Characterizing a Mouse Model for Nonphotic Clock Resetting Studies

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What Makes Our Clock Tick?

An internal "clock" that resides in the brain, known collectively as circadian rhythms, regulates and coordinates different systems in the body to an approximately 24-hour cycle. Our clock is responsible for many physiological functions, ranging from sleep and wake cycles at the behavioral level, to communicating to our body at the molecular level, requesting the release or inhibition of particular hormones to bring about a desired response in order to maintain homeostasis. Because human health can be significantly influenced by disruption in circadian rhythms, studies on how these clocks reset are important.

Since many genetic modifications exist for the mouse model, the mouse is a very useful model organism to study genes associated with resetting of circadian rhythms. One of our current goals is to characterize the conditions under which mice show optimal clock resetting.

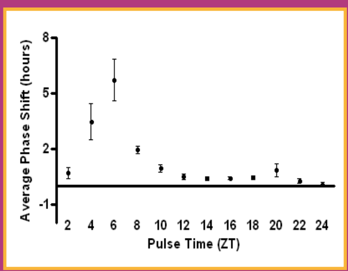
When Do Mice Best Reset Their Clock?

- In cages with running wheels, male mice were held for 3 weeks in 12 hours of light/12 hours of dim light to entrain each individual's clock to a common rhythm. Entrainment was determined by when the mice began running each night (onset of activity).
- We observed clock resetting (phase shifting) in response to light-to-dark transitions at different time points (phases) of the circadian cycle in mice.
- Phase shifting data during different phases were used to generate a phase response curve as shown below.
- These results are currently used in our pilot studies on nonphotic clock resetting in mice.

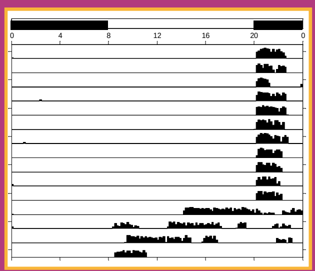
Sex-Specific Aspects of Clock Resetting Exist in Mice

- In cages with running wheels, 10 female and 10 male mice were held for 3 weeks in 12 hours of light/12 hours of dim light to entrain each individual's clock to a common rhythm. Entrainment was determined based on when the mice began running each night (onset of activity).
- We compared several animal responses to a transition to constant darkness in the middle of the subjective day (ZT 6), when mice best phase-shift. This may not be reflective of what happens at all phases.
- Results: **Males were found to phase shift significantly greater than females, and females typically had a delayed onset of activity rather than an early onset as males had.**

Phase Response Curve



Greatest Phase Shift at ZT6



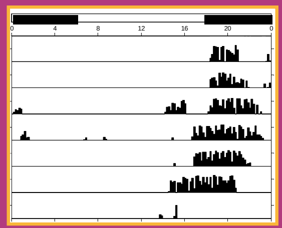
Time (Hours)

FIGURE KEY

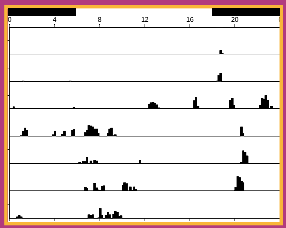
- Transition to constant darkness at ZT 6 on this day (indicated by arrow)
- Each black bin represents number of wheel revolutions per 10 minutes
- Each row is one day (24 hours)
- Pre- and Post-pulse (lights off) onsets were measured one day before pulse and one day after pulse, respectively.

Results: **Mice showed large phase shifts during the middle of the subjective day, with the greatest phase shifts observed at Zeitgeber Time (ZT) 6. No significant phase shifting occurred in response to light-to-dark transitions during the subjective night. This was expected since other organisms, such as hamsters, also do not significantly reset their clock in response to light-to-dark transitions during the subjective night.**

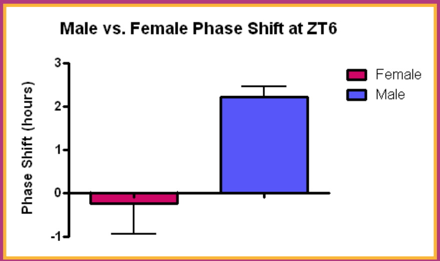
Male Phase Shift at ZT6



Female Phase Shift at ZT6



Time (Hours)



Credit is rightly given to:
- *Sarah Tillman for her pioneer work on circadian rhythms in mice*
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