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## Strengthening Mouse Circadian Rhythms under Dim Light at Night Through Arousal

Biello, S., Johnston, H., Meikle, A.



Daily entrainment or synchronisation of the mammalian circadian clock is responsible for the regulation of:

- **Food intake timings**
- **Energy expenditure**
- **Timings of sleep**

The synchronisation of circadian rhythms is thought to be primarily achieved by the synchronisation of the clock to the environmental 24-h light-dark cycle, in which light is the natural time-giver.

**Artificial light** and **urbanization** has increasingly contributed to the effect on health by directly decreasing the timing cues of the light dark cycle, with secondary effects on the rhythmicity of social and sleeping patterns.



Obayashi et al., 2014; Stenvers et al. 2016



McFadden et al. 2014; Fonken et al. 2010



# Non-Photic Interventions

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Buhr, Yoo & Takahashi, 2010



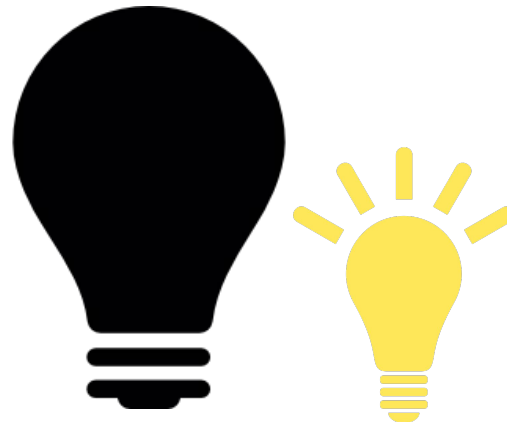
Janik & Bereton, 2017



Van Reeth & Turek, 1966



Mrosovsky, 1988





## Wheel-Running

- ▶ Locomotor activity creates arousal which aids the synchronization to an zeitgeber, creating activity feedback
  - ▶ Edgar & Dement (1991)
- ▶ Free-Access to wheel-running has positive effects on the circadian system
  - ▶ Yamamada et al. (1988)
  - ▶ Leise et al. (2013)
- ▶ Scheduled-Access to wheel-running has stronger effects on the circadian system
  - ▶ Edgar & Dement (1991)
  - ▶ Yamanka et al., (2013)



## HOWEVER

No study has investigated the strength of scheduled-access to wheel-running as an intervention for improving synchrony under **dim light at night**, in comparison to free-access to wheel-running.



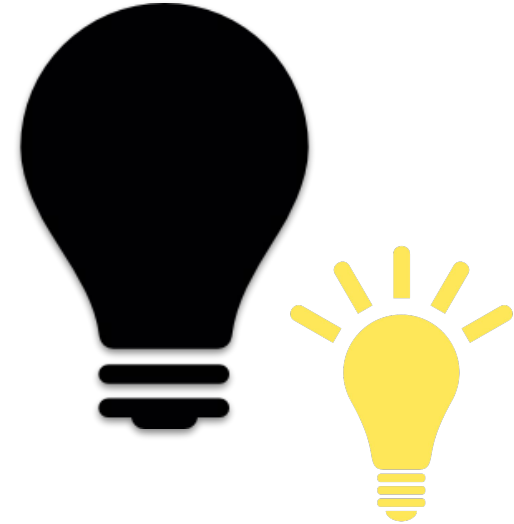
## Dark Pulses

Periods of complete darkness used to induce arousal and behavioural responses in nocturnal animals

- ▶ Animals typically respond in a 'non-photic' fashion
  - ▶ Phase Response Curve

Do dark pulses work through induced activity?

- ▶ Restriction of movement during pulse reduces effects
  - ▶ (Reebs, Lavery & Mrosovsky, 1989)
- ▶ Level of locomotor activity induced in each hamster correlates to phase shift magnitude
  - ▶ (Canal & Piggins, 2006)





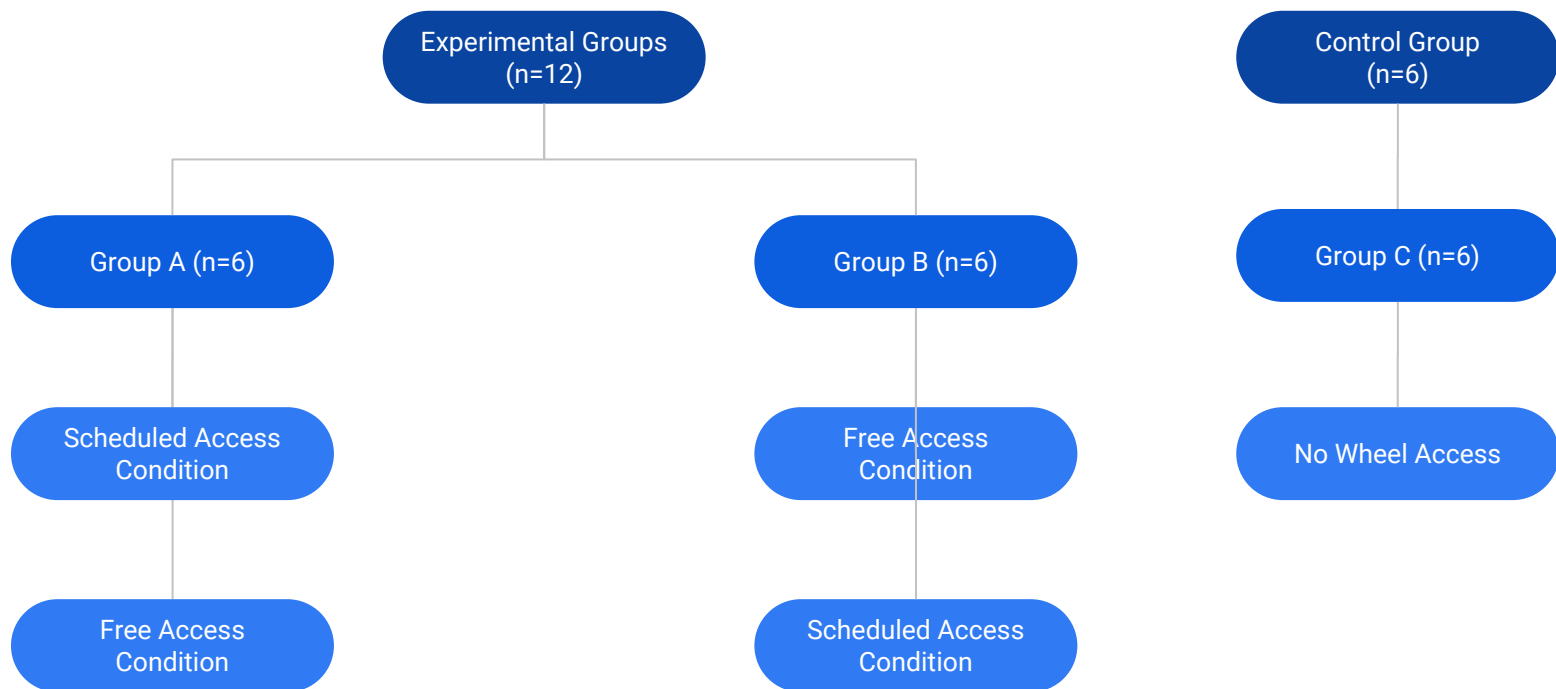
**AIM:** To Investigate the effects of **Scheduled-Access to Wheel-Running**, comparative to **Free-Access Wheel-Running**, in order to understand the influence on circadian synchrony under dim light at night.

- 1) Scheduled-access to wheel-running will have a more significant effect on improving entrainment of circadian rhythms than free-access to wheel-running, by having a lower fragmentation (IV) and higher stability (IS)
- 2) Scheduled and free access to wheel running will have a more significant effect on improving entrainment of circadian rhythms than no access to wheel-running, by having a lower fragmentation (IV) and higher stability (IS).

# Study 1: Strengthening Circadian Rhythms through Scheduled Wheel-Running



- ▶ Within-Subjects Design: Exploration of Hypotheses (1)
- ▶ Between-Subjects Design: Exploration of Hypotheses (2)





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# Study 1: Strengthening Circadian Rhythms through Scheduled Wheel-Running

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- ▶ Scheduled-Access to Wheel-Running
  - ▶ 9am -12pm
  
- ▶ Light Cycle
  - ▶ Bright lights (L) were switched on at 3am and dim lights (DL) were switched on at 3pm (12L:12DL)
  
- ▶ Activity Sensors and Wheel-Clickers to measure activity.

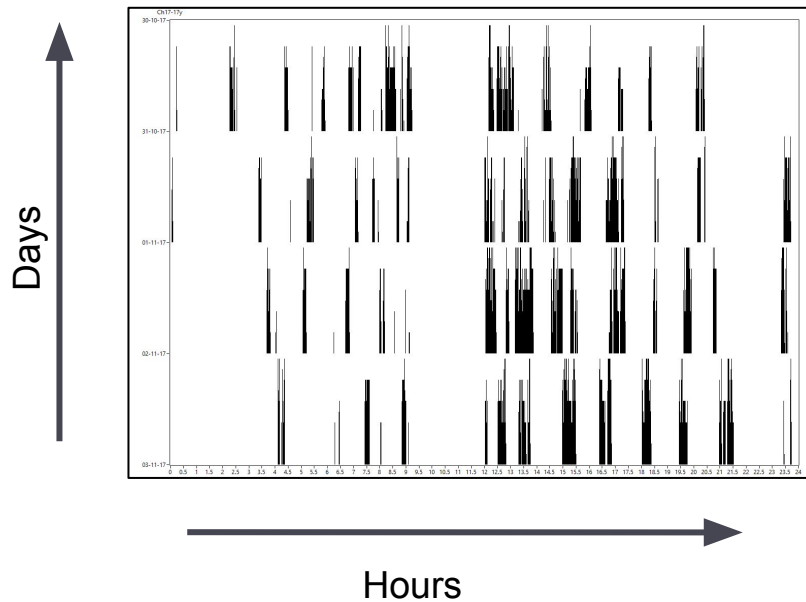




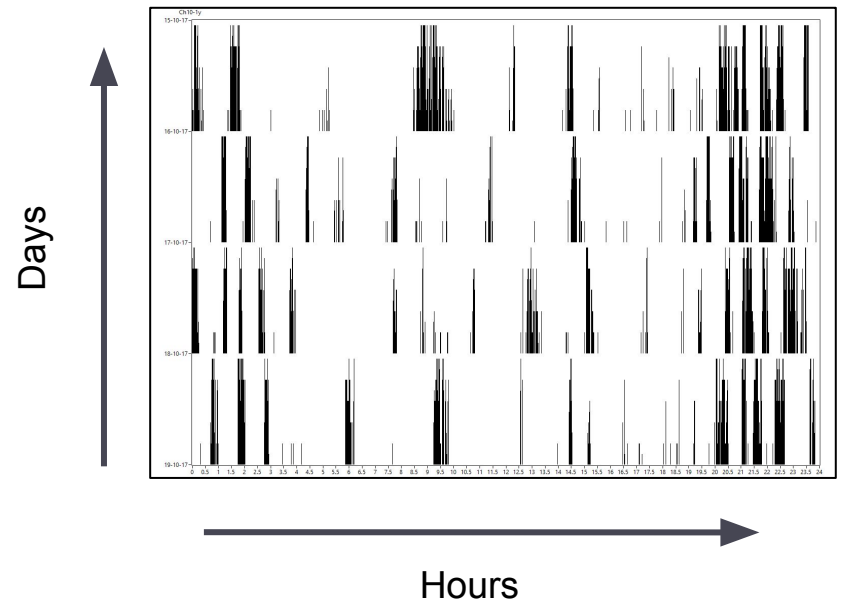


## Study 1: Results

Scheduled Access Actigraph



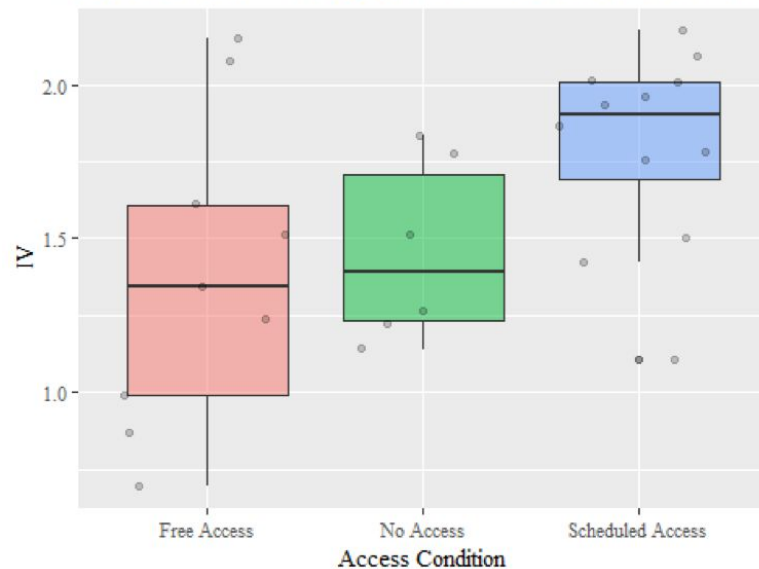
No Access Actigraph



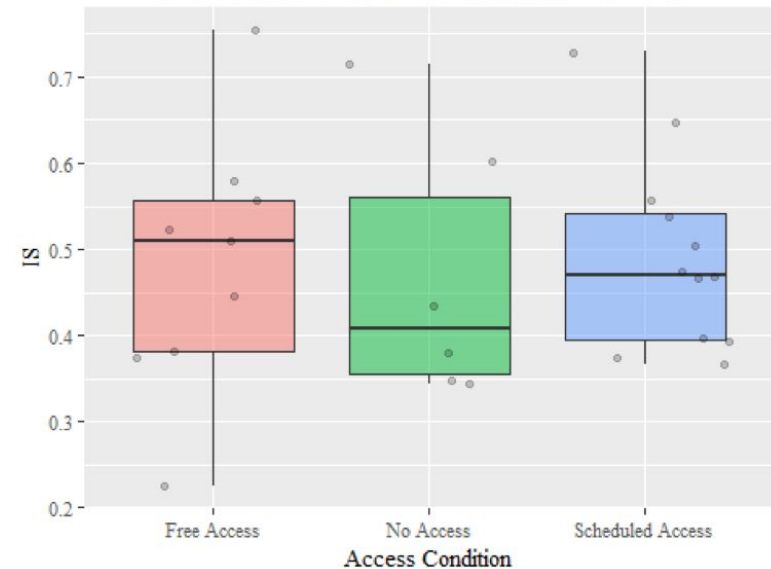


## Study 1: Results

Rhythm Fragmentation (IV) Across Wheel Access Conditions



Stability (IS) Across Wheel Access Conditions



# Study 2: Strengthening Circadian Rhythms through Scheduled Dark Pulses

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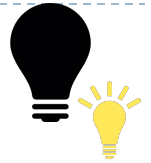


- ▶ **Aim:**
  - ▶ To improve circadian rhythms in mice housed under dim light through the presence of a daily 3-hr dark pulse
  
- ▶ **Hypotheses**
  - ▶ The presence of a dark pulse will increase rhythm stability (interdaily stability) and reduce rhythm fragmentation (intradaily variability)
  - ▶ The magnitude of these effects will be stronger in young mice compared to old



# Study 2: Strengthening Circadian Rhythms through Scheduled Dark Pulses

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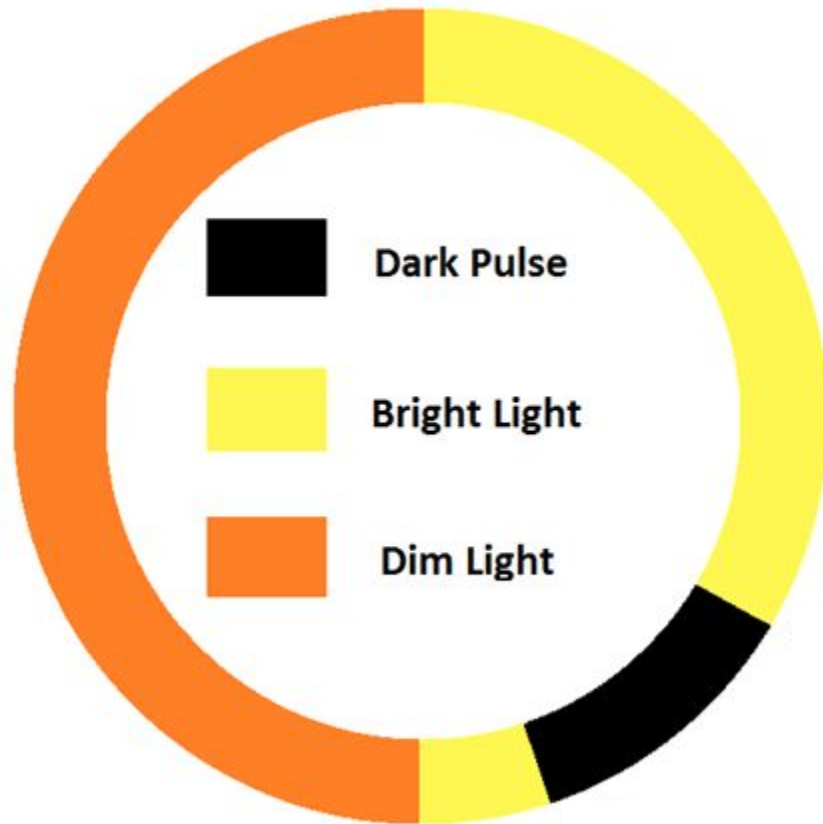
## ► Design

- Cross sectional, counterbalanced mixed design.



# Study 2: Strengthening Circadian Rhythms through Scheduled Dark Pulses

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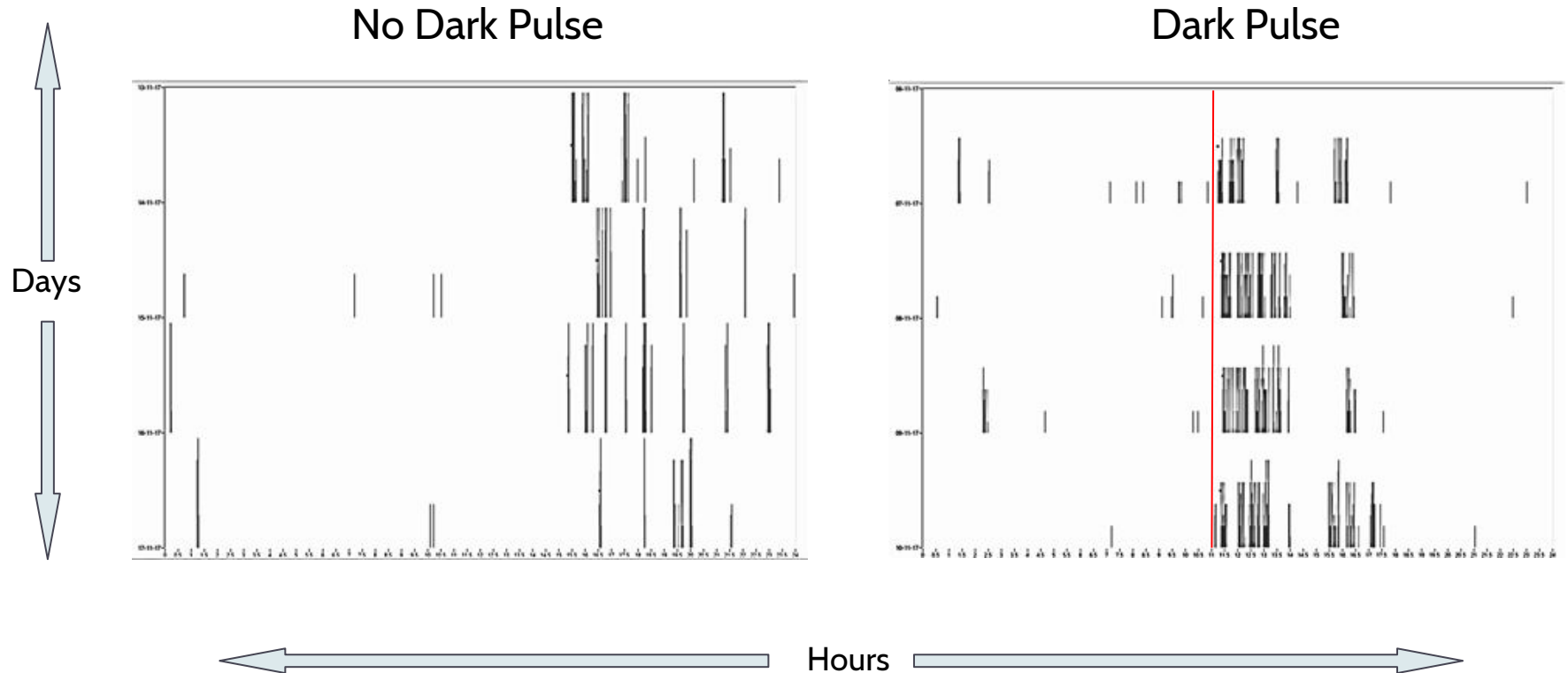


- ▶ Light Cycle
  - ▶ Same as previous study
  - ▶ (dim lights 3pm-3am)
- ▶ Dark Pulses
  - ▶ 5 consecutive days
  - ▶ 3hrs from 11am-2pm





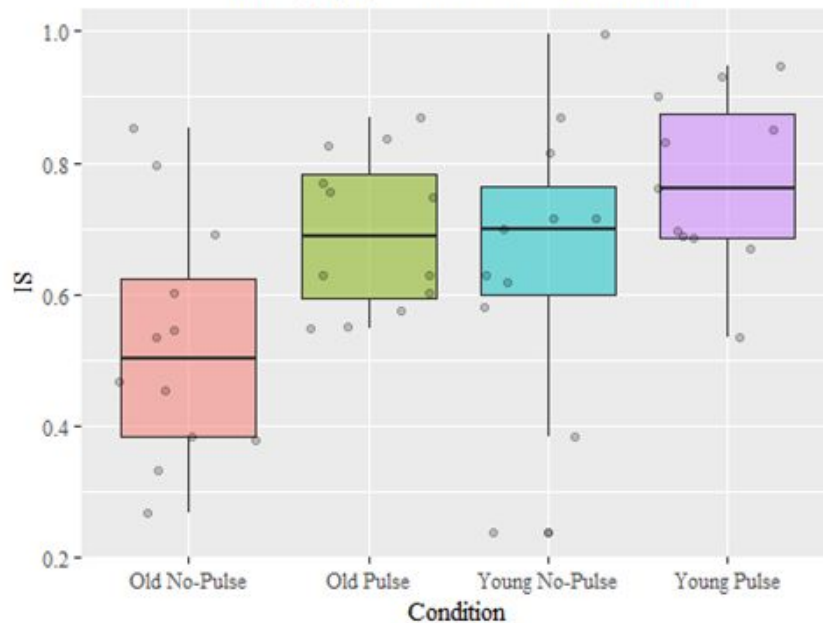
## Study 2: Results



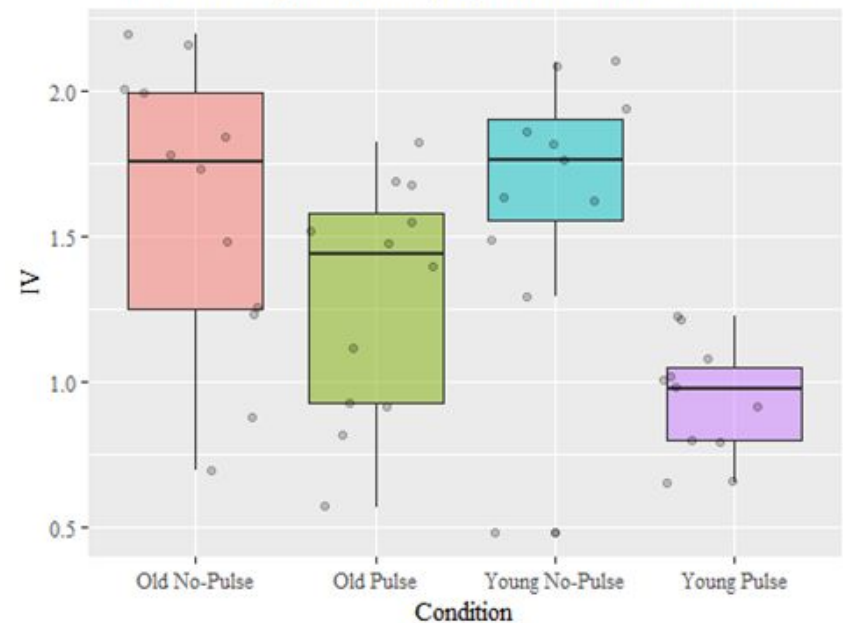


## Study 2: Results

Stability (IS) Across Pulse Conditions



Rhythm Fragmentation (IV) Across Pulse Conditions





### Study 1 (wheels)

- ▶ No significant results were obtained, which would appear to not be in line with previous findings (Edgar & Dement, 1991, Schroeder et al. 2012, Wolff & Esser, 2012; Yasumoto et al. 2015)

### ▶ Study 2 (Pulses)

- ▶ Significant findings that dark pulses improved rhythms on measures of stability and fragmentation
- ▶ Age differences



# Discussion

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## Potential Explanations:

- ▶ Level of arousal
- ▶ Scanners v wheels
- ▶ Intradaily Variability and Interdaily Stability



# Conclusion

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- ▶ Improvements in circadian rhythms can be made when both the light cycle and activity level are altered
- ▶ Suggestions for future research
  - ▶ additional outcome measures
  - ▶ long-term effects





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# References

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