F385. Arousal from torpor advances circadian phase without effect on period in mice

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Abstract:

Daily torpor is an energy-conserving physiological state, employed by a wide variety of animals to survive periods of food scarcity or challenging environmental conditions by transiently reducing metabolic rate, body temperature, and activity. Its impact on circadian rhythms remains poorly defined. While the circadian clock is known to be temperature-compensated, and some evidence exists regarding seasonal hibernators, it is unclear if the pacemaker continues to oscillate, arrests, or shifts phase during daily torpor.

We investigated these dynamics in mice using a fasting-induced torpor (FIT, n=12) model (food deprivation starting at 12 hours after lights on, at Zeitgeber Time (ZT) 12) and a "synthetic" torpor (ST, n=4) model, induced via chemogenetic activation of neurons in the Preoptic Area (POA) of the hypothalamus. To isolate the specific effect of torpor on circadian rhythms, we employed a within-subject crossover design. We monitored wheel-running activity and core body temperature in the same mice in constant darkness (DD) following arousal from a torpor bout (Torpor DD), and after a matched control period without manipulation (Control DD). This allowed us to directly evaluate changes in the intrinsic circadian free-running period (τ) and phase within each animal, free from the confounding effects of photic entrainment. We used Lomb-Scargle periodograms, fitted over the 5 days following torpor, and paired t-tests to quantify and compare τ between Torpor DD and Control DD. To quantify phase shifts, we calculated the "activity onset deviation" (AO deviation): the difference between observed activity onsets and those predicted by projecting the baseline phase (mean activity onset time of the 5 days prior to DD) forward using the individual τ from Control DD. A two-way repeated measures ANOVA (or mixed-effect model in case of missing datapoints), for the factors “Time” and “Experimental Condition”, followed by Sidak's multiple comparisons tests was used for statistical analysis.

Our results demonstrate that torpor did not significantly alter τ in either model (FIT: Torpor DD: 24.15±0.06 hours vs. Control DD: 24.1±0.06 hours; paired t-test: $t_{(11)}$=1.076, p=0.305; ST: Torpor DD: 23.78±0.17 hours vs. Control DD: 24.07±0.15 hours; paired t-test: $t_{(3)}$=1.509, p=0.228). This indicates that during torpor the clock does not "freeze" or lose organization despite the profound drop in core body temperature. However, the expression of a torpor bout was associated with a consistent phase advance in activity onset, for both FIT (mean AO deviation: 40.8 ± 7.8 minutes) and ST (mean AO deviation: 46.8 ± 30.6 minutes). Although the magnitude of the observed phase advance was similar for FIT and ST, this reached statistical significance for FIT ("Experimental Condition" $F_{(1,11)}$=27.04, p< 0.001) but not for ST ("Experimental Condition" $F_{(1,3)}$=2.266, p=0.229), likely due to current sample size limitations (experiments ongoing). Notably, arousal from torpor tended to occur during the late subjective day, a time window when non-photic arousal stimuli are known to exert a potent entraining effect on the central circadian oscillator, resulting in a phase advance. Our study therefore suggests that emergence from torpor, and the associated behavioural arousal, can represent the stimulus responsible for the observed phase shift.