A. Basic and Translational Sleep and Circadian Science

Generalized linear mixed models revealed associations of leukocyte counts with rest-activity behavior and cortisol concentration in most cell types (p<.05). Moreover, the found photoperiodic effects on diurnal rhythms in rest-activity behavior and cortisol concentration are in agreement with research in humans and primates. **Conclusion:** The present study revealed photoperiodic effects on diurnal rhythms in the immune system, rest-activity behavior, and cortisol concentration in pigs and strengthens the importance of the domestic pig as suitable model for chronoimmunology.

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TIMING OF DAILY RHYTHM OF CARDIAC AUTONOMIC CONTROL CONTRIBUTES TO WEIGHT LOSS RESISTANCE, INDEPENDENT OF DAILY ENERGY INTAKE AND PHYSICAL ACTIVITY LEVEL

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Introduction: Obesity is a major health problem. Many treatments have been designed to help overweight/obese people to lose weight, but their effectiveness is highly variable. The same treatments may work for some persons while others have no responses — weight loss resistance. We tested whether the daily rhythm of cardiac autonomic control contributes to weight loss resistance.

Methods: We studied 39 overweight/obese Caucasian women (BMI>25; age: 21–62 years old) who completed (1) an obesity dietary treatment of up to 30 weeks with weekly assessments of body weight, and (2) ambulatory monitoring of electrocardiogram (ECG) for up to 3.5 days. Heartbeat intervals were derived from ECG. Cardiac autonomic control was assessed in each 1-h bin by examining the temporal correlation in heartbeat fluctuations — a nonlinear measure that quantifies the delicate dynamic interplay between sympathetic and vagal outflows. Daily rhythm was estimated using the cosinor analysis.

Results: Weight loss was highly variable (range: 0.68%-21.78 % of initial body weight). The correlation in heartbeat fluctuations displayed a 24-h rhythm (p<0.0001) with fewer correlations (more random) during the nighttime. The phase (peak timing) of the rhythm was highly variable, i.e., 10AM to 8PM for most participants, and after midnight in four participants. Weight loss evolution depended on the phase (p=0.006) in a nonlinear manner. Specifically, participants with the phase between 2PM-8PM lost weight faster than those with phases before 2PM and those after 8PM. The effect was independent of total energy intake, physical activity level, and sleep/wake schedules.

Conclusion: Cardiac autonomic control in overweight/obese women displayed a daily rhythm. The timing of the rhythm had previously un-identified contributions to weight loss. The inter-individual differences in the timing may reflect different circadian regulation of autonomic function and its interaction with the daily behavioral cycle. **Support:** This work was supported by NIH grants R01AG048108, RF1AG059867, RF1AG064312, R01AG017917, and R01NS078009.

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RECURRENT CIRCADIAN DISRUPTION WHILE MINIMIZING SLEEP LOSS IN HUMANS IMPAIRS GLUCOSE TOLERANCE ONLY IN THE PRESENCE OF HIGH-FAT DIET

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Introduction: Nearly 14% of Americans experience chronic circadian disruption due to shift work, increasing their risk of obesity and cardiometabolic disorders. These disorders are also exacerbated by modern eating habits such as frequent snacking and consumption of high-fat foods. Here we used a forced desynchrony protocol to investigate the effect of 3 weeks of recurrent circadian disruption (RCD) with minimal sleep loss on glucose metabolism in humans on a lower or higher fat diet (LFD and HFD, respectively). Methods: Six healthy adults (38-69yrs; 3f) participated in a 37-day inpatient protocol with LFD (25-27% fat) and 15.67-hr fasting duration, or HFD (45-50% fat) and 13-hr fasting duration. The protocol included three weeks of RCD consisting of 28-hr "days" with 11.67-hr sleep opportunities (=10hrs/24hr). Glucose and insulin responses to a standardized breakfast were conducted at baseline, at an aligned circadian phase after 2-3 weeks of exposure to RCD, and after 1 week of recovery. Frequent blood samples were assayed for glucose and insulin; the Area-Under-Curve was calculated from start of breakfast through postprandial minute 180. Results: Total Sleep Time was similar in Baseline and RCD in both groups. Participants on the LFD showed no change in glucose AUC during RCD compared to Baseline. Insulin AUC was lower during RCD (p=0.0269) and Recovery (p=0.0443) than Baseline. In contrast, participants on the HFD showed a significant increase in glucose AUC during RCD compared to Baseline (p<0.0001); AUC returned to Baseline during Recovery. There was no significant change in insulin AUC on the HFD.

Conclusion: RCD (in the absence of sleep loss) led to impaired glucose tolerance when combined with HFD, but not when combined with LFD. These results suggest that LFD may be part of healthy strategies for people experiencing RCD.

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