

Sex-Dependent Effects of Bisphenol-A Exposure on Obesity Development in Mice

^{1,2}Mavanji V, ¹Kram B, ¹Ahmed A, ¹Sandoval Caballero CL, ¹Roemer Z, ^{1,3}Kotz CM.

¹Department of Integrative Biology and Physiology, University of Minnesota, Minneapolis, Minnesota, USA; ²Research Service, Minneapolis VA Healthcare System, Minneapolis, Minnesota, USA

³GRECC, Minneapolis VA Healthcare System, Minneapolis, Minnesota, USA



Endocrine Disrupting Chemicals as Obesogens

- Bisphenol A (BPA), a widely used plastic-related chemical and endocrine disruptor, which accumulates in adipose tissue once inside the body.
- BPA has been shown to promote obesity through increased adipogenesis.
- Endocrine disruptors may contribute to obesity by impairing the secretion or sensitivity of various hormones such as GLP-1.
- BPA is also a xenoestrogen, which suggests there may be alternative mechanisms and effects between sexes.

Research Objective and Hypothesis

- This study investigates how exposure to BPA during the perinatal period contributes to the development of metabolic disease, specifically obesity and Type 2 Diabetes Mellitus (T2D).
- We hypothesize that developmental BPA exposure alters normal metabolic regulation, leading to increased adiposity index (fat mass/lean mass), weight gain, and food intake by disrupting key metabolic hormones.

Methods

- Pregnant CD-1 mice are exposed to BPA or a placebo through extended-release pellets from gestational day 8 to weaning.
- Offspring are assigned by sex to either a high-fat diet (HFD) or a low-fat chow diet (High carbohydrate diet, HCD), resulting in 10 mice per sex per diet group.
- Over 6 months, body weight, body composition, food intake, physical activity, and energy expenditure are measured.
- At 6 months, mice undergo an oral glucose tolerance test, followed by sacrifice for endpoint analyses.

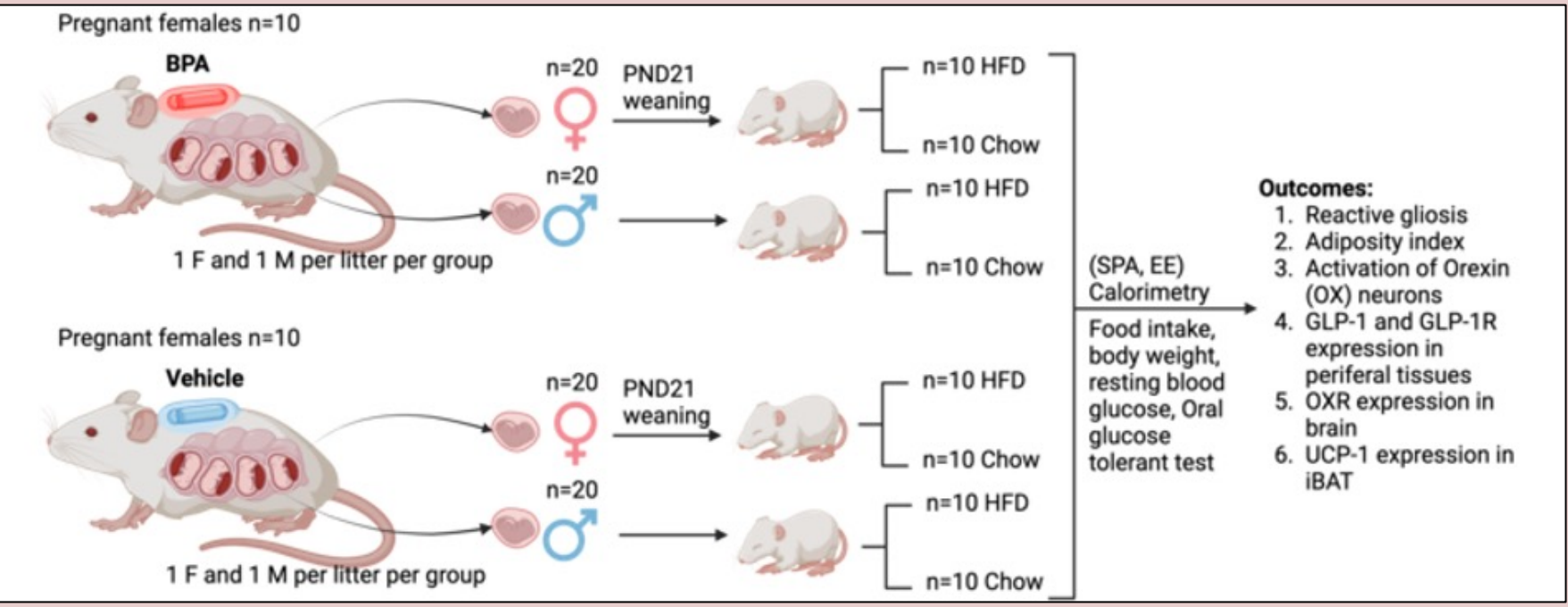


Figure 1: Study design

Results

- Females exposed to BPA exhibit a significantly higher body weight and adiposity index regardless of the diet
- Males exposed to BPA and HFD consistently ate more grams of food and gained higher body weight over the duration of the study
- Females exposed to BPA exhibit a significantly higher fat mass, energy efficiency and lower lean mass regardless of the diet
- Interestingly, males exposed to BPA and HCD had higher locomotor counts, and females exposed to BPA and HFD had a lower fall latency.

Results (Contd.)

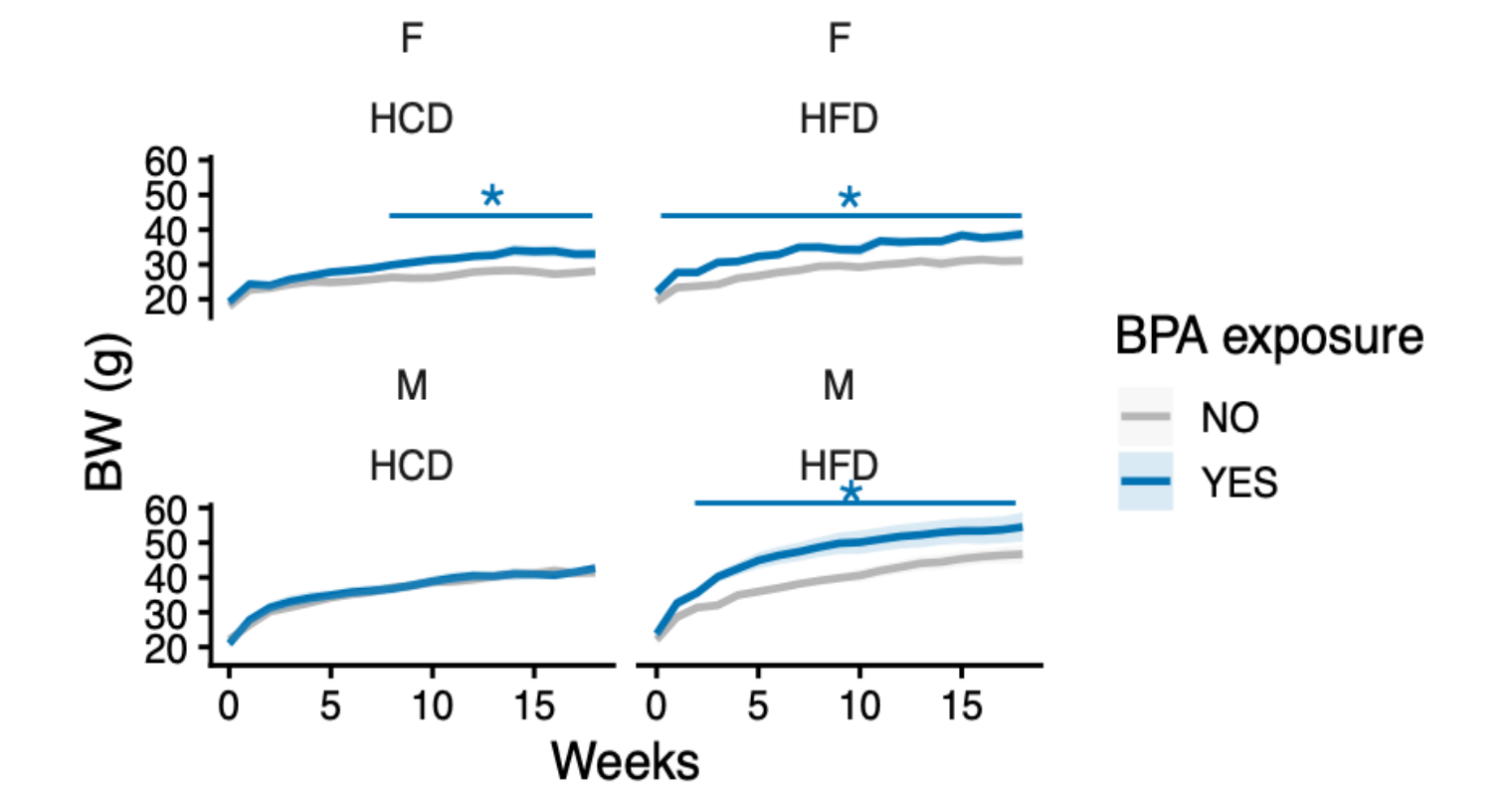


Figure 2: Body weight

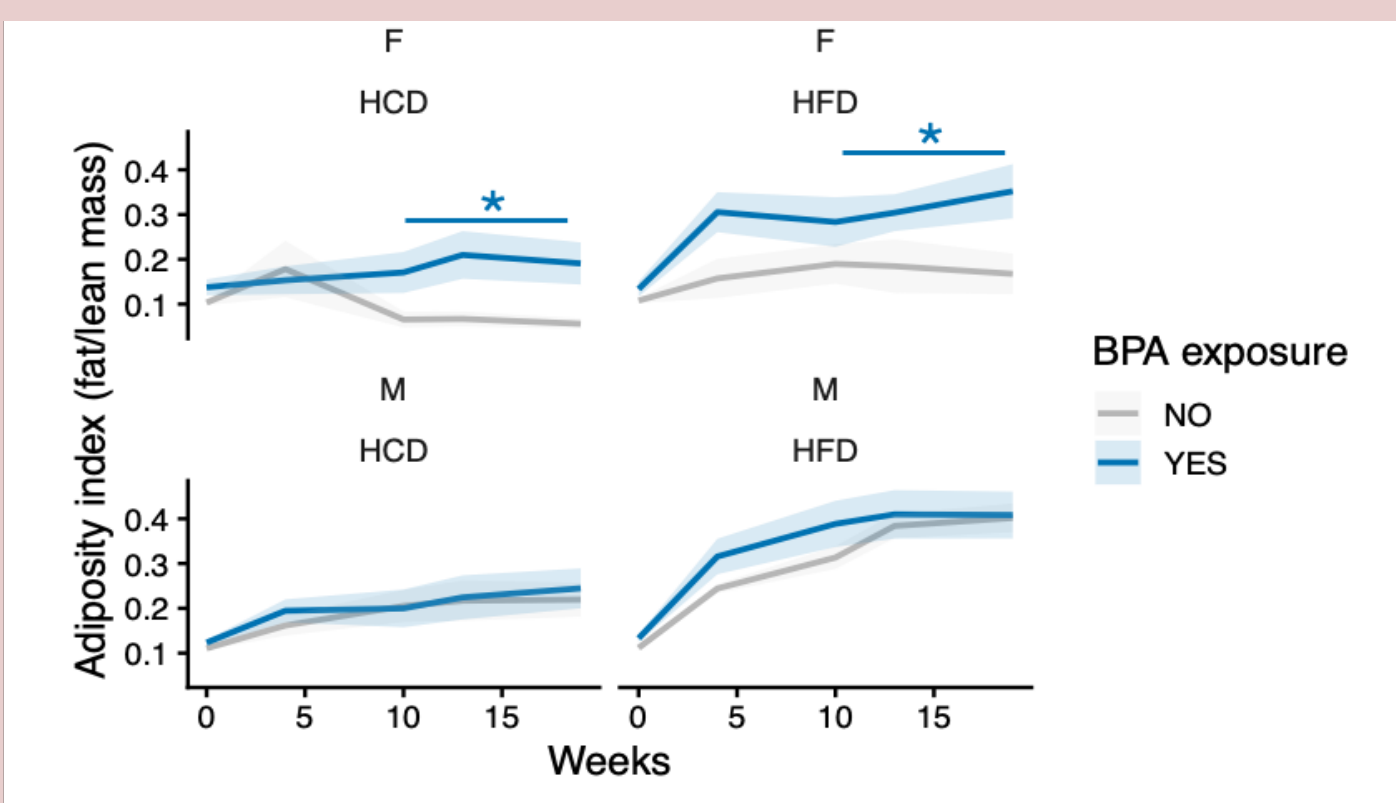


Figure 3: Adiposity indices

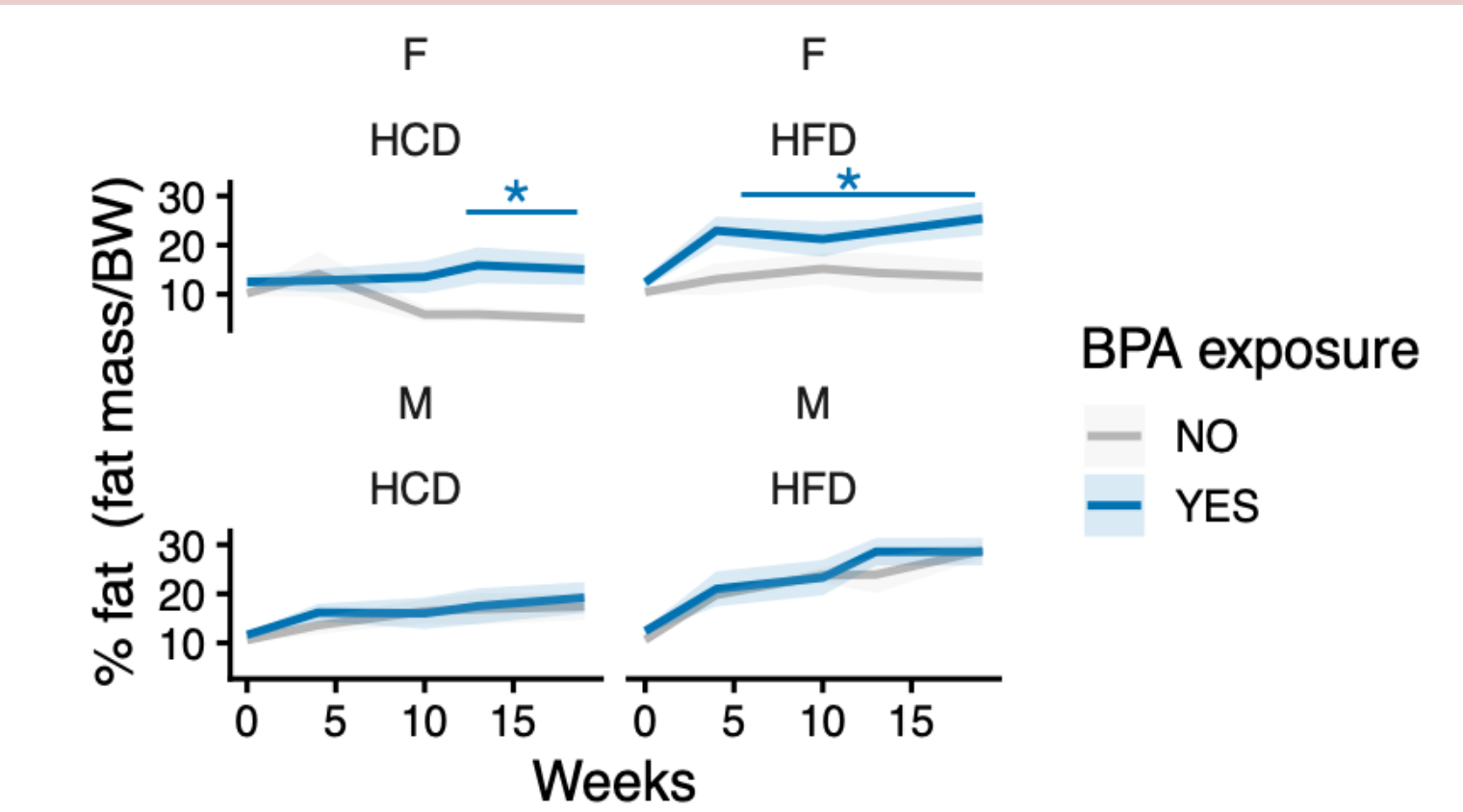


Figure 4 : Percent fat mass

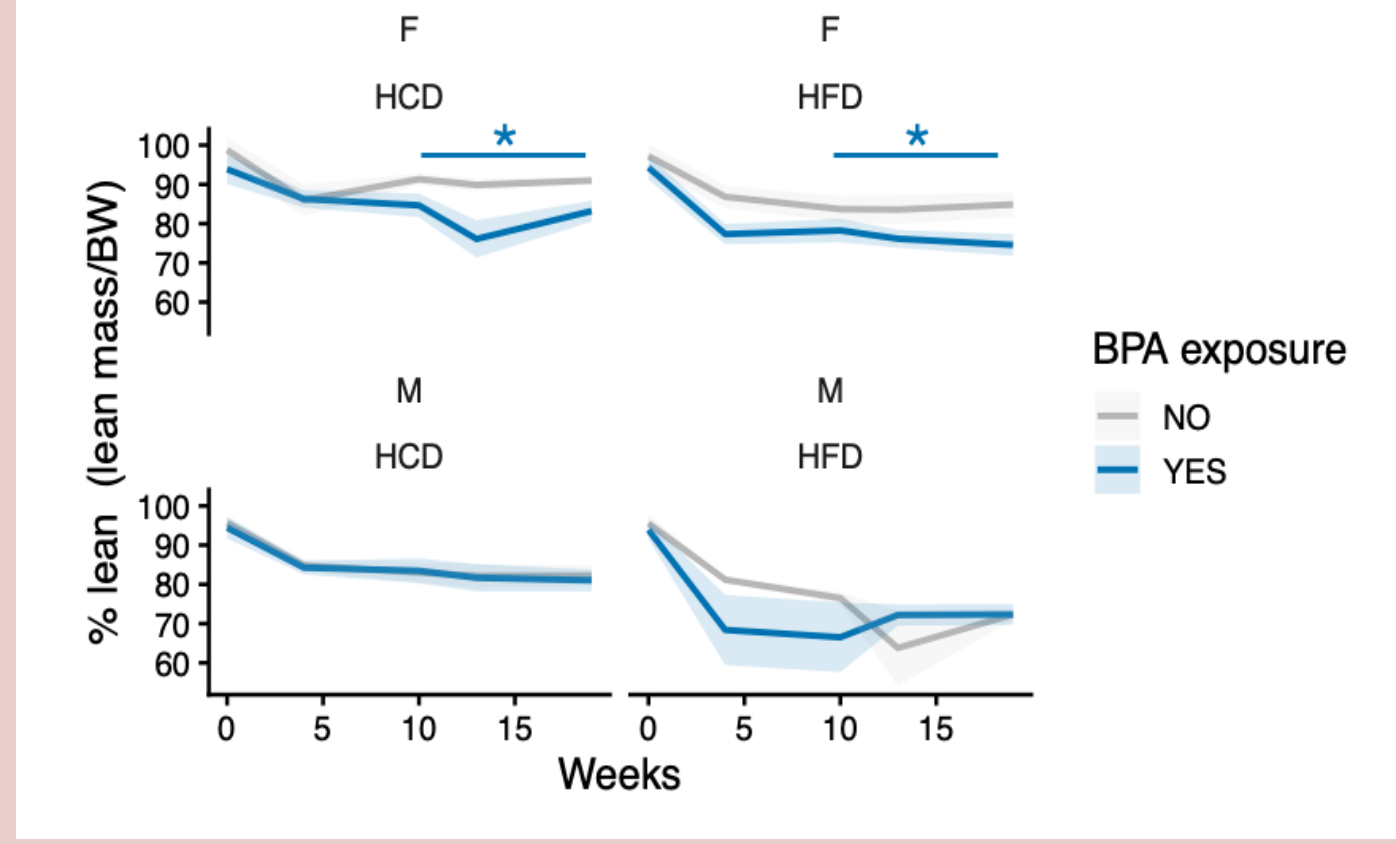


Figure 5 : Percent lean mass

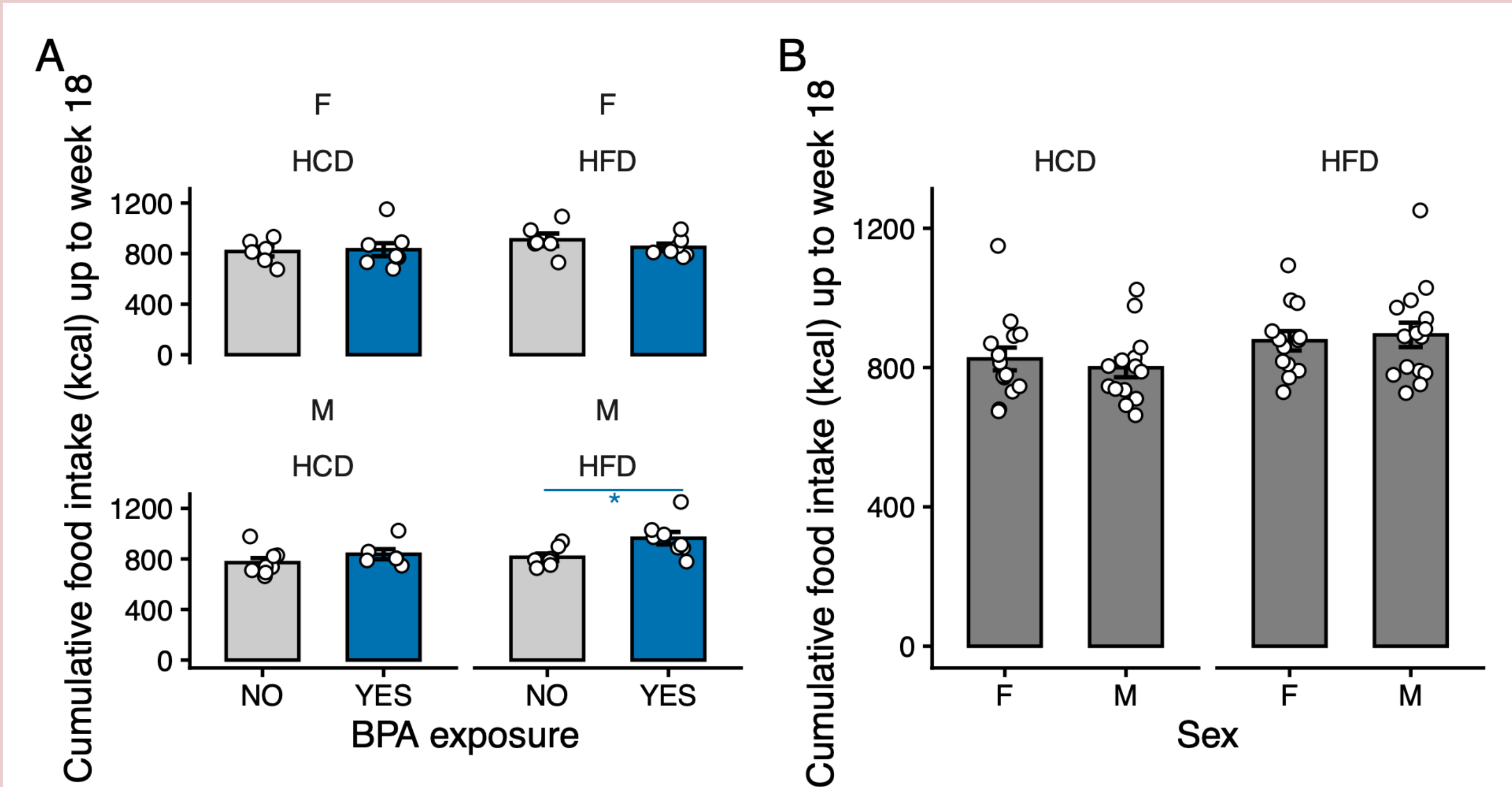


Figure 6: Cumulative food intake

Conclusions

- Exposure to BPA in utero has a sex dependent effect on both food intake, body weight, fat mass, lean mass, adiposity index, locomotion and fall latency.
- Interestingly, some of these effects are not muted in the HCD groups, suggesting that the effects of BPA exposure does not depend on type of diet.
- Future studies will further isolate the mechanism behind these sex dependent effects.

Results (Contd.)

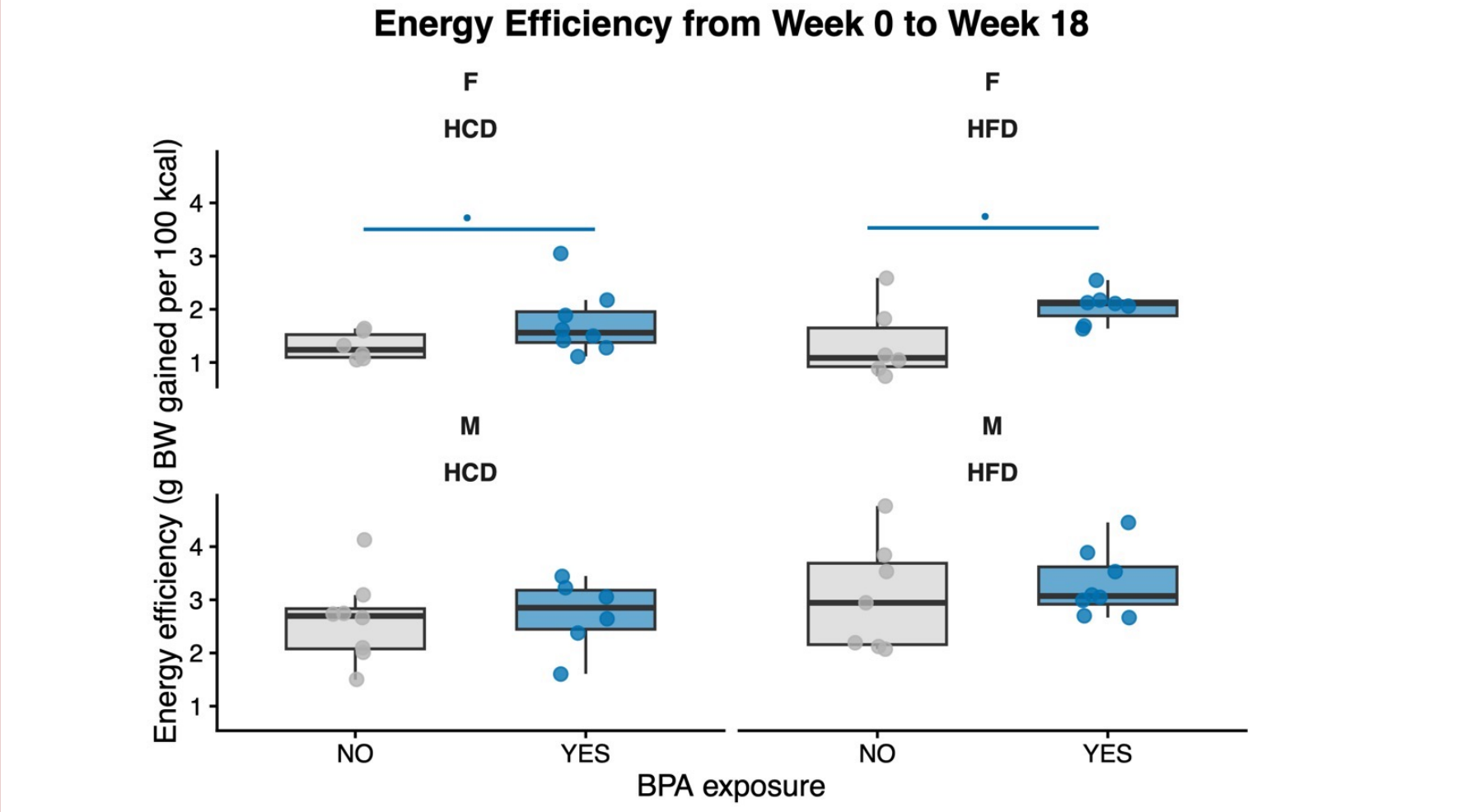


Figure 7: Energy efficiency

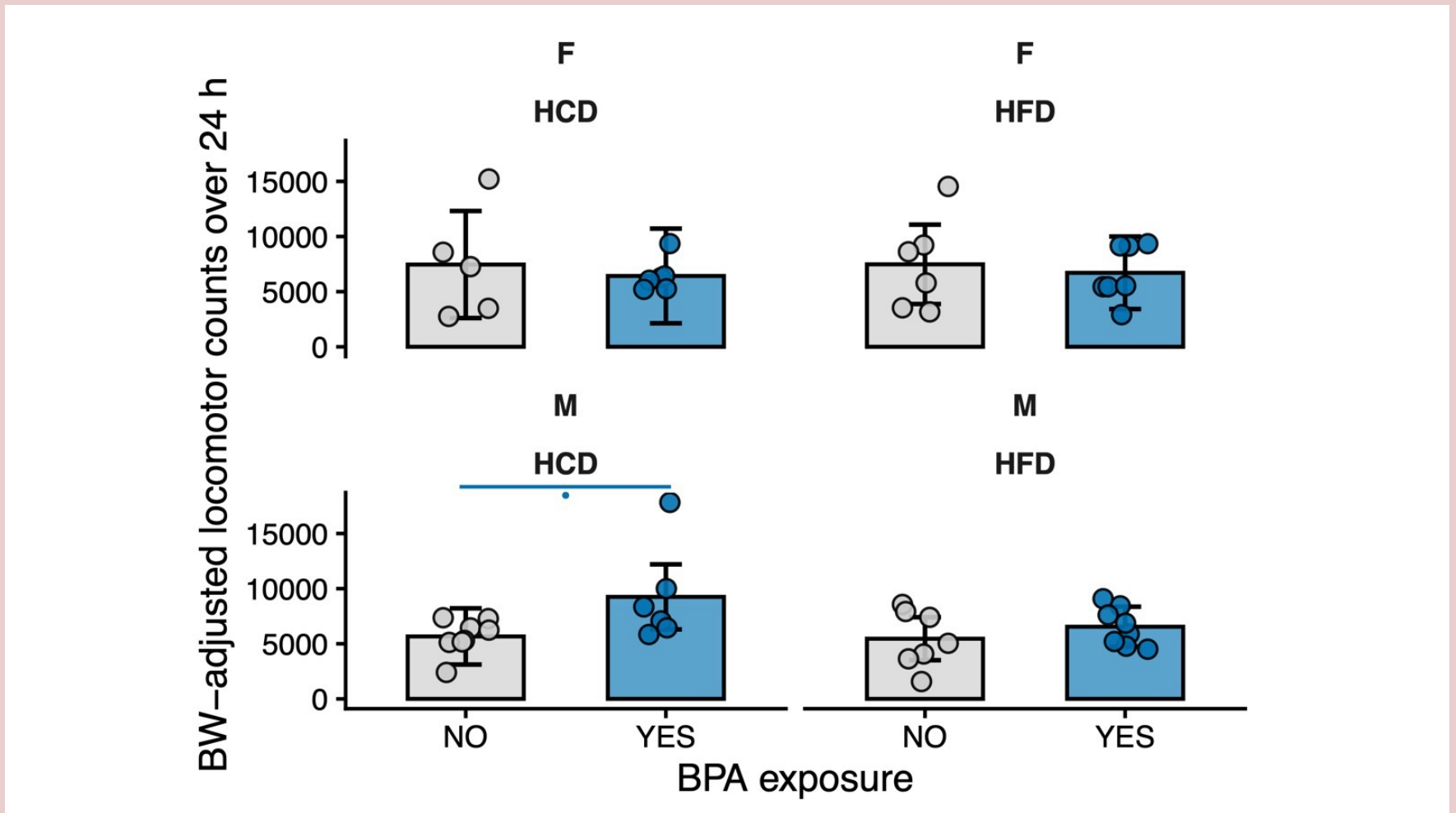


Figure 8: Locomotor counts

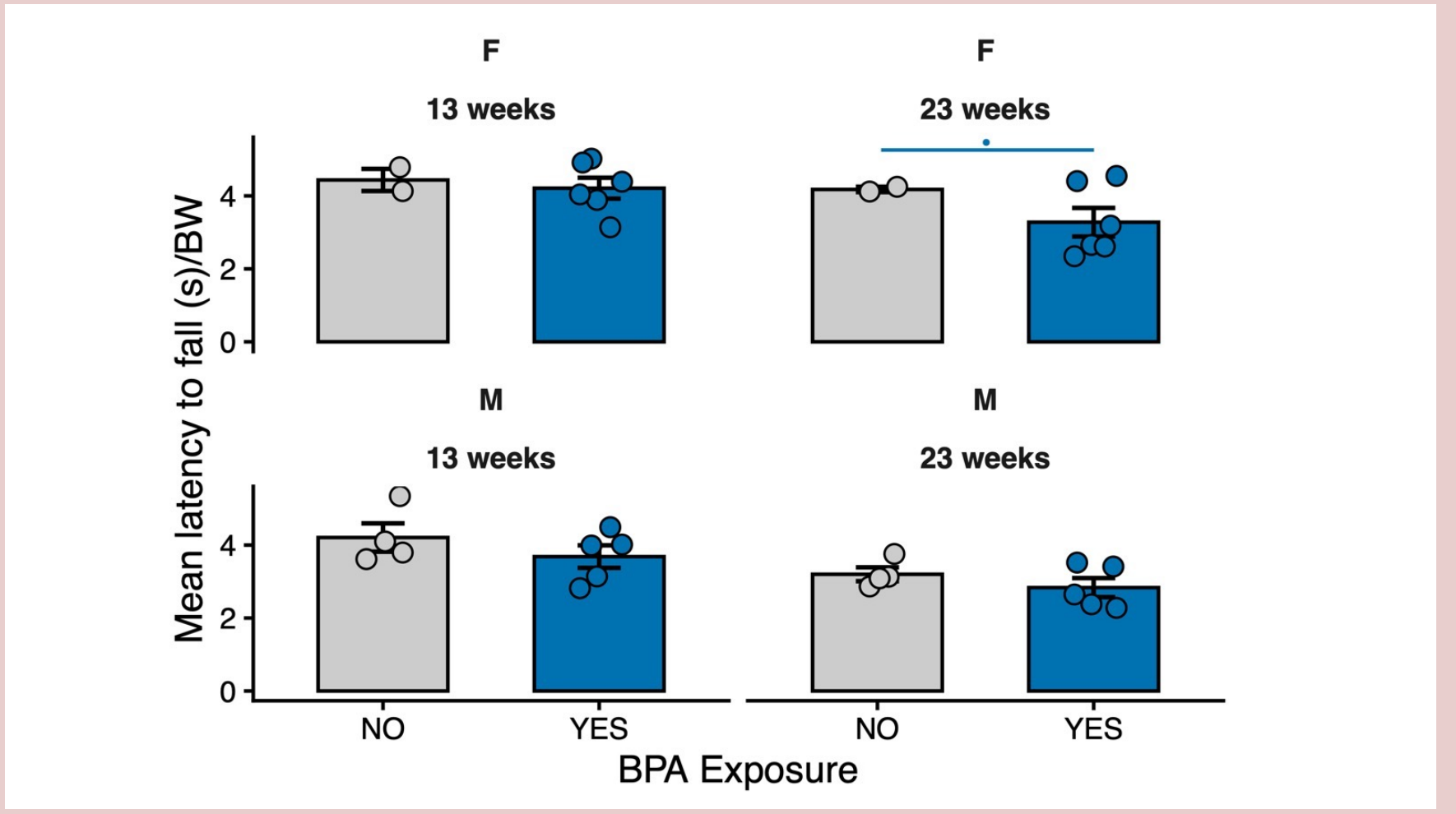


Figure 9: Latency to fall