

Glucose Clearance Recovery in Hibernating Arctic Ground Squirrels During Early Arousal

Hannah Hausmann^{1,2} Nicholas Clark^{1,2}, Bernard W. Laughlin², Jet Nguyen², Samantha Medbury², Kay Quintana Torres², Neeraj K. Lal^{1,3} Kelly Drew^{1,2}

¹Department of Chemistry and Biochemistry, University of Alaska Fairbanks ²Institute of Arctic Biology and Center for Translational Research in Metabolism, University of Alaska Fairbanks ³Monell Chemical Senses Center, Philadelphia, Pennsylvania, USA

Introduction

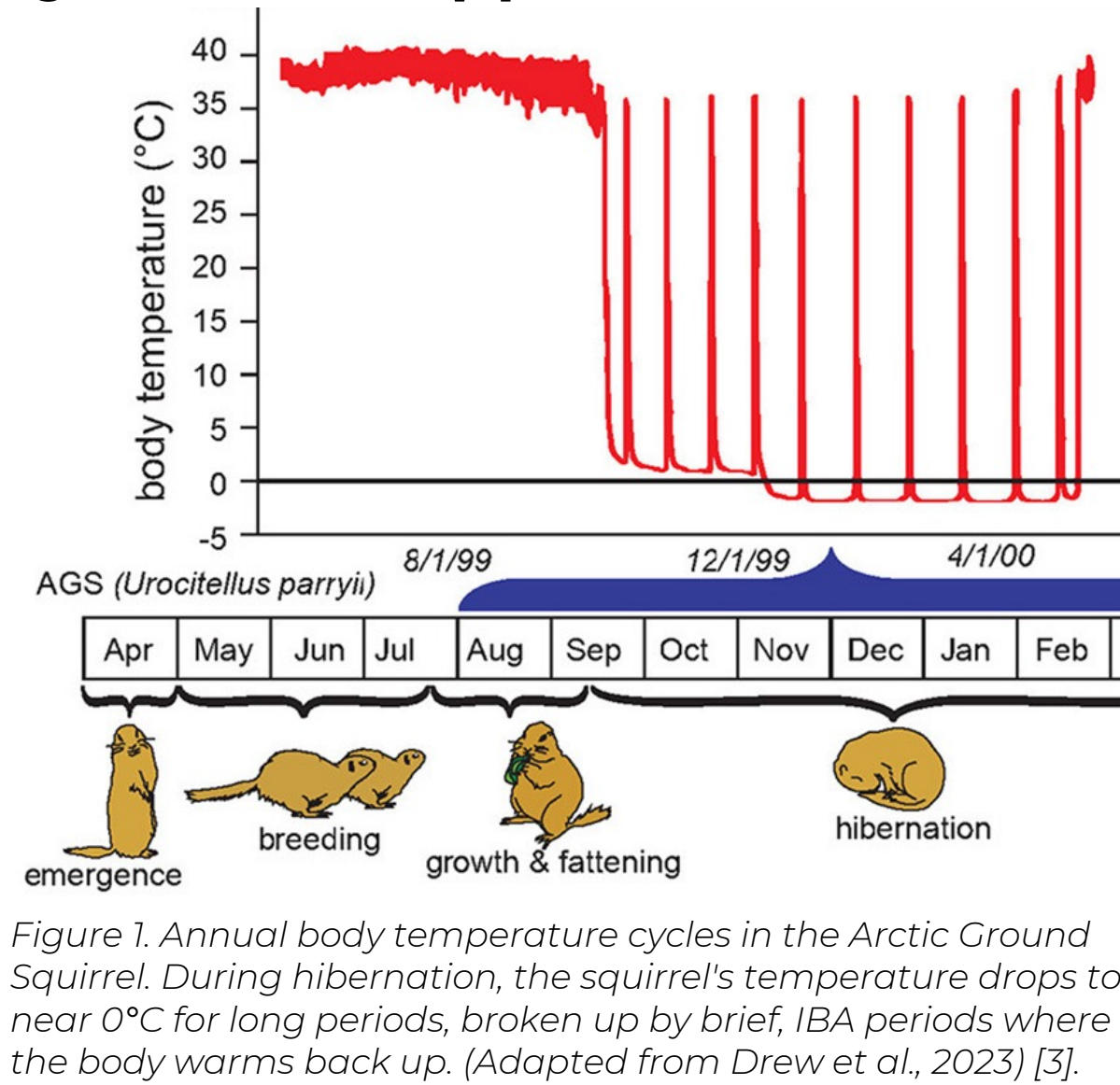
Arctic ground squirrel hibernation represents an extreme model of reversible insulin sensitivity and metabolic flexibility.

During hibernation, basal metabolic rate is suppressed by more than 98%, and carbohydrate metabolism is severely suppressed [1].

Medical cooling and synthetic (CHA-induced) torpor often cause harmful hyperglycemia in non-hibernators. The arctic ground squirrel provides a natural blueprint for regulating glucose clearance during hibernation [2].

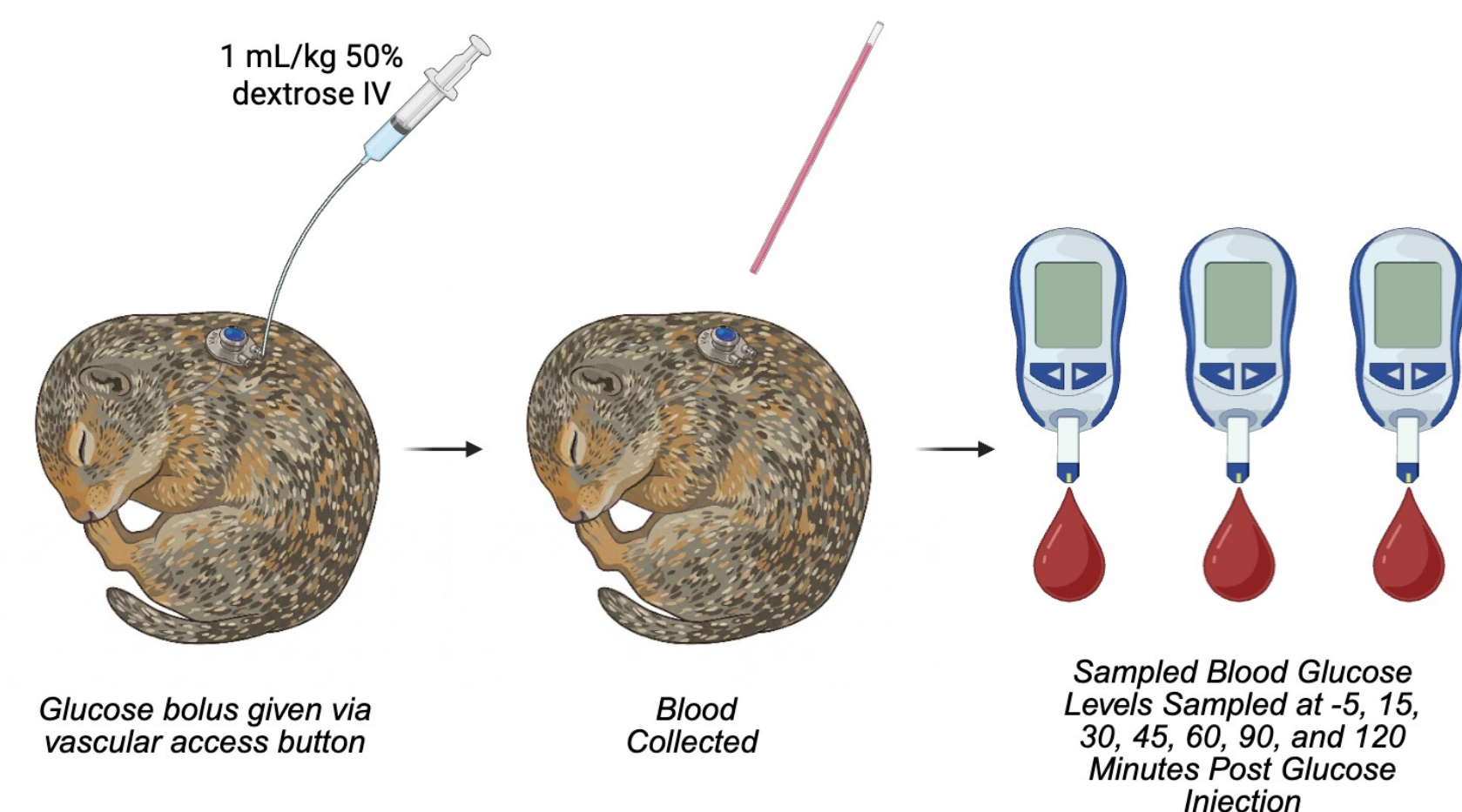
Objective: Determine how early arousal from a hibernation state influences glucose clearance.

Hypothesis: Glucose clearance is suppressed during torpor but recovers during early arousal with processes independent of body temperature.

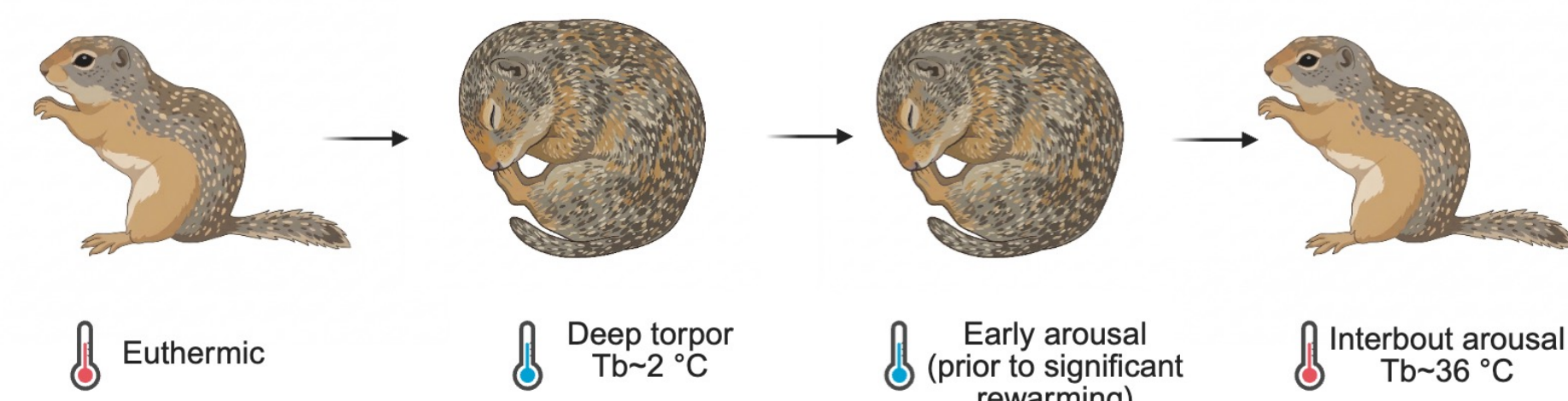


Methodology

Yearling female arctic ground squirrels (n=3) were instrumented with femoral artery and vein catheters (Instechlabs.com) and abdominal temperature transmitters (DSI Inc). Animals were initially housed at 16°C under a 12:12 L:D photoperiod. Beginning Sept 21, the light cycle was adjusted to mimic the North Slope of Alaska, transitioning to a winter 4L:20D cycle on Oct 7. Ambient temperature was ramped from 16°C to 2°C between Oct 4 and Oct 6.

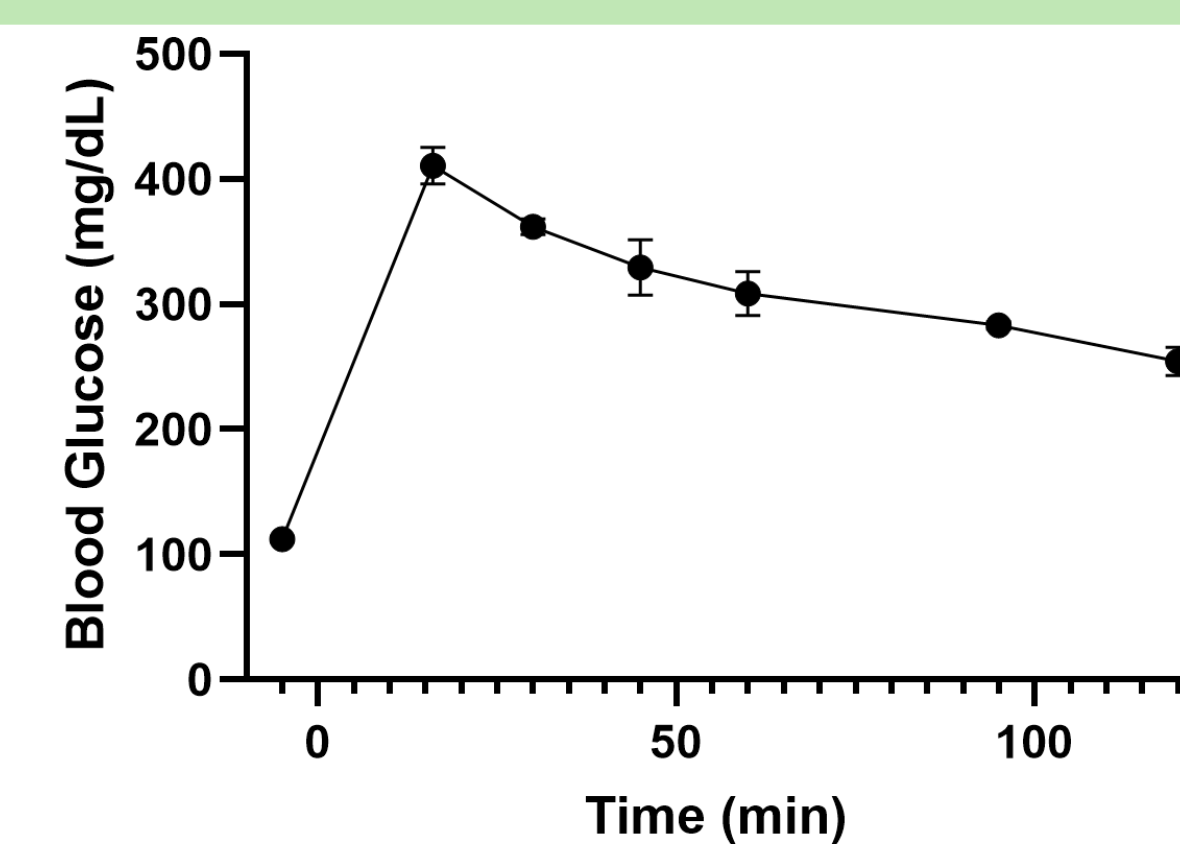


Glucose tolerance tests were performed across four distinct physiological states. Sampling began in September at the end of the seasonal fattening phase (Prehibernation, euthermic), and during the hibernation season at time points defined as Hibernating, Early Arousal, and Interbout Arousal (IBA)).

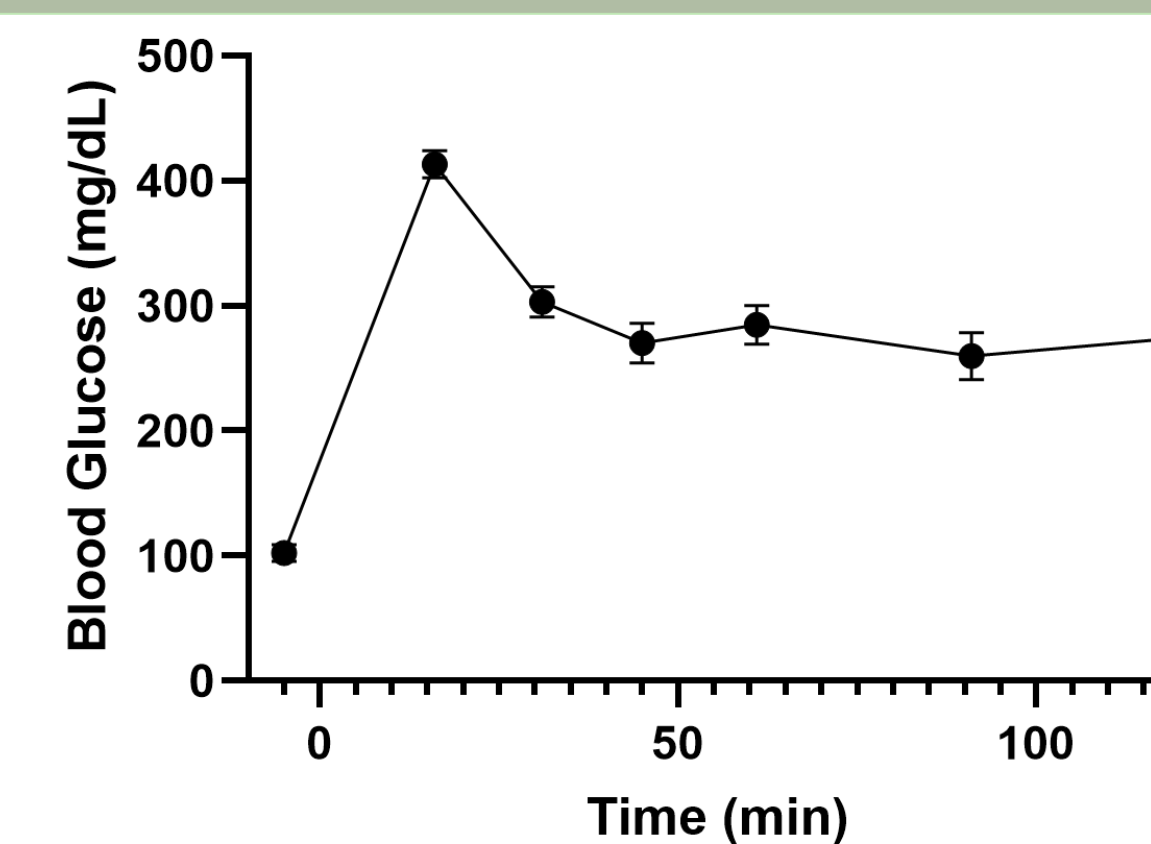


Results

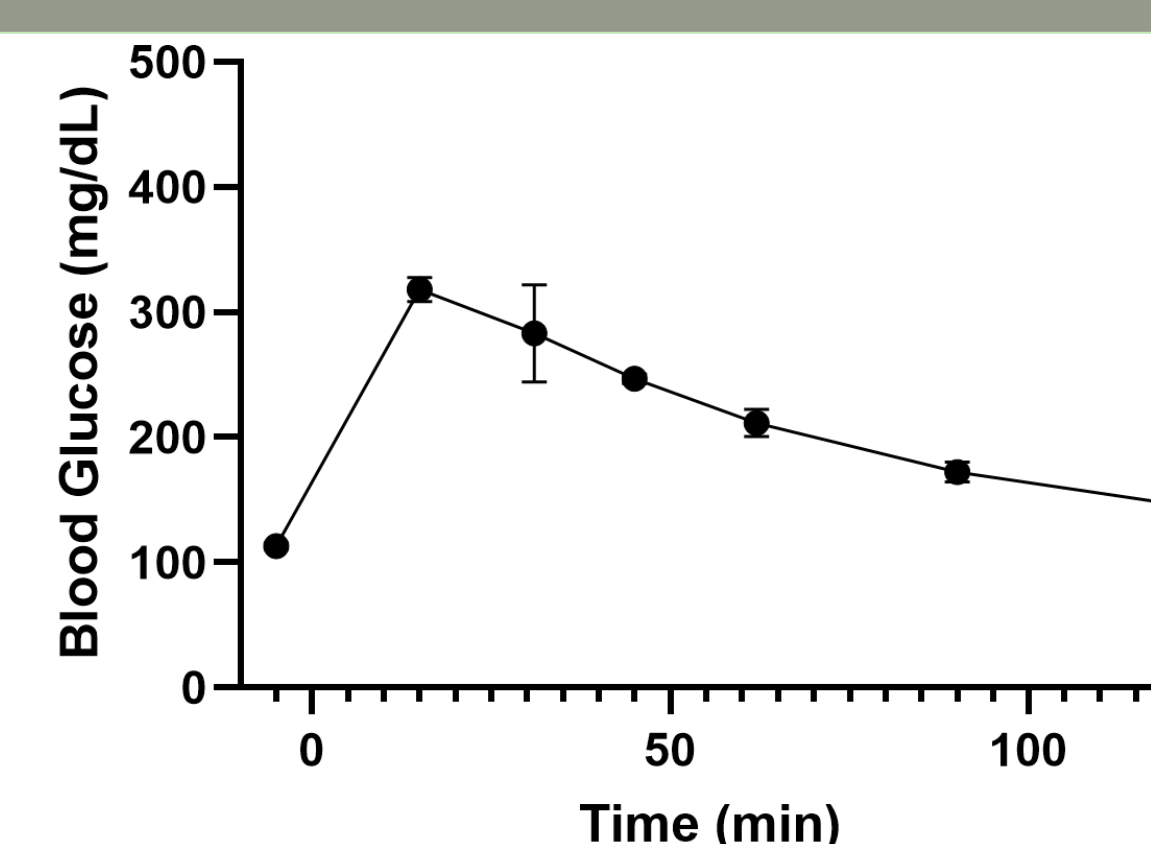
Glucose Clearance (Cold Hibernating)



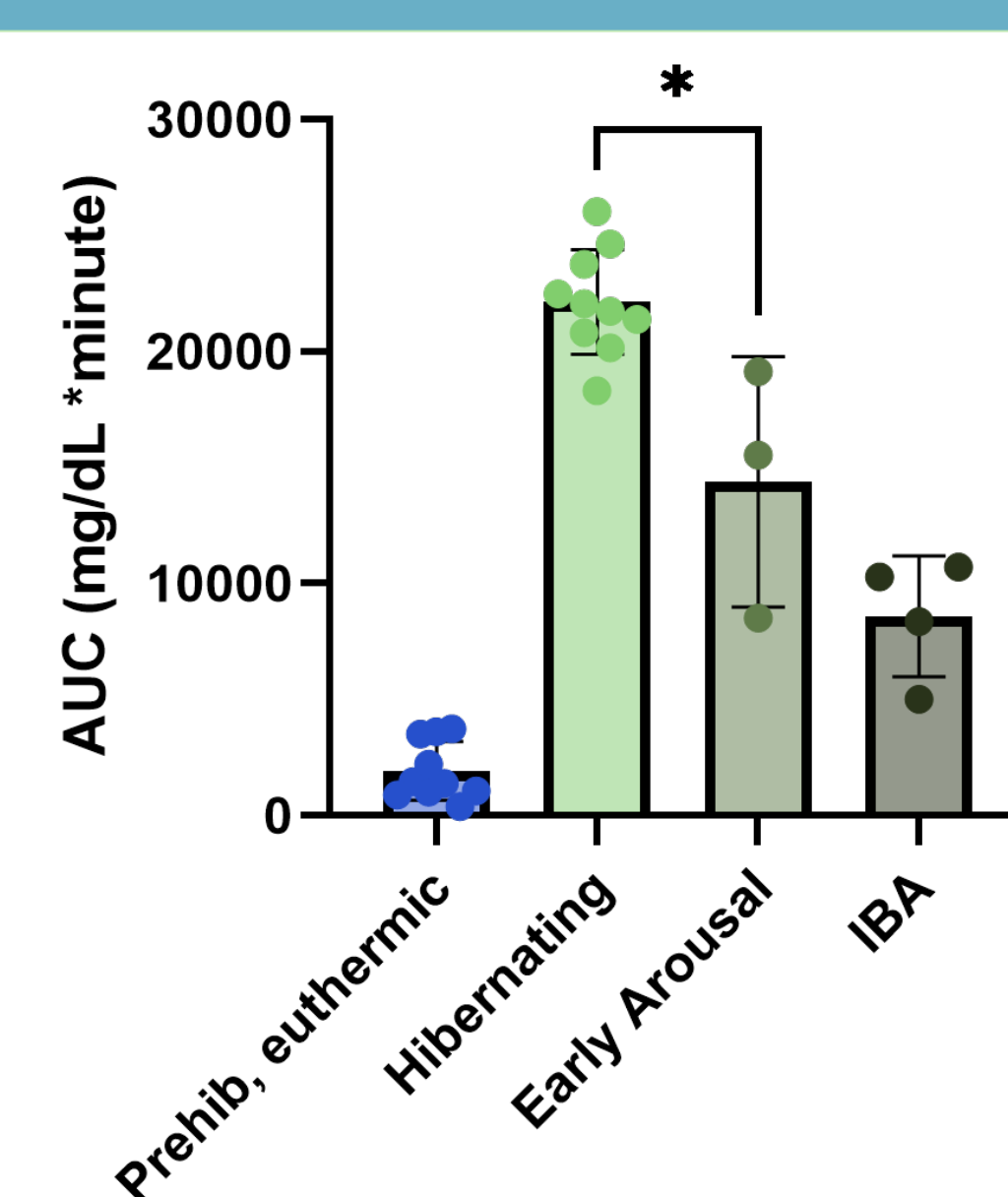
Glucose Clearance (Early Arousal)



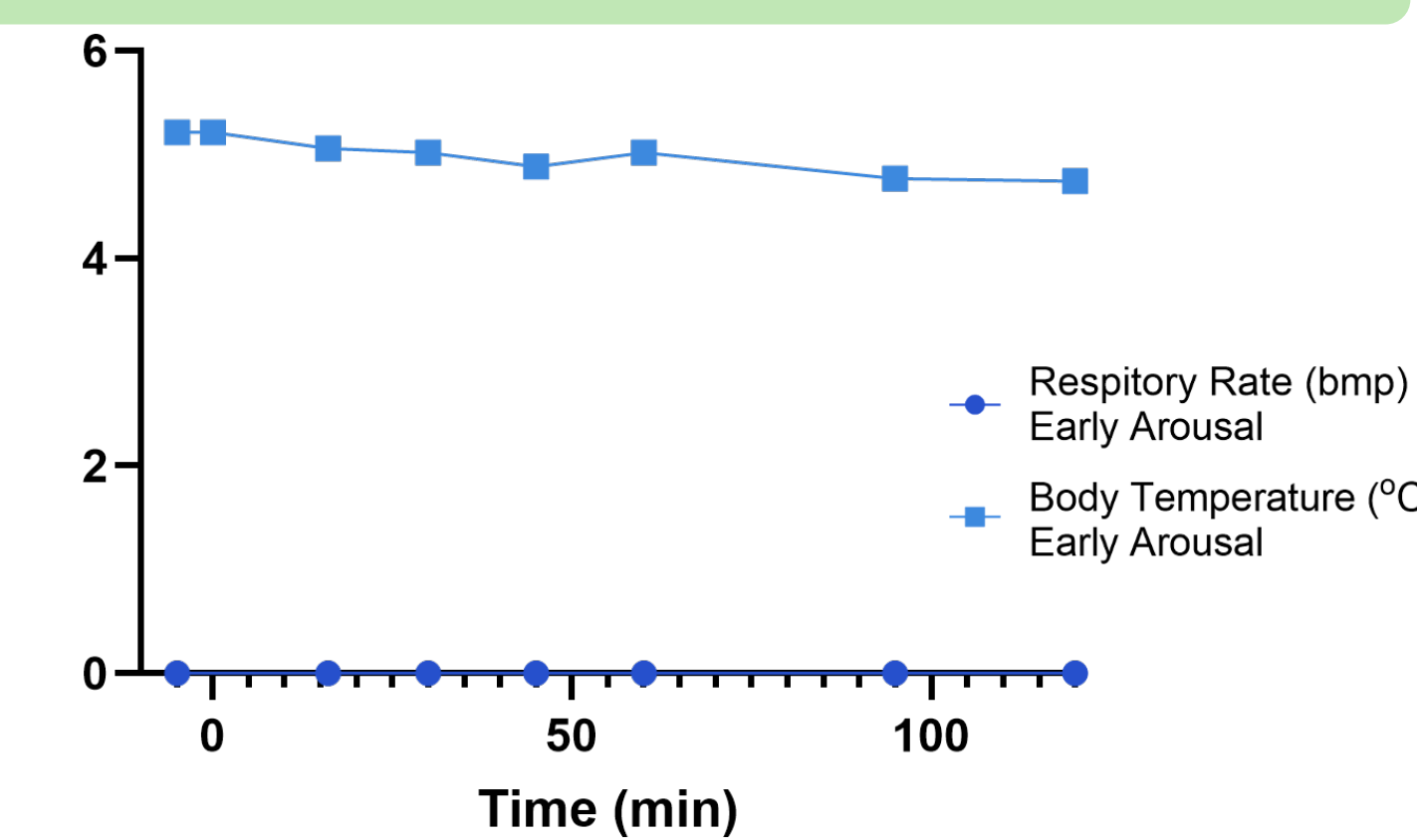
Glucose Clearance (IBA)



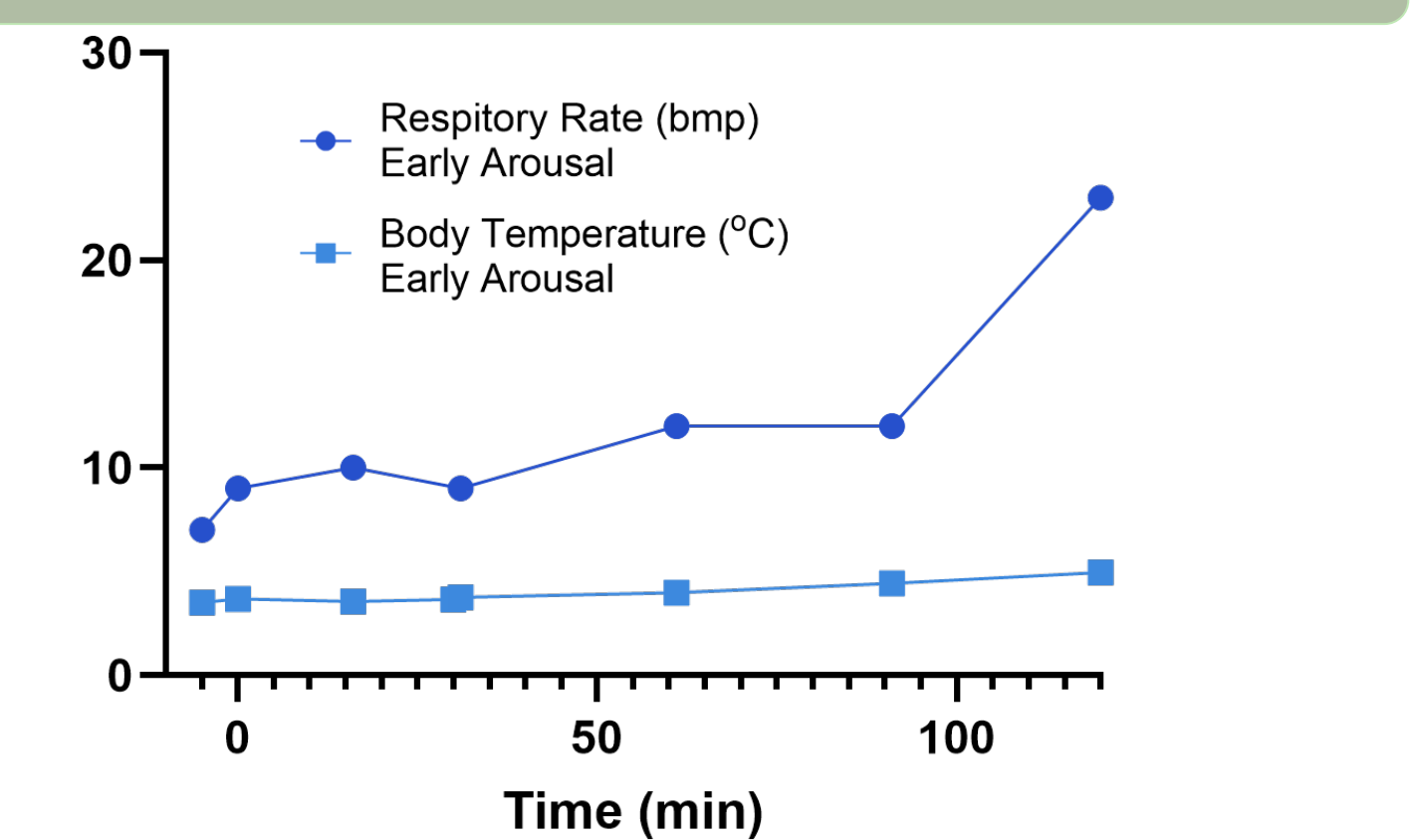
AUC of Glucose Clearance



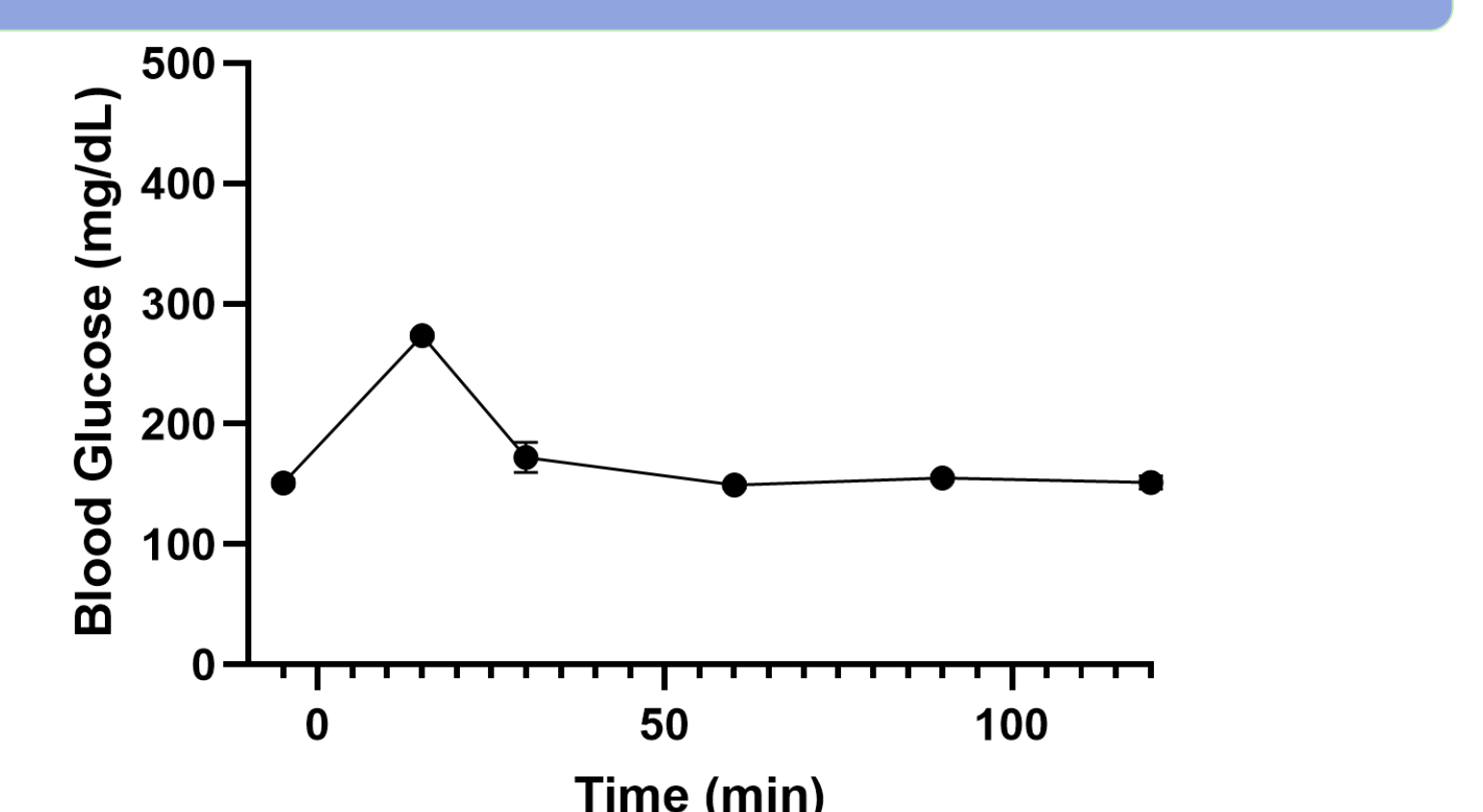
Respiratory Rate & Body Temperature (Hibernating)



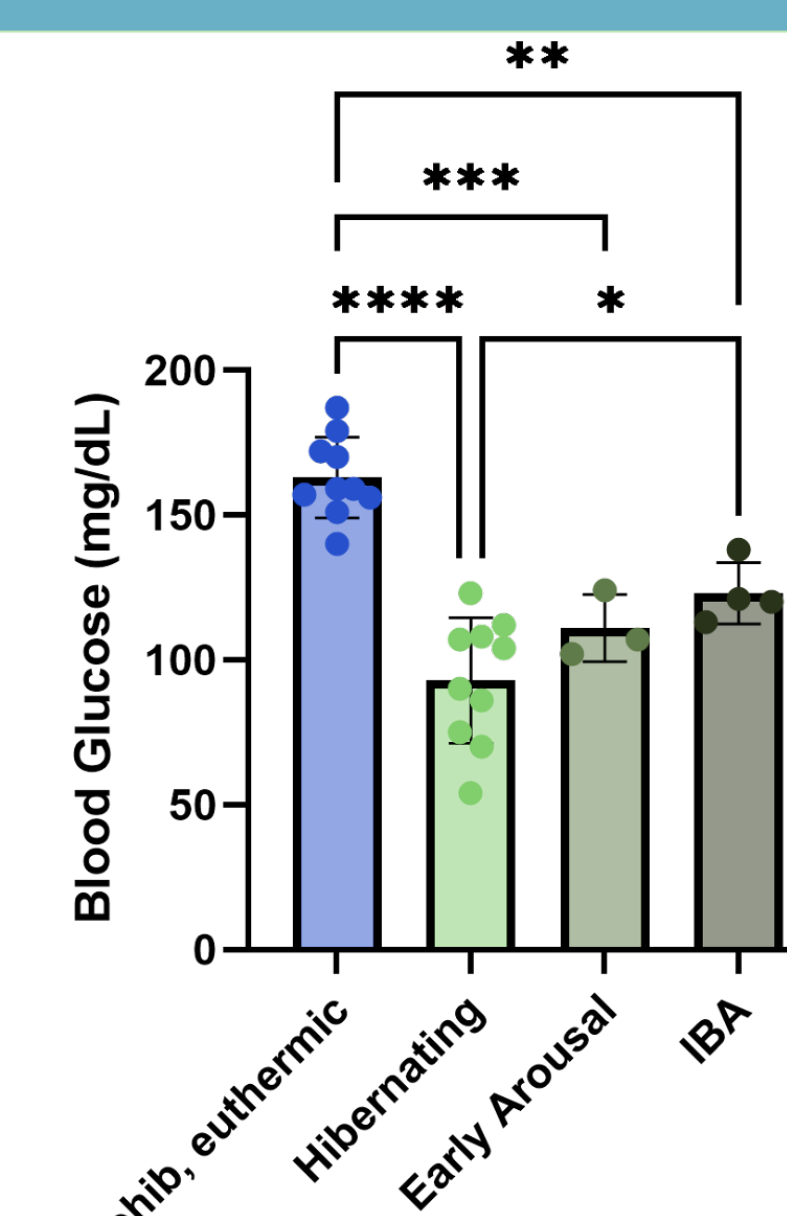
Respiratory Rate & Body Temperature (Early Arousal)



Glucose Clearance (Prehibernation Euthermic), Tb 36.7



Average Baseline Glucose



Conclusion

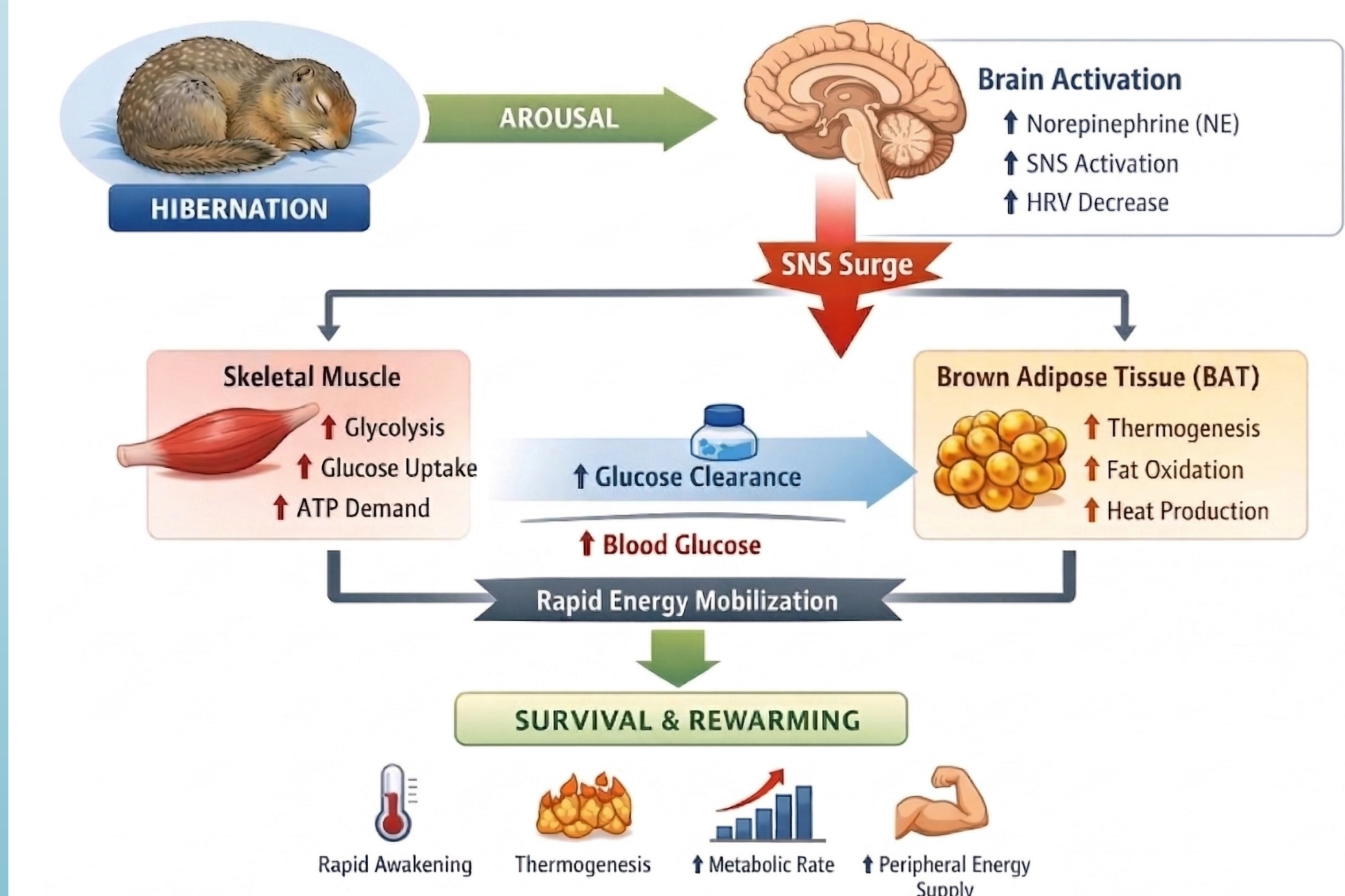
Arctic ground squirrels were evaluated following their seasonal fattening phase.

Deep torpor significantly reduces glucose clearance, mirroring the overall suppression of basal metabolic rate during hibernation.

Glucose clearance is restored abruptly at the onset of early arousal, preceding any measurable increase in body temperature.

These results indicate that the processes restoring glucose utilization are initiated before thermal recovery.

This early restoration implies that neural or circulatory mechanisms, rather than temperature-dependent enzyme kinetics, trigger the reactivation of carbohydrate metabolism.



Acknowledgements

This work was supported by the Branco Weiss Fellowship (to N.L.), NASA grants NNX13AB28A and 22-EPSCoR-0018, and NIH grants P20GM130443 and P20GM103395, and Alaska Space Grant Undergraduate Research support to HH, JN, KQT and Graduate Student support to NBC (80NSSC20M0070)

References

- [1] Frerichs, K. U., Diemel, G. A., Cruz, N. F., Sokoloff, L., & Hallenbeck, J. M. (1995, Feb). Rates of glucose utilization in brain of active and hibernating ground squirrels. *Am J Physiol*, 268(2 Pt 2), R445-453. <https://doi.org/10.1152/ajpregu.1995.268.2.R445>
- [2] Laughlin, B. W.; Bailey, I. R.; Rice, S. A.; Barati, Z.; Bogren, L. K.; Drew, K. L. Precise control of target temperature using N6-cyclohexyladenosine and real-time control of surface temperature. *Ther. Hypothermia Temp. Manag.* 2018, 8 (3), 154-161.
- [3] Drew, K. L.; Bhowmick, S.; Laughlin, B. W.; Goropashnaya, A. V.; Tøien, Ø.; Sugiura, M. H.; Wong, A.; Pourrezaei, K.; Barati, Z.; Chen, C.-Y. Opportunities and Barriers to Translating the Hibernation Phenotype for Neurocritical Care. *Front. Neurol.* 2023, 14, 1009718.