

Dynamics of Protein Restriction on Protein Preference in Male C57BL/6J Mice

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Introduction/Background

- Animals must respond to macronutrient deficiencies to survive.¹
- Animals exhibit behavioral and physiological adaptations to macronutrient deficiency.²
- Protein may be the most important macronutrient to regulate because it cannot be stored in the body.³
- Animals fed a low protein diet consume more food and exhibit a higher preference for protein solution versus carbohydrate solution compared to animals fed a normal protein diet.⁴

Research Questions

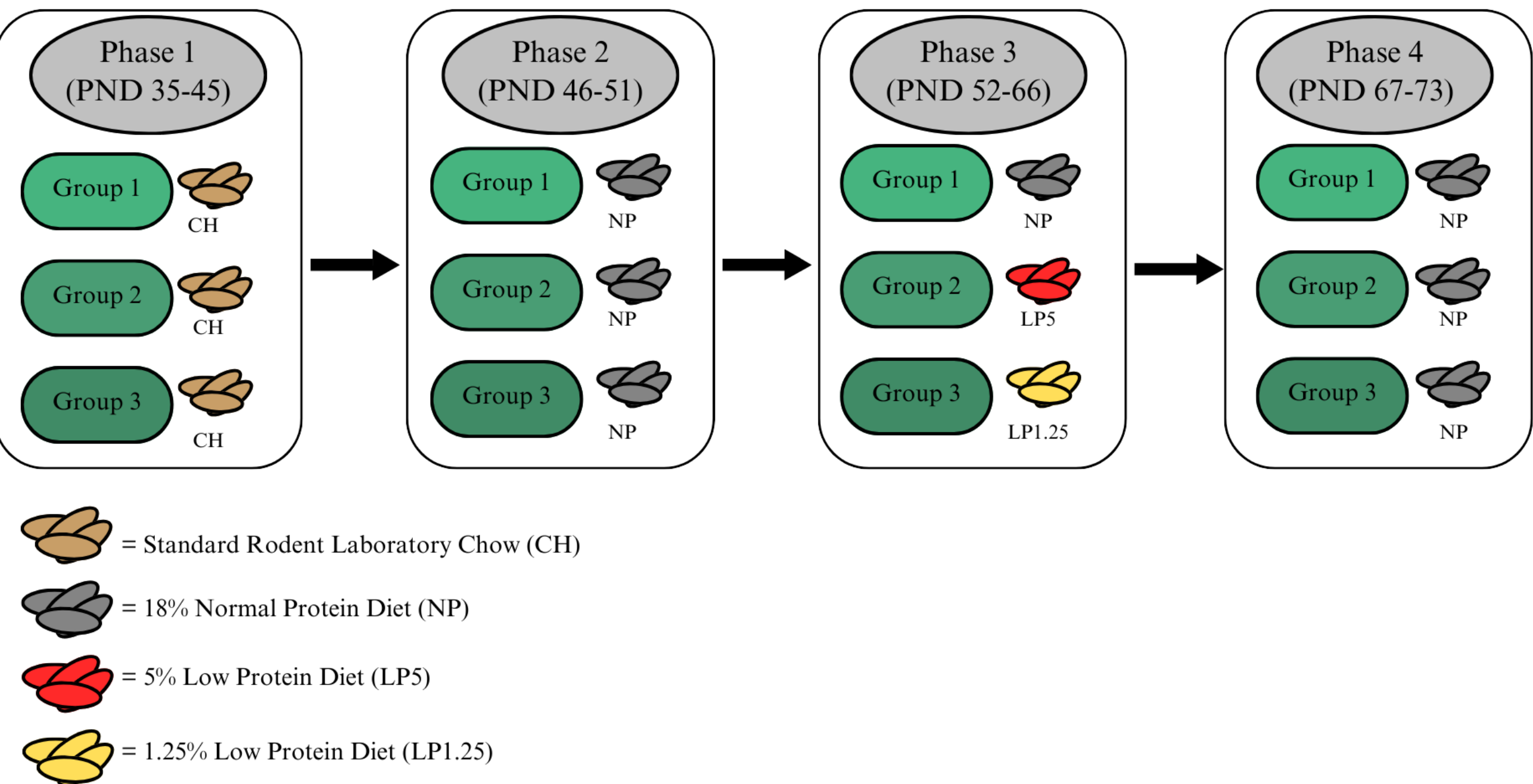
- How does protein preference shift dynamically with changes in dietary protein?
- Is preference dependent on degree of restriction?
- Does preference persist after normalization of protein intake?

Methods

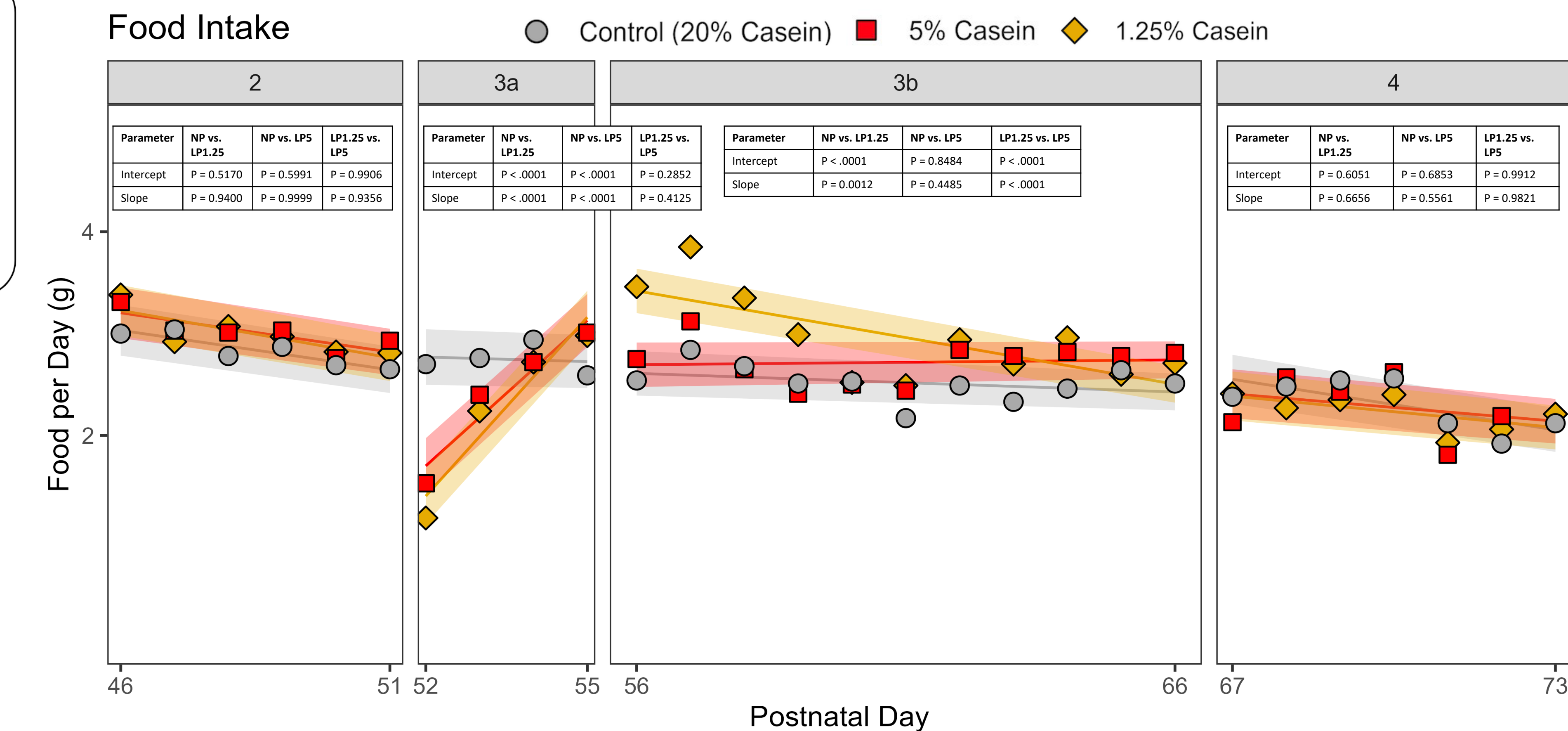
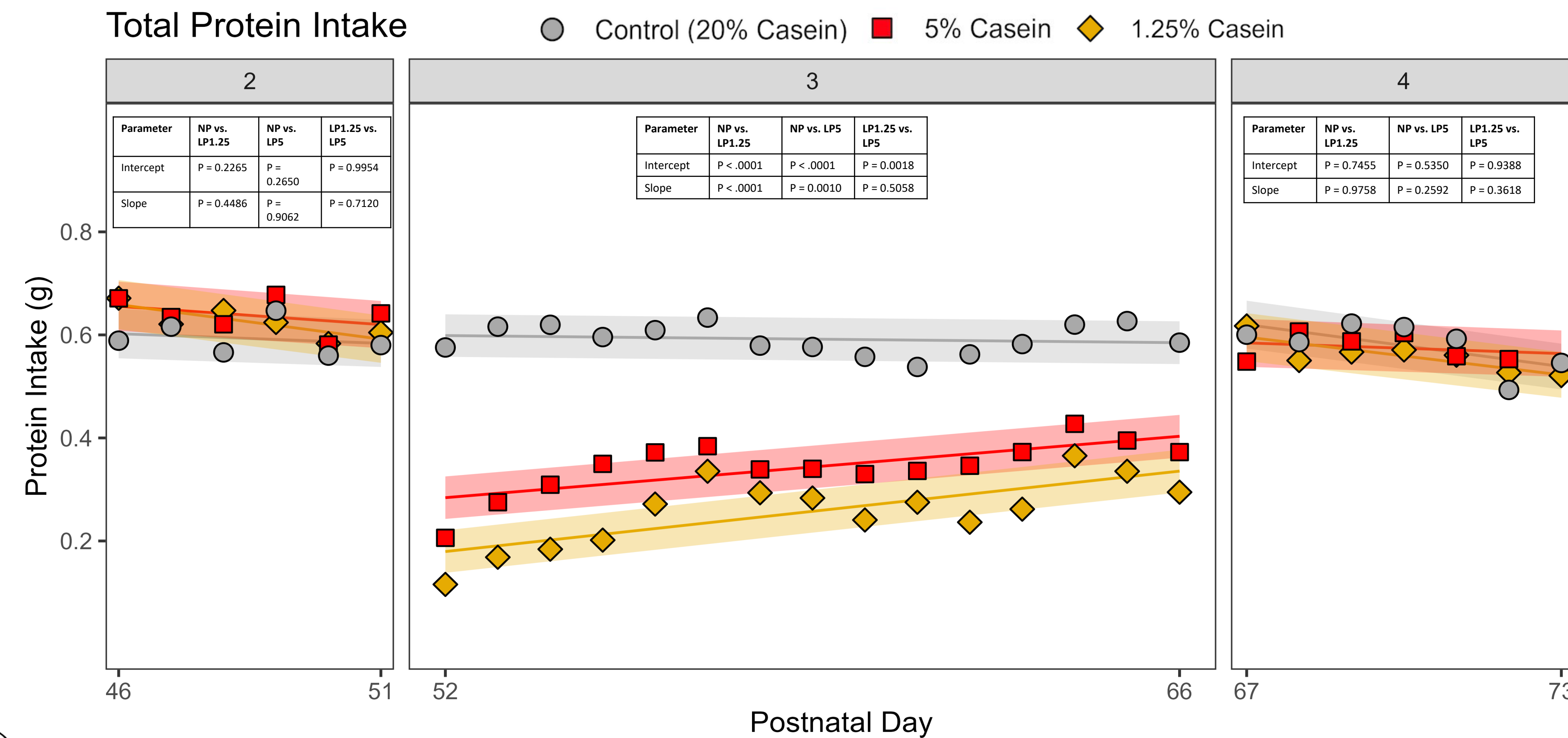
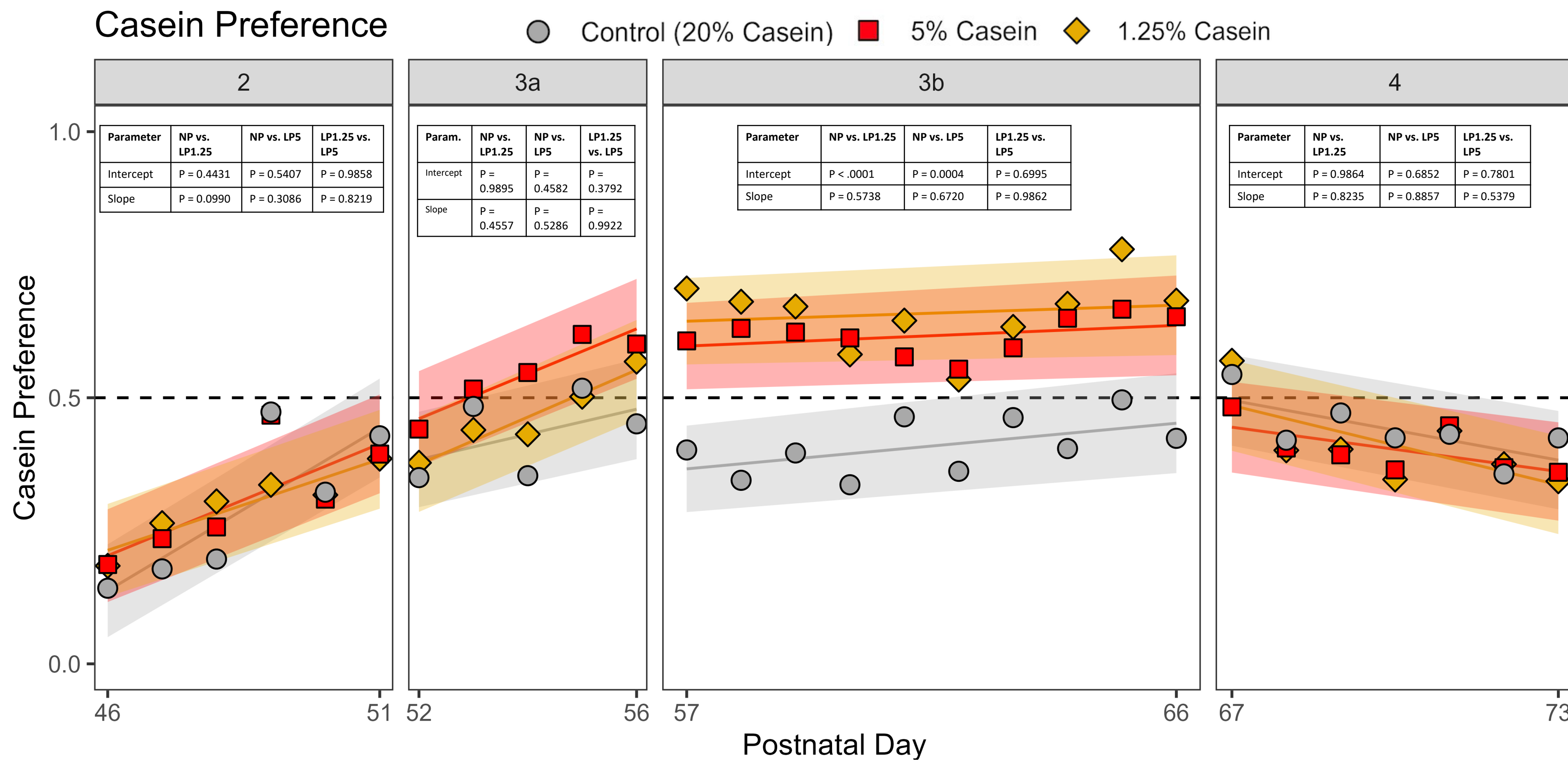
- **Subjects:** 30 male C57BL/6J mice.
- **Housing:** Individually housed in temperature and humidity-controlled rooms on 12-hour light/dark cycles.
- **Preference assessment:** All mice had 24-hour/day access to 4% casein (protein) + 0.2% saccharin solution, 4% maltodextrin (carbohydrate) + 0.2% saccharin solution, and food.



- **Outcomes:** Casein preference, total protein intake, and food intake
- **Timeline**



Results



Conclusions

1. Initial development of preference occurred gradually.
2. Preference for casein decreased rapidly following normalization of protein intake.
3. Shifts in casein preference were consistent with between-group studies.⁴
4. Shifts in preference did not require pre-exposure to diets without solutions.
5. Casein preference did not depend on degree of dietary protein restriction, suggesting possible ceiling effect on solution intake.
6. Prior protein restriction did not induce persistent effects on preference, contrary to some suggestions⁵, perhaps because continuous exposure to solutions allowed more rapid learning of post-ingestive consequences.

References

- ¹Kanarek, R. B. (1985). Determinants of dietary self-selection in experimental animals. *American Journal of Clinical Nutrition*, 42(5), 940-950. <https://doi.org/10.1093/ajcn/42.5.940>
- ²Torres, F., Khan, S., Fernandez-Kim, S. O., Spann, R., Albarado, D., Wagner, T. J., Morrison, C. D., & Soto, P. L. (2022). Dynamic effects of dietary protein restriction on body weights, food consumption, and protein preference in C57BL/6J and *Fgf21*-KO mice. *Journal of the Experimental Analysis of Behavior*, 117(3), 346-362. <https://doi.org/10.1002/jeab.745>
- ³Simpson, S. J., Le Couteur, D. G., James, D. E., George, J., Gunton, J. E., Solon-Biet, S. M., & Raubenheimer, D. (2017). The Geometric Framework for Nutrition as a tool in precision medicine. *Nutrition and Healthy Aging*, 4(3), 217-226. <https://doi.org/10.3233/NHA-170027>
- ⁴Murphy, M., Peters, K. Z., Denton, B. S., Lee, K. A., Chadchankar, H., & McCutcheon, J. E. (2018). Restriction of dietary protein leads to conditioned protein preference and elevated palatability of protein-containing food in rats. *Physiology & Behavior*, 184, 235-241. <https://doi.org/10.1016/j.physbeh.2017.12.011>
- ⁵Soto, P. L., & Morrison, C. D. (2024). Persistent behavioral and physiological effects of dietary protein restriction. *bioRxiv*, 2024.2003.2004.583396. <https://doi.org/10.1101/2024.03.04.583396>

Acknowledgements

Funding provided by AREA Grant R15DK139555 from the National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute of General Medical Sciences

