on these preliminary studies, this thesis was set out to investigate two hypothesis; 1) the circadian system becomes more sensitive to short-wavelength light (blue) in the early morning (5:00 – 6:00 am) compared to the early night (1:00 to 2:00 am), and 2) a combination of photoreceptors participate in circadian phototransduction.

In order to test these hypotheses, a set of light goggles were used to provide a constant irradiance and spectral wavelength to each subject while the researchers ran two one-hour treatments at different times in the night (1:00 – 2:00 and 5:00 – 6:00). On the next round, the subjects received a different irradiance and spectral wavelength. The irradiances provided by the light goggles were calculated so that they would produce the same response by the circadian system (40% melatonin suppression) if a single photoreceptor peaking at 480nm was responsible for circadian phototransduction. The irradiances used was 0.292 W/m^2 of 445nm (blue) light and 0.529 W/m^2 of 525nm (green) light. Before, during, and after being exposed to the light the subjects provided both blood and saliva for radioimmunoassay analysis as well as pupil size measurements using an entopic pupilometer. Melatonin suppression was calculated as the percentage difference of the melatonin concentration from 2:00 to 1:00 (or from 6:00 to 5:00 for the later condition). The ratio of the two different light source's effect on melatonin

concentration at the same time of night was used to determine if the shorter wavelength light source became more effective at stimulating the circadian system later at night.

One tail t-test revealed a significant increase ($p=0.03$) in plasma melatonin suppression ratio after the 445 nm treatment compared to the 525 nm treatment, suggesting an increase in short wavelength sensitivity at the end of the night. The saliva melatonin suppression ratio did not show a significant change between time 1 and time 2 ($p=0.19$). In fact, the saliva melatonin suppression ratio suggests an increase in the response to the 525 nm rather than an increase in response to 445 nm towards the end of the night. In another analysis, where low melatonin levels were removed from the data set and data set was normalized, the suppression ratio at time 1 was significantly lower ($p=0.03$) than in time 2, suggesting a change in spectral sensitivity in the expected direction. The pupil measurements, however, did not show any change from time 1 to time 2 and thus no significant effect of spectrum. Moreover, the melatonin suppression obtained in time 1 was much lower than predicted by the model.

These results presented here suggest, but do not confirm a change in spectral sensitivity of the circadian system over the course of the night. The lower than predicted melatonin suppressions do at least follow past studies using very short wavelength light sources. Several possible explanations are presented for this as well as for the high variability of melatonin concentrations found.