

Rhett White's URDC Poster Supplemental Materials

Poster link -

<https://docs.google.com/presentation/d/17zcvCjhBbUrbnFyzSDL29S-6d4OiE1Hj0usaGi6V6UI/edit?usp=sharing>

VIDEO WITH SUBTITLE:

https://drive.google.com/file/d/1gHbQI9z3bHBFFPuXmLZzx5F_dQnwlu3S/view?usp=sharing

Dim Light at Night Exacerbates Pain Associated with Chemotherapy

Rhett White¹, Jacob R. Bumgarner¹, William H. Walker II¹, Jennifer A. Liu¹, Hecmarie Melendez-Fernandez¹, James C. Walton¹, & Randy J. Nelson¹

Introduction

- Circadian rhythms are cyclical endogenous physiological processes that exhibit a period of ~24 hours. These rhythms are synchronized to the environment primarily by daytime light exposure. Proper synchrony of these rhythms is optimal for health³
- In contrast, exposure to dim light at night (dLAN, ~5 lx) disrupts circadian rhythms and has many negative health effects, such as heightened pain sensitivity and inflammation²
- Chemotherapy induced peripheral neuropathy (CIPN) has many negative effects on treatment outcome and patient well-being; there are currently no approved preventative agents^{4,5}
- Paclitaxel is a commonly used platinum-based taxane chemotherapy agent used for various forms of cancer⁶

Experimental Question

Does dim light at night exacerbate allodynia (i.e., pain in response to stimuli that usually do not provoke pain) associated with CIPN?

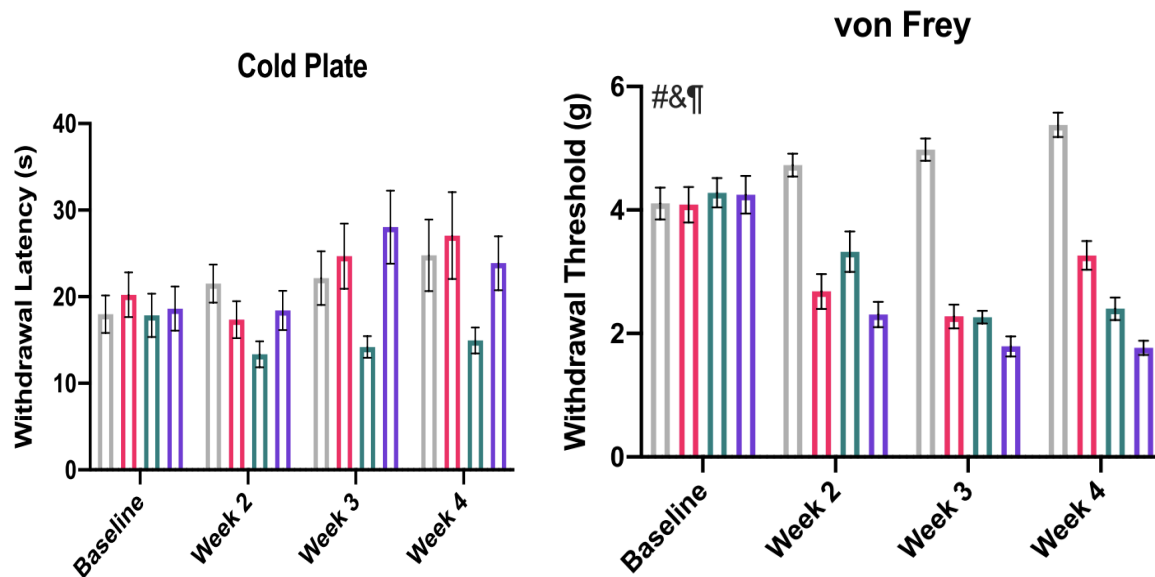
Hypothesis/Prediction

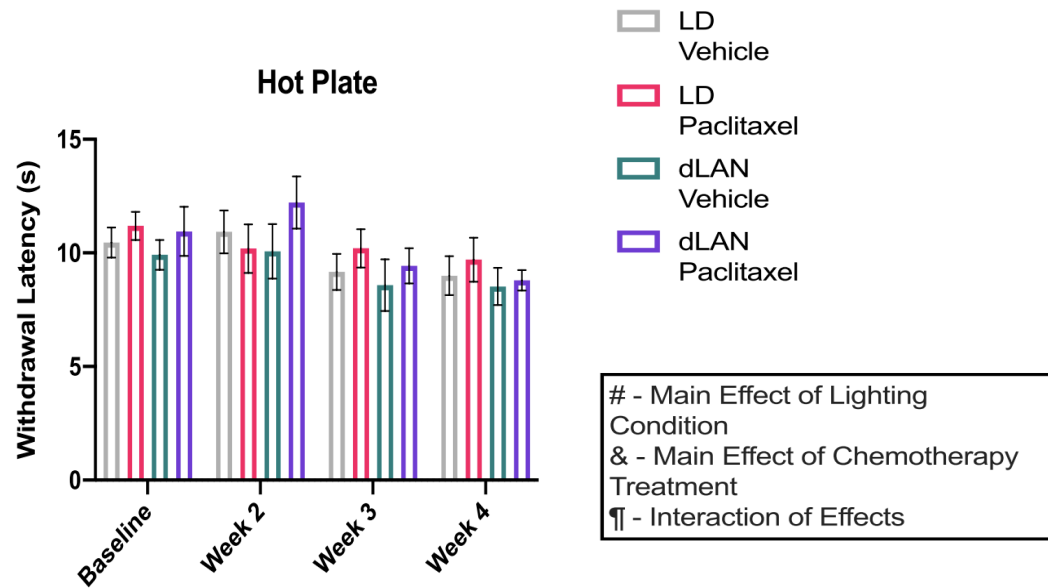
We hypothesized that dLAN exacerbates pain behavior associated with CIPN in female CFW mice.

Methods

- Female CFW mice received a 5-day injection regimen of either paclitaxel or vehicle and were placed in dark nights (LD) or dLAN conditions starting on the first night of injections (2mg/kg/day)^{1,6}
- Baseline pain was assessed, then weekly pain behavior began after one week of injections for 4-weeks
- dLAN began on the first night of injections
- Following the final day of pain testing, the periaqueductal gray (PAG) and rostral ventromedial medulla (RVM) were dissected for qRT-PCR analysis

Results





Results

- dLAN exacerbated mechanical allodynia associated with paclitaxel treatment relative to paclitaxel treated mice in LD conditions
- Exacerbated allodynia was associated with upregulated *Il-6* in the RVM in the dLAN paclitaxel group
- No significant differences were seen in other gene expression analysis or pain assessments

Conclusions

- This study represents an important step in examining the relationship between disrupted circadian rhythms and pain
- Future pain management strategies may need to consider the effects of disrupted circadian rhythms on therapeutic outcomes

Acknowledgments

This research was funded by the National Institutes of Health - 5U54GM104942-04

References

1. Bruera G et al. (2018). Dose-finding study of oxaliplatin associated to capecitabine-based preoperative chemoradiotherapy in locally advanced rectal cancer. *Oncotarget* 9, 17906.
2. Bumgarner JR, Walker WH, Liu JA, Walton JC, Nelson RJ. (2020). Dim light at night exposure induces cold hyperalgesia and mechanical allodynia in male mice. *Neuroscience* 434, 111.

3. Golombek DA, Rosenstein RE. (2010). Physiology of circadian entrainment. *Physiological reviews* 90, 1063-1102.
4. Hershman DL et al. (2014). Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. *Journal of Clinical Oncology* 32, 1941-1967.
5. Mols F, Beijers T, Vreugdenhil G, van de Poll-Franse L. (2014). Chemotherapy-induced peripheral neuropathy and its association with quality of life: a systematic review. *Supportive Care in Cancer* 22, 2261-2269.
6. Reagan-Shaw S, Nihal M, Ahmad N. (2008). Dose translation from animal to human studies revisited. *The FASEB Journal* 22, 659-661.