Bridging Animal Models to Human Health Outcomes

Disruption of the 24-hour light-dark cycle has been linked to increased risk for diseases among shift workers. The present study investigated how circadian disruption, similar to that experienced by shift workers, affected glucose intolerance in mice. Phasor magnitude was used as a measure of circadian entrainment. It was hypothesized that a shorter phasor magnitude would be associated with higher glucose intolerance.

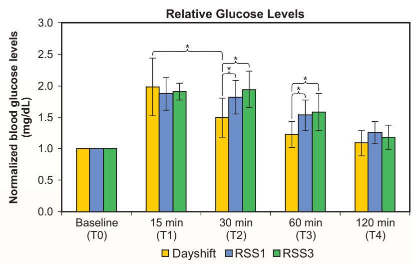

Figure 1: Mean ± standard deviation (SD) of the normalized blood glucose levels measured at each of the four time points.

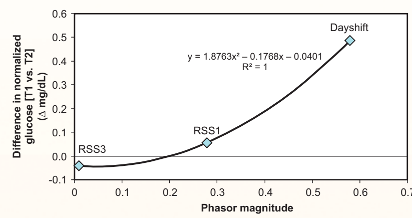

Figure 2: Relationship between phasor magnitude, a measure of circadian entrainment, and the difference in glucose levels measured 15 min and 30 min after glucose administration.

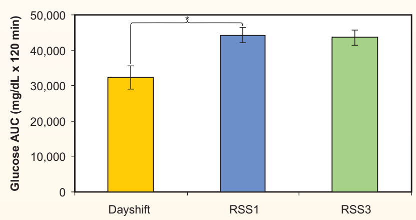

Figure 3: Mean ± SD of the area under the curve (AUC) for all three lighting conditions.

Methods

Twelve individually housed C57BL6 male mice were exposed to 12 hours of light and 12 hours of dark (12L:12D) for a minimum of two consecutive weeks. The mice were then exposed to a light-dark pattern experienced by a rotating-shift worker (RSS1 or RSS3). In the RSS1 condition, the mice experienced a reversed light-dark pattern once per week, for three consecutive weeks. In the RSS3 condition, the mice were given a reversed light-dark pattern for three days in a row per week. This pattern was repeated for three consecutive weeks. In between the three light-dark conditions, the mice remained in 12L:12D for two weeks to wash out the previous effects.

Glucose levels were assessed via oral glucose tolerance test (OGTT). The area under the curve (AUC) was also calculated following the OGTT. Twelve additional animals were given running wheels and experienced the same three lighting conditions as those subjected to the OGTT. Phasor magnitudes were calculated using the light-dark and activity-rest patterns obtained from these animals.

Results

Glucose intolerance significantly increased after animals experienced the RSS1 and RSS3 conditions (Figure 1). As shown in Figure 2, the shorter the phasor magnitude, the smaller the difference in glucose levels measured 30 minutes after glucose administration, suggesting a negative correlation between phasor magnitude and glucose tolerance. The rotating-shift schedules were also associated with significantly higher glucose AUC than the 12L:12D schedule (Figure 3). These results suggest that even one night of shift work may be detrimental to health, at least in the short term.

Conclusions

The present study offers a method to bridge animal models and ecological data from shift workers.

- Phasor analyses make it possible to perform direct comparisons between ecological measurements of circadian entrainment in humans and laboratory measurements of circadian entrainment in mice (Radetsky et al. 2013).
- Phasor magnitude is inversely correlated with glucose intolerance.

Citation

Radetsky L, Rea MS, Bierman A, Figueiro MG. Circadian disruption: comparing humans to mice. *Chronobiology International*, 2013; 30(8):1066-1071.

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