On the Maturation of Circadian Rhythms in Core Body Temperature in Mice

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FUNDING: NINDS K08NS110924, NINDS R01NS13199, BCM Office of Research Seed Funding

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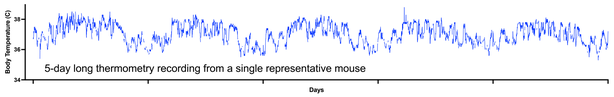
Oura Ring4

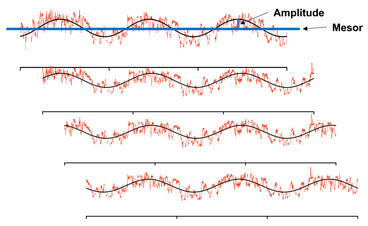
Background

Body temperature is a critical physiological parameter that affects (or is affected by) a host of biological processes. Circadian fluctuations in body temperature can be tightly coupled with circadian oscillations in activity and heart rate, but are less sensitive to environmental influences. Continuously collected measures of peripheral body temperature are now frequently provided by consumer wearables (E.g., Oura ring, Embrace). Despite its known biological relevance, continuous measurements of body temperature in rodent studies are often ignored because of the practical difficulties associated with repeated rectal probe-based techniques, the need for thermal imaging and/or the invasiveness of large telemeter implants. In this study, we employed lightweight radiofrequency ID (RFID) chips to continuously measure body temperature in group housed mice from early peri-weaning periods (P20) through to adulthood (P75). Our goal was to identify objective, home-cage based, digital biomarkers of physiological maturation that may be distorted in models of neurodevelopmental disorders.

Methods

Continuous thermometry was achieved using the UID Mouse Matrix, as follows. Wildtype mice (Tac:N:NIHS-BC background) were subcutaneously implanted with cylindrical RFID chips measuring 2x13mm (<1g) over the left thigh. Group housed mice in shoebox cages starting at postnatal day 20 (P20) or beyond were positioned over base plates that contain 8 antenna zones. Antennas were designed to record identifying information (implant ID), zone position and core body temperature from the RFID. Cage changes were conducted every 7-8 days. Mice were housed in a temperature and humidity- controlled satellite facility, with lights off between 1700 and 0500. Individual mouse level temperature data was obtained as time series at a sampling rate of 0.016Hz (1 value per minute). Time series of body temperature fluctuations were segmented into 3-day windows tallied every 6h. For each 3d window, we applied the cosinor model to calculate the **amplitude** and **mesor of** circadian temperature changes. In addition, we calculated a series of nonparametric measures, including **interdaily stability (IS)**, **intradaily variability (IV)** and **Shannon entropy.** We also applied detrended fluctuation analysis to calculate the scaling exponent **α** from the slope of the log-log plot of fluctuation versus window seizure.





α (fractal complexity)

$$F(s) \propto s^{\alpha} \implies \alpha = \frac{d \log F(s)}{d \log s}$$

Calculated by dividing the 3-day recording into non-overlapping windows at multiple scales (60, 360, 720, 1080 and 1440 minutes), detrending each window with a first-order polynomial, computing root mean square fluctuations at each scale, and estimating the slope of the log-log plot of fluctuation vs window size.

Intradaily Variability

$$\mathrm{IV} = \frac{\sum_{t=2}^{T}\left(x_t - x_{t-1}\right)^2/(T-1)}{\sum_{t=1}^{T}\left(x_t - \bar{x}\right)^2/T}.$$

Calculated as the ratio of the mean squared difference between successive hourly averaged temperature values to the total variance of hourly averaged temperatures, quantifying fragmentation of temperature rhythms within each day.

Interdaily Stability

$$\mathrm{IS} = \frac{\sum_{s=1}^{24}\left(\bar{x}_s - \bar{x}\right)^2/24}{\sum_{t=1}^{T}\left(x_t - \bar{x}\right)^2/T},$$

Calculated as the ratio of the variance of hourly mean temperature across the 24-hour day to the total variance of all hourly temperature values, quantifying the strength of coupling between the rest-activity rhythm and the 24-hour light-dark cycle.

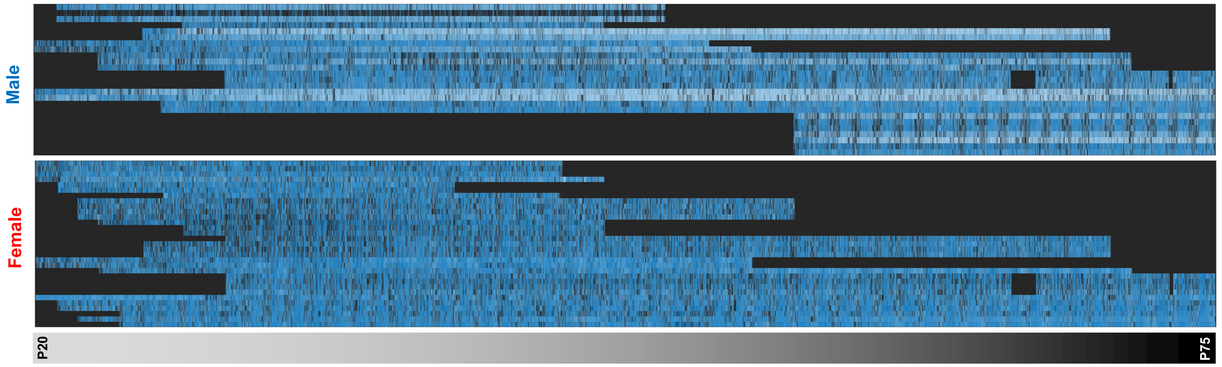
Shannon Entropy

$$H = -\sum_{i=1}^{k} p_i \log_2 p_i$$

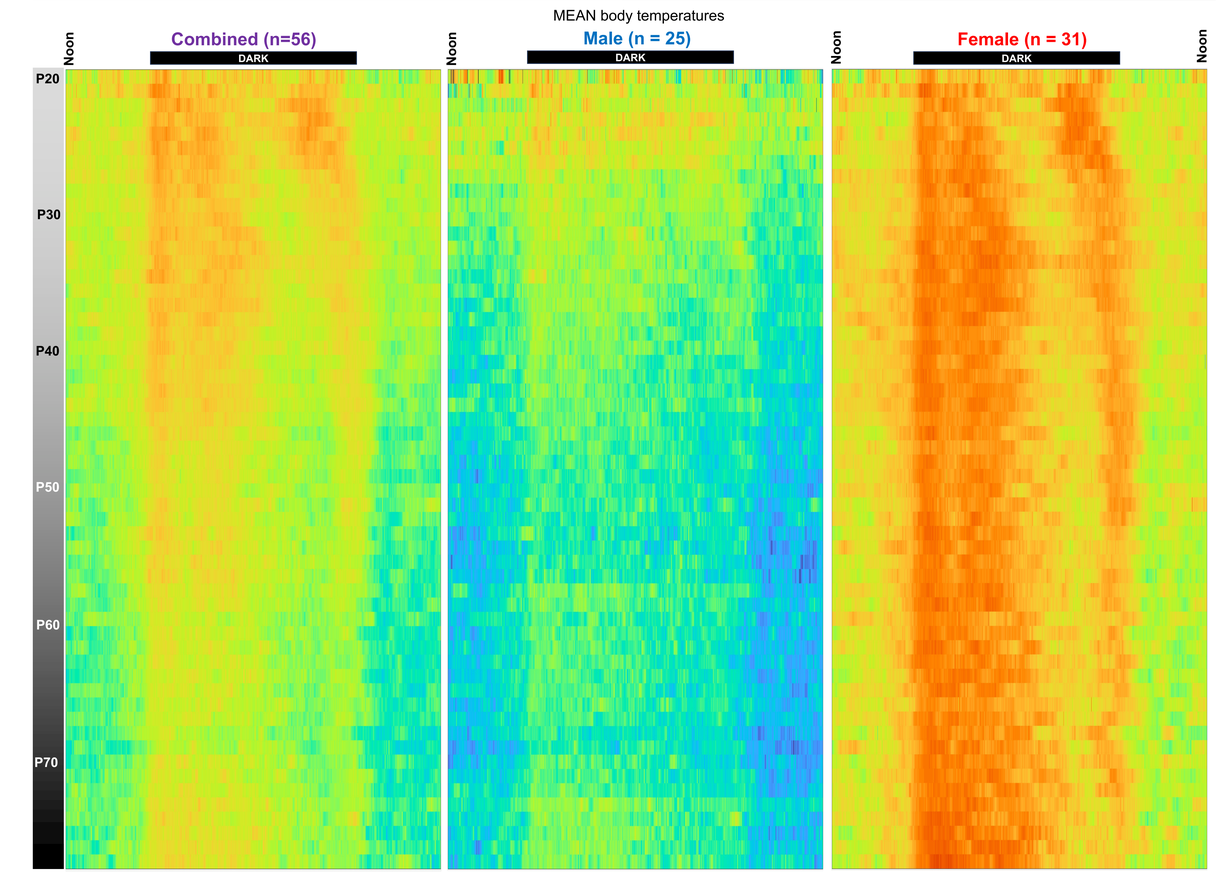
Quantifies the distributional complexity of temperature values within each window

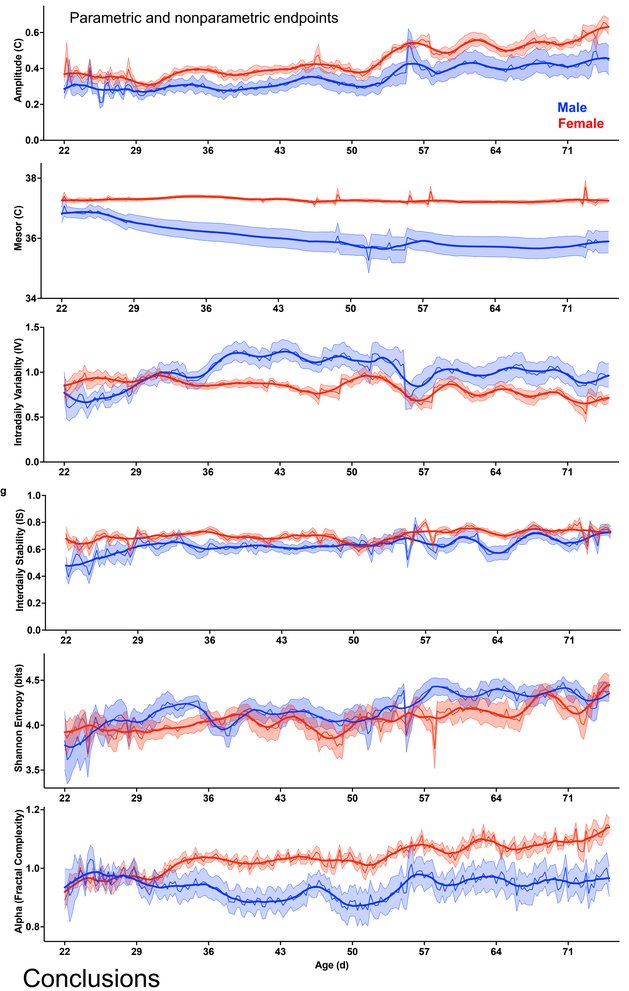
Results

Continuous thermometry was recorded from cohorts of group housed mice.



MEAN body temperatures





Conclusions

In this study, we leverage continuous thermometry (achieved via subcutaneously implanted temperature transponders) to describe neurodevelopmental changes in naturally occurring circadian rhythms of body temperature. Between P20 and P75, we find:

- Gradual increases in circadian amplitude
- Gradual reductions in circadian mesor (in males but not female mice)
- Gradual reductions in fractal complexity (in females but not males)
- No obvious monotonic changes in interdaily stability or intradaily variability

These findings are consistent with cross-sectional data collected from human subjects (Ley et al JAMA Internal Medicine 2023), showing that body temperatures are higher in female subjects. In ongoing studies, we are actively exploring how these “growth” curves are disrupted in mouse models of neurodevelopmental disorders with or without spontaneous seizures.