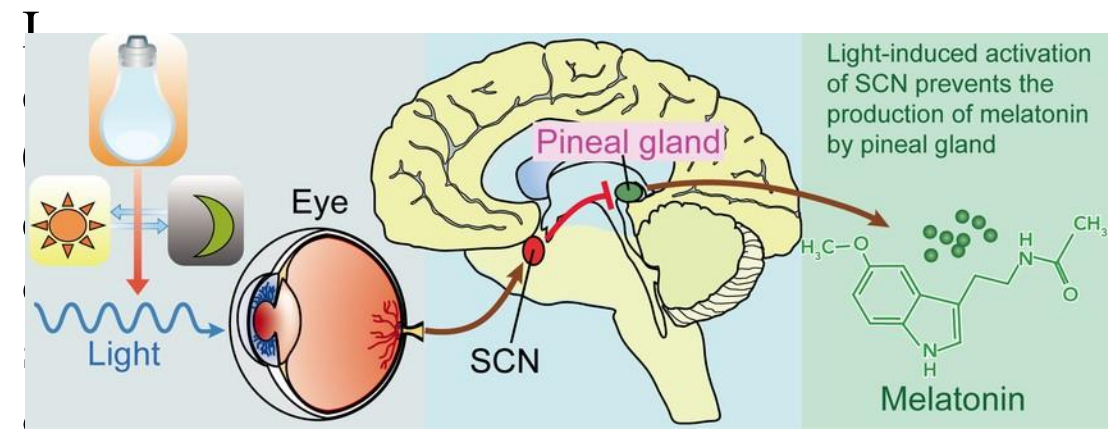


# Rhythms and Blues

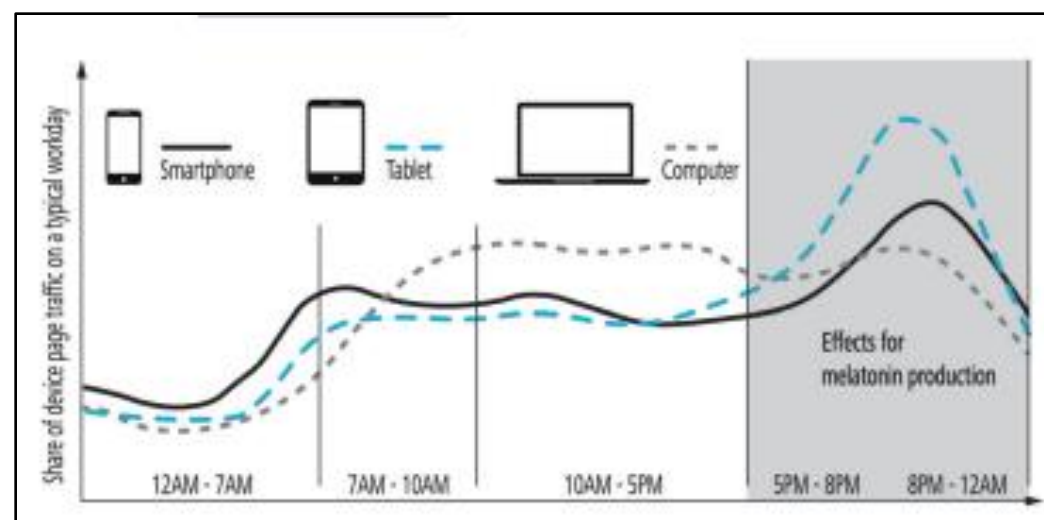
## Evaluating the Impact of Artificial Light Exposure and Circadian Disruption on

### Biobehavioral Systems in *Drosophila melanogaster*

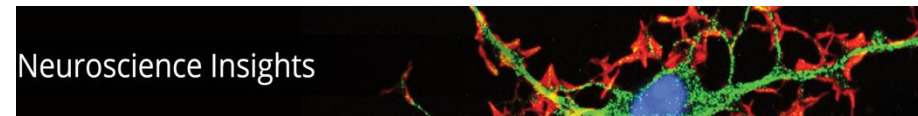
**INTRODUCTION:** Circadian rhythms: physical, mental, and behavioral changes that follow a 24-hour cycle regulated by a master clock in the brain called the Suprachiasmatic Nucleus or SCN (Zhiqiang et al., 2016). Circadian disruptions can affect many systems including learning, memory, metabolism and cardiovascular health (Videnovic and Zee, 2015). Artificial blue light from LED lighting, smartphones and tablets could negatively impact sleep quality, circadian phase, and cycle durations in all organ systems (Wahl et al, 2019) but its precise impact on mental and physical health outcomes is not well known. Limitations of human studies and mammalian models: time, space, and ethical considerations. *Drosophila melanogaster* is a well-established model organism to study sleep/circadian alterations.



Melanopsin present in retinal ganglion cells reacts to light stimuli (natural or artificial) by transmitting signals to the SCN. SCN activation inhibits the pineal gland's melatonin production [8].



LED Usage modelled during the day [7].



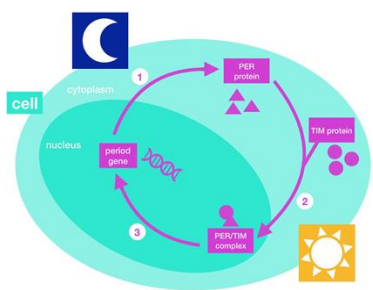


**Disclosure:** Phase I results have been published. **Dozing Off with *Drosophila*: The Effect of Disrupted Circadian Rhythms and Sleep Disturbance on Mortality, Mood, and Addiction.** *Neuroscience Insights*. 2023;18.

### OBJECTIVES:

**Phase I:** to create an animal model of circadian dysfunction (CD) and sleep deprivation (SD), using *Drosophila melanogaster* and examine whether such disruptions in circadian and sleep physiology can negatively impact physical and mental well-being.

**Phase II:** to compare health outcomes of the circadian mutant flies, studied in phase I, to a model of circadian disruption induced by exposure to blue light.

### RESEARCH METHODOLOGY PHASES I and II.


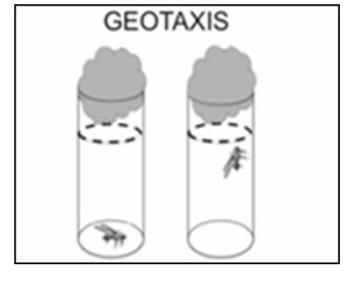
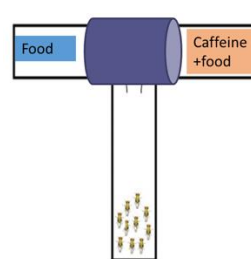
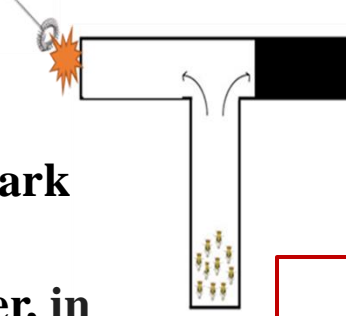

EXPOSURES		
Circadian Dysfunction	Sleep Deprivation	Blue Light Exposure
Rhythmless flies with <i>Tim<sup>01</sup></i> mutation.	<b>Periodic light exposure &amp; mechanical stimulation.</b>	Periods: (7 am – 3 pm) or 12 hours (7 am to 7 pm).
		
PER and TIM protein cycles.[1]	Image taken by finalist, 2024	Image on right taken by finalist, 2024. Image on left: <a href="https://www.woodenearth.com/blogs/wooden-blog/can-desk-lamps-hurt-your-eyes">https://www.woodenearth.com/blogs/wooden-blog/can-desk-lamps-hurt-your-eyes</a>

Fly Stocks (wild-type (Samarkand strain) and Timeless *y[1] w[\*]*; *tim[01]* *Drosophila*) were obtained from Bloomington Stock Center (Bloomington, Indiana) and raised at 23° C on standard cornmeal-molasses medium.

### REFERENCES

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### OUTCOMES

Longevity (Mortality)	Mood (Climbing Behavior)	Addiction (Propensity to Caffeine)	Cognition (Memory and Learning)	Aging/Intestinal Integrity (Smurf Assay)
Measured as percentage of flies surviving over time. <i>Tim<sup>01</sup></i> mutation disrupts multiple biologic clocks theoretically causing multi-system dysfunction. Image taken by finalist, 2024 	Flies who have depression induced pharmacologically show a loss of climbing motivation, or despair like behavior (Moulin et al. 2021).  Flies climbing up to Escape- geotaxis [7].	Flies are an established model to study drug addiction such as voluntary ethanol consumption (Deveneni and Heberlein, 2012).  Choice chamber to assess preference for caffeinated food [3]	Flies were taught to suppress their natural affinity to light by subjecting them to an aversive stimulus coupled with light exposure.  Light-Dark Choice Chamber, in which flies learn to avoid light that is paired with an aversive stimulus [3].	Intestinal integrity assessed by distribution of a blue food dye (FD&C blue dye #1) throughout the body.  Image obtained from <a href="https://cartooncharacters.fandom.com/wiki/Sloppy_Smurf">https://cartooncharacters.fandom.com/wiki/Sloppy_Smurf</a>

### RESULTS PHASE I

**Longevity:** Survival curve analysis showed that Flies with the timeless gene mutation (*tim01*) have a significantly shorter lifespan than controls. **Depressed Mood/Impaired Geotaxis:** Geotaxis was not significantly impaired by sleep deprivation (OR 1.89, P = 0.24), but it was negatively affected by circadian dysfunction (OR 3.26, P = 0.024). **Caffeine Preference/Addiction:** Both the CD (OR 26.3, P<0.001) and SD (OR 5.43, P = 0.017) groups showed a preference for caffeine containing food, after 72 hours of exposure to it, with the CD group much more affected than the SD group.

### RESULTS PHASE II

**Longevity:** Wild type flies exposed to 12:12 light:dark cycles lived the *tim<sup>01</sup>* mutants and the flies exposed to 12 hours of blue light (p< 0.001). The flies exposed to blue light for 8 hours did not have any impact on their lifespan when compared to the control flies. There was also a significant difference between the flies exposed to 12 hours versus 8 hours of blue light (p <0.0001, hazard ratio of 1.5, 1.01-2.2). **Substance Addiction :**The circadian mutant group were almost 11 times as likely to prefer caffeinated media compared to the controls (P<.0001). The BL12 group was also more likely to prefer caffeine containing media compared with the controls (Odds Ratio 6.07, P=0.0007), as were the BL8 group (Odds Ratio 6.48, P=0.0003). **Cognitive Function:** The learning index was defined as the percentage of flies that successfully suppressed phototaxis (or the innate desire to migrate towards light) and migrated to the unlit side of the chamber. *Tim<sup>01</sup>* flies demonstrated significant impairment in memory and learning compared to the control flies (p-value 0.0288). Flies exposed to blue light for 12 hours also had impaired memory and learning (p-value 0.0089) as did the flies exposed to blue light for 8 hours (0.0083). **Intestinal Barrier Dysfunction (Aging):** In the group of flies with the circadian mutation, 23.1% of flies exhibited the *Smurf* phenotype compared to controls at 0% (p-value 0.0248). Exposure to blue light for 12 hours, caused 13.6% of flies to exhibit the *Smurf* phenotype, but did not reach statistical significance (p-value 0.2326).

### CONCLUSIONS

**Sleep and circadian disturbances can negatively influence physical and mental wellbeing and the accompanying molecular mechanisms, as well as disrupted brain physiology, must be studied. It is critical to identify and minimize social and environmental disruptors of such biologic rhythms.**

**Research in both animal and human systems looking at specific amounts, types, and timing of blue light exposure is critical.**

**The health implications of a digital world can no longer be ignored and must be subjected to closer biologic scrutiny and reasonable regulations.**

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