

Use of Environmental Light Cycles to Distinguish Circadian Regulation from Direct Light Modulation of Learning and Mood

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ABSTRACT

Previous work has suggested that circadian rhythms regulate cognitive functions and mood in human and mice. However, previous experiments housed mice in regular daily light: dark cycles preventing the dissociation of light from circadian rhythms. In light of recent findings in human, that light directly modulates attention and mood, we wanted to create light cycles which would allow the dissociation of light from circadian rhythms. Here we describe two light cycles, the first allows the measurement of behaviors in the absence of “white” light, and the second prevents mice from photoentraining but does not cause sleep disruption or circadian arrhythmicity. These cycles have allowed us to determine the circadian and light effects on learning and mood.

Abstract Keywords

Circadian rhythms, light, learning and mood.

INTRODUCTION

Short day length and irregular light schedules cause mood disorders, cognitive dysfunction, and fatigue as observed in seasonal affective disorder (SAD), shift work, and transmeridian travel. A common feature of all these situations relates to changes in the duration or time of light input. The circuitry and function of how light regulates cognitive functions in SAD, shift work and transmeridian

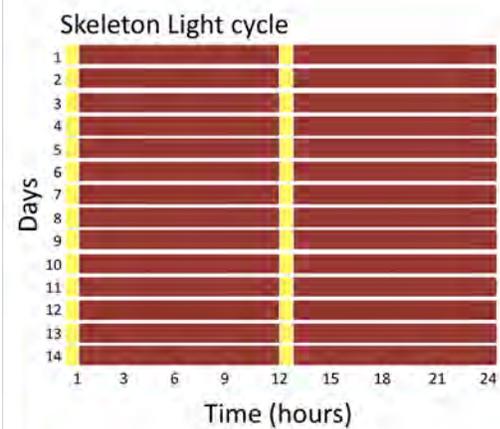
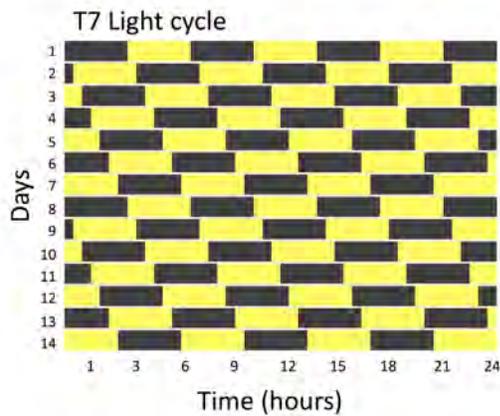
travel has been confounded by sleep and circadian disruptions. To begin to understand how light and circadian rhythmicity affect shift work differentially, it is necessary to have light environments that allow the isolation of each factor. Historically, this has been vary difficult to accomplish as daily light cycles are used to synchronize circadian rhythms. We have utilized two previously characterized light cycles, one which allow animals to photoentrain with only two hours of light each day, and another which does not allow circadian photoentrainment, but does not disrupt circadian rhythmicity.

METHODS

In our first light cycle, we administer two light pulses each day, which outline the typical light period (ie: first light pulse from 700-800 and second light pulse from 1800-1900). The remainder of the day is illuminated with dim red light, which does not affect the circadian system. We are then able to use behavior tests with red illumination to determine the circadian regulation of cognitive functions without any confounding issues of light on the circadian system.

The second light cycle consists of an ultradian light schedule of 7 hours (T7: 3.5 hours of light followed by 3.5 hours of darkness). We have shown previously that mice housed in this light cycle sleep equivalent amounts when compared to mice housed in a 24 hour light cycle. Using this light cycle we have found that mice are unable to predict the onset of lights and consequently adopt a 24.5 hour period. This slightly longer than 24 hour period allows the 3.5 hour light pulses to hit all phases of the circadian cycle within two days. In this setup, we are able to test the effect of chronic light pulses on behavior without the

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confounding factors of sleep disruption and circadian arhythmicity.

FINDINGS

Using these light cycles we have found that circadian phase does not influence the ability of mice to learn spatial or recognition tasks. However, mice housed in the T7 light cycle show decreased ability to learn a spatial task and are unable to discriminate objects in a simple recognition task indicating that chronic light pulses disrupt the ability of mice to form hippocampal dependent memories. Previously hippocampal dependent learning and memory has been linked to depression related increases in glucocorticoid levels. We therefore asked if the changes found in learning were due to increased depression like behavior in mice housed in a T7 cycle. We used forced swim tests and corticosterone measurements to assay depression like

behaviors. Mice housed in the T7 light cycle found showed increased time spent floating and increased levels of corticosterone in indicating that chronic exposure to light pulses increases depression like behaviors which then leads to an decreased ability to learn. To test the hypothesis that depression like behaviors precede the decreased ability to learn, we treated the depression behavior with an antidepressant, desipramine, prior to performing the learning assay. We found that mice housed in the T7 cycle that were treated with antidepressants, showed a complete recovery in their ability to learn hippocampal dependent tasks.

CONCLUSIONS

Our ability to house mice in light cycles which dissociate circadian photoentrainment from the direct influence of light on behavior has allowed us to show that circadian rhythmicity does not affect hippocampal dependent learning and that light modulates learn and mood in mice, confounding previous experiments on the topic.

Ethical Statement

All work described here has been approved by the Johns Hopkins University IUCAC committee.

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