Effects of Dim Light at Night and Di-(2-Ethylhexyl) Phthalate on Locomotor Rhythms and Feeding Behavior

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INTRODUCTION

The circadian system is an organism's internal biological clock, responsible for regulating physical and behavioral activities that follow a daily 24-hour cycle such as sleep patterns, feeding habits, and hormone release. These rhythms are controlled by the suprachiasmatic nucleus, housed in the brain's hypothalamus.

Circadian disruption occurs due to an interruption in the daily cycle. In humans, circadian disruption is caused by several factors, including light at night, shift work, and jet-lag. This creates problems in the synchronization of behavioral and physical activities and can lead to long-term health conditions. Furthermore, di-(2-ethylhexyl) phthalate (DEHP) is a ubiquitous chemical that has been shown to induce endocrine disruption, which may further modify circadian disruption.

This study aims to test the connection between circadian and endocrine disruption. We expect to find abnormal locomotor activity and feeding behavior changes in both the circadian and endocrine disrupted groups. In the combined disruption group, we expect to see an additive effect of the two models of disruption.

METHODS

- Male and female CD-1 mice organized into 3 treatment groups and 1 control

	Circadian Disruption	Endocrine Disruption
Control	No; 12 h light:12 h dark cycle	No; corn oil
DEHP	No; 12 h light:12 h dark cycle	Yes; 50 µg/kg/day DEHP
dLAN	Yes: 5 lux dim light during dark phase	No; corn oil
DEHP-dLAN	Yes; 5 lux dim light during dark phase	Yes; 50 µg/kg/day DEHP

- Human exposure to DEHP is from 0 to 200 µg/kg/day
- 5 lux corresponds to urban sky
- Animals were acclimated for two weeks and oral dosing started after acclimation and was conducted daily at ZT0 (hours after lights-on) for 30 days
- Locomotor and feeding behavior data taken for 30 days
  - Locomotor data collected from running wheel activity
    - Percent diurnal activity: 100 x [(Activity during light phase)/(Total activity)]
  - Feeding behavior data collected by measuring food weight 2 hours before lights on (Dark phase) and 2 hours before lights off (Light phase)
- Two days of rest were given after the 30 day data collection
- After 2 days of rest, the elevated plus maze was conducted to measure anxiety-like behavior
- An additional 2 days of rest were given before collections of brain, liver, ovary, testes, white fat

LOCOMOTOR ACTIVITY RESULTS

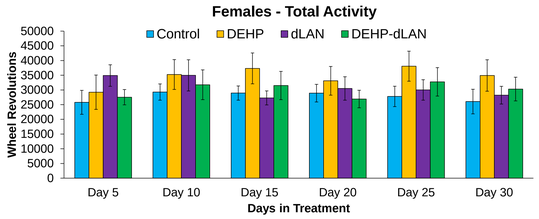

Figure 1. Average activity on running wheel for female mice. There was no significant difference seen in the activity in any of the treatment groups compared to the control. The error bars are SEM. n=8 for all treatments.

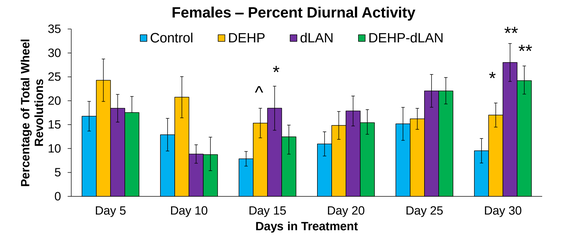

Figure 2. Average percent diurnal activity in female mice. After 15 days of treatment, DEHP and dLAN groups showed increased diurnal activity. After 30 days of treatment, DEHP, DEHP-dLAN, and dLAN groups showed increased average diurnal activity. ^p<0.10, *p<0.05, **p<0.001. The error bars are SEM. n=8 for all treatments.

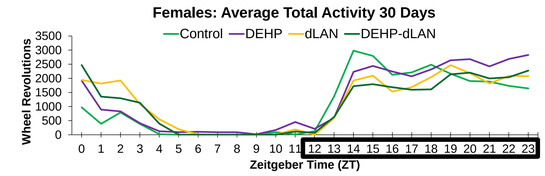

Figure 3. Average total activity across the 30th day of treatment in female mice. Zeitgeber time (ZT) is the number of hours after lights were turned on. Mice in all three treatment groups showed increased activity at ZT0 and decreased activity in the dark phase (post ZT12). DEHP mice increased activity in the dark phase at ZT19. n=8 for all groups.

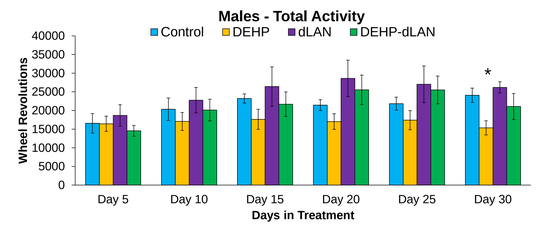

Figure 4. Average activity on running wheel for male mice. DEHP treated mice had significantly lowered activity after 30 days of treatment. *p<0.05. The error bars are SEM. n=8 for all treatments.

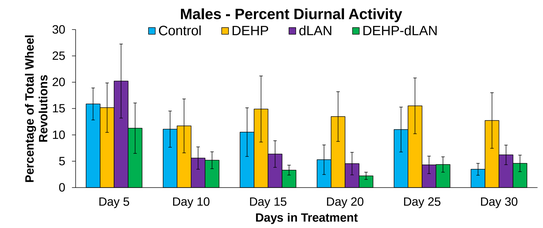

Figure 5. Average percent diurnal activity in male mice. There was no significant effect of any treatment on diurnal activity in males. The error bars are SEM. n=8 for all treatments.

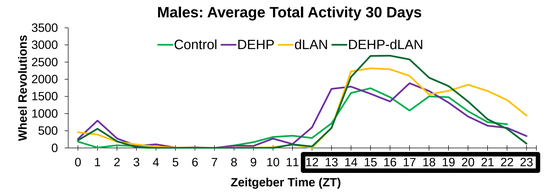

Figure 6. Average total activity across the 30th day of treatment in male mice. Zeitgeber time (ZT) is the number of hours after lights were turned on. The mice in dLAN and DEHP-dLAN groups showed increased activity in the dark phase. n= 8 for all treatment groups.

FEEDING BEHAVIOR RESULTS

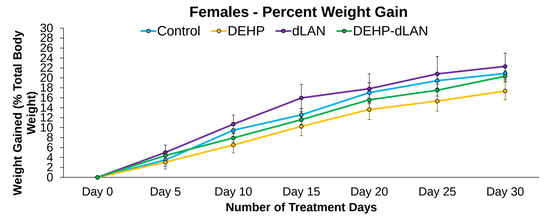

Figure 7. Average percent weight gained in female mice. There was no significant difference in any treatment groups on weight gain. The error bars are SEM. n=8 for all treatments.

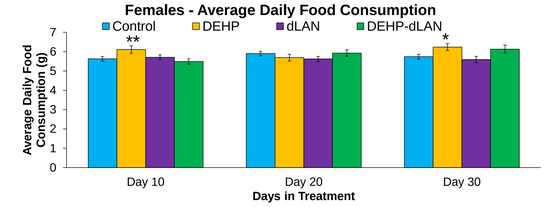

Figure 8. Average food consumption in female mice. DEHP treated mice had significantly higher food consumption at and after 10 and 30 days of treatment. *p<0.05, **p<0.01 The error bars are SEM. n=8 for all treatments.

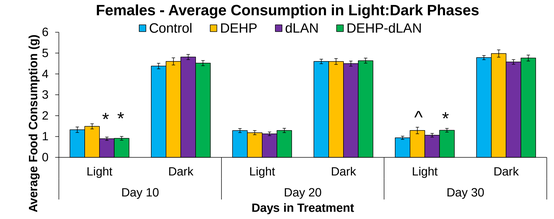

Figure 9. Average food consumed in the light and dark phases in female mice. At day 10 during the light phase, dLAN and DEHP-dLAN treated mice had reduced food consumption. At day 30, DEHP and DEHP-dLAN treatments had higher food consumption during the light phase. ^p<0.10, *p<0.05. The error bars are SEM. n=8 for all treatments.

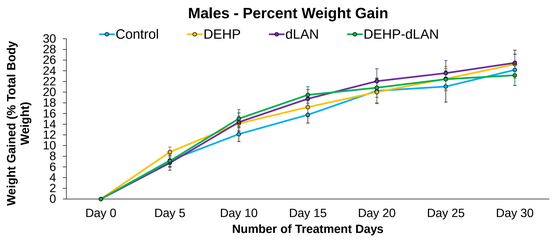

Figure 10. Average percent weight gained in male mice. There was no significant difference in weight gain of any treatment. The error bars are SEM. n=8 for all treatments.

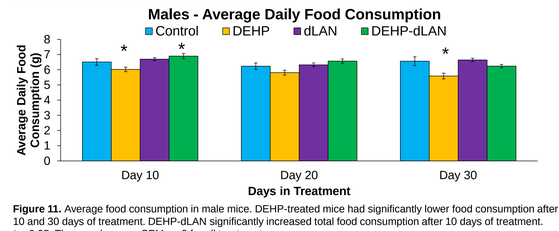

Figure 11. Average food consumption in male mice. DEHP-treated mice had significantly lower food consumption after 10 and 30 days of treatment. DEHP-dLAN significantly increased total food consumption after 10 days of treatment. *p<0.05. The error bars are SEM. n=8 for all treatments.

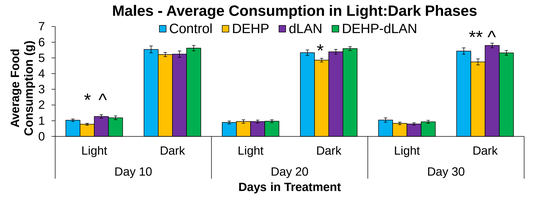

Figure 12. Average food consumed in the light and dark phases in male mice. At 10 days, DEHP decreased and dLAN increased food consumption in the light phase. DEHP-treated mice reduced food intake after 20 days in the dark phase. At Day 30, DEHP decreased and dLAN increased food intake in the dark phase. ^p<0.10, *p<0.05. The error bars are SEM. n=8 for all treatments.

CONCLUSIONS

- Weight was not significantly affected by any of the treatments
- **DEHP-dLAN treatment** did not have an additive affect on feeding behavior and locomotor activity but the treatment did have a significant impact on measures in our model
  - DEHP-dLAN treatment changed the locomotor activity and feeding behavior in females
  - DEHP-dLAN changed feeding behavior in males but locomotor activity was not affected
- **DEHP treatment** impacted both feeding behavior and locomotor activity in male and female mice
- **dLAN treatment** modified the locomotor activity and feeding behavior in females
  - In males, dLAN changed feeding patterns but not locomotor activity

The data show that exposure to endocrine and circadian disruptors commonly found in the environment do modify behaviors

FUTURE DIRECTIONS

- Assess the effects of circadian and endocrine disruption on anxiety-like behavior using elevated plus maze data
- Analyze vaginal lavage slides to determine any effects on estrous cyclicity in females
- Use the brains for gene expression studies in the suprachiasmatic nucleus and other brain regions

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