Binge eating and the endogenous GLP-1 system

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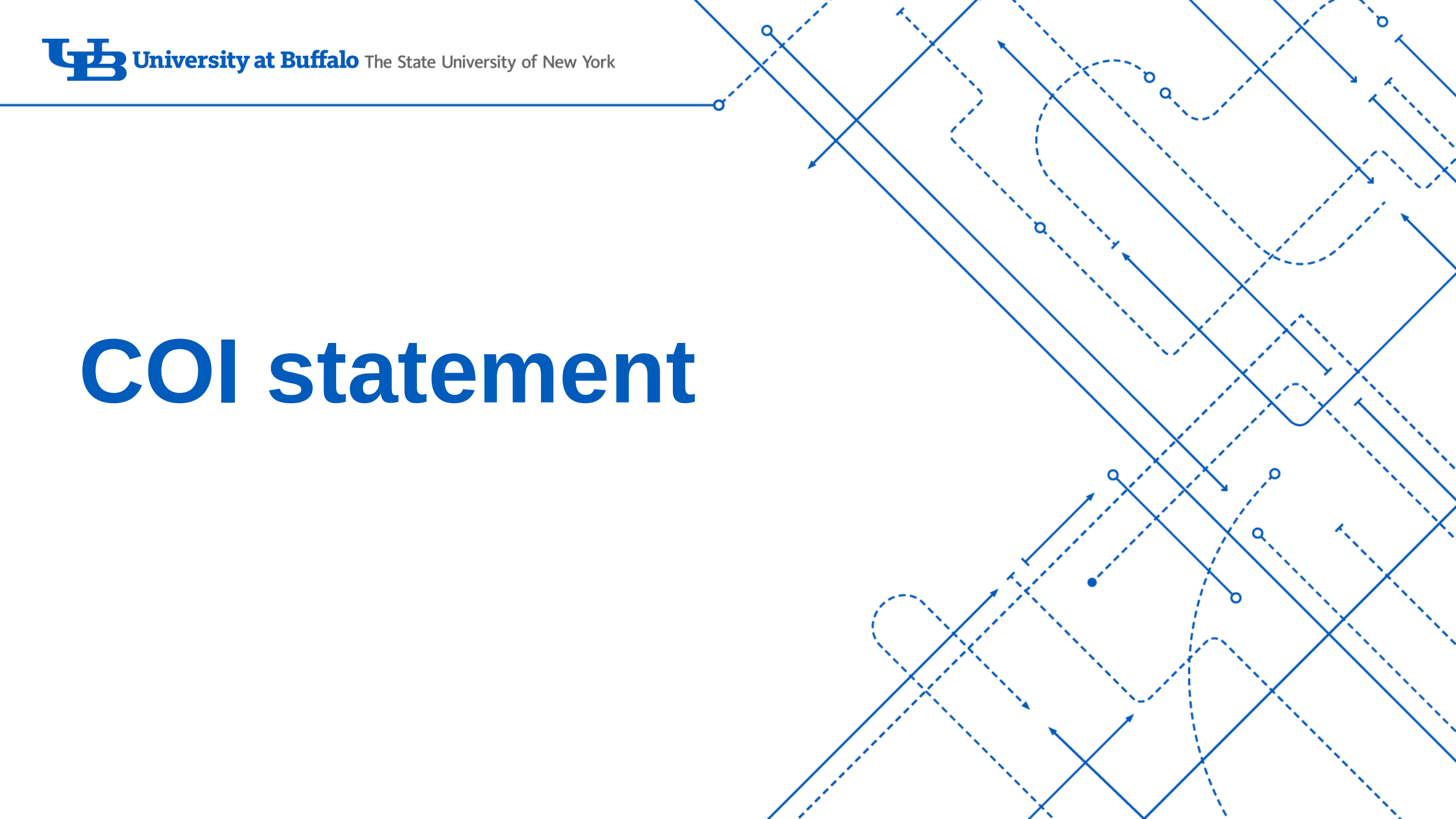
COI statement



Binge eating: framing the issue

- Consuming a larger-than-normal amount of food, in a discrete period of time
  - Incidence >5% (Hudson et al., 2007)
  - Associated with obesity, other comorbidities
- Feature of clinical eating disorders – binge eating disorder (BED), bulimia nervosa (BN)
- Current treatment options for BED are limited
  - Cognitive behavioral therapy
  - Lisdexamfetamine (psychostimulant; FDA-approved)
  - Off-label use of pharmacotherapy

GLP-1: potential treatment for binge eating / BED?

- GLP-1 system could be a potential pharmacotherapeutic target to reduce binge eating behavior and to treat BED (McElroy et al., 2018; Balantekin, Kretz, & Mietlicki-Baase, 2024)

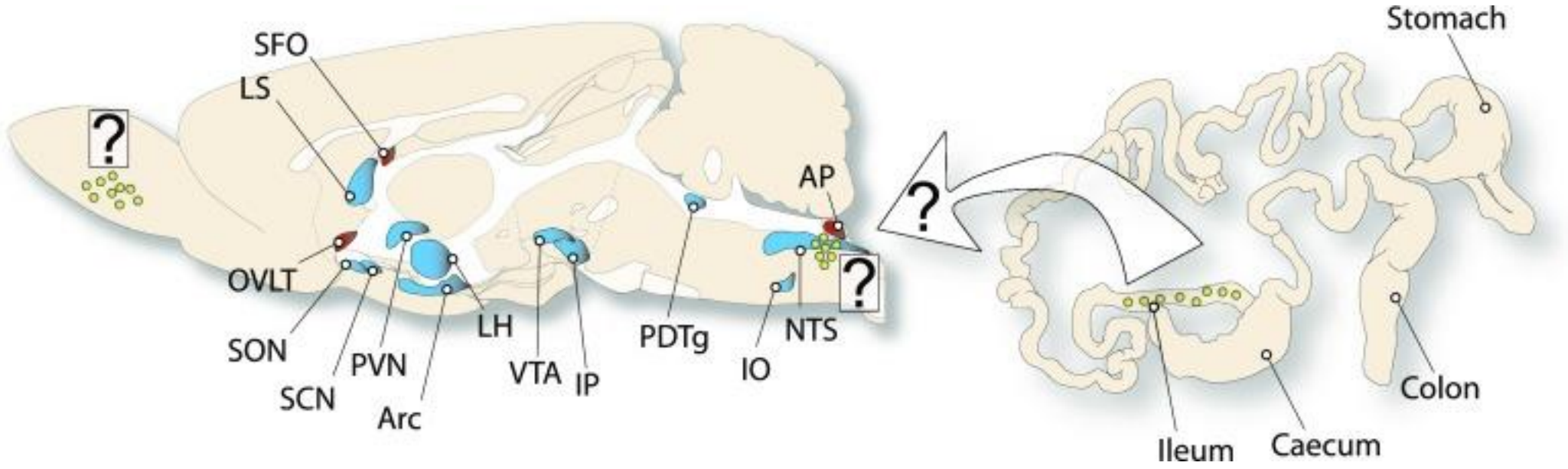


Image: Daniels & Mietlicki-Baase (2019)

Why focus on the hindbrain?

- **Nucleus tractus solitarius (NTS)** – produces *preproglucagon* (PPG), the precursor to glucagon-like peptide-1
- Direct projections to areas of the brain relevant for food intake and food reward

- *How do we model binge eating in rodents?*

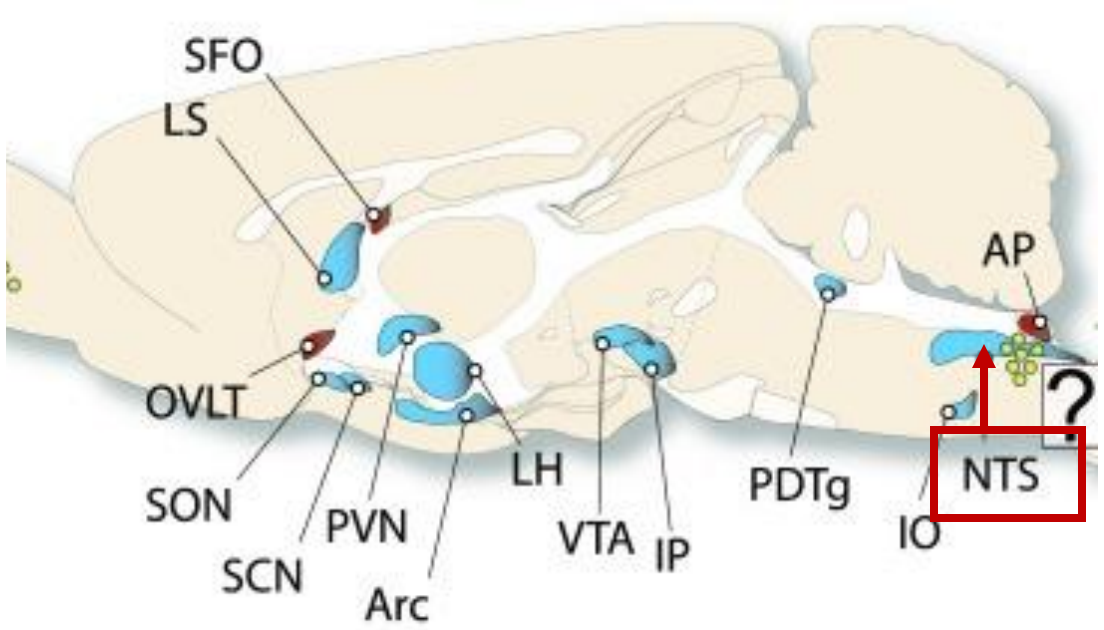
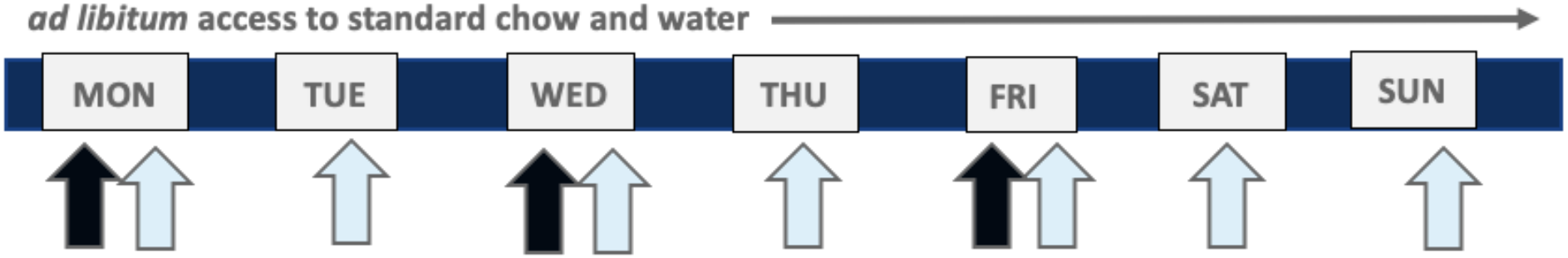


Image modified from Daniels & Mietlicki-Baase (2019)

Intermittent access to palatable food drives overconsumption in rodents – ”binge-like eating”

Controls: palatable food every day (1h)

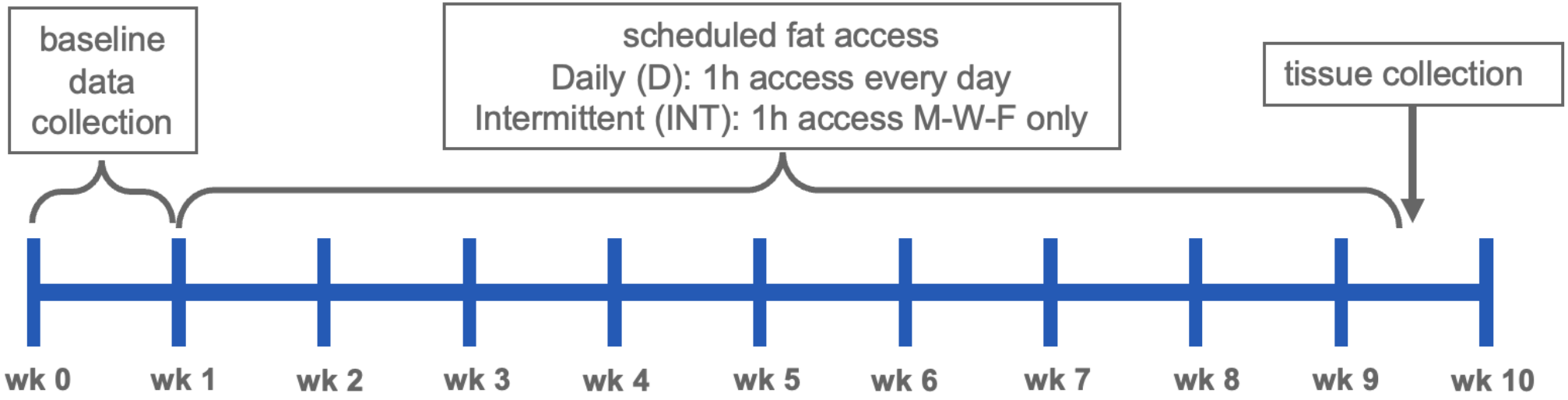
Intermittent access: palatable food only 3d/wk (1h), drives overeating when PF is available (“binge sessions”)



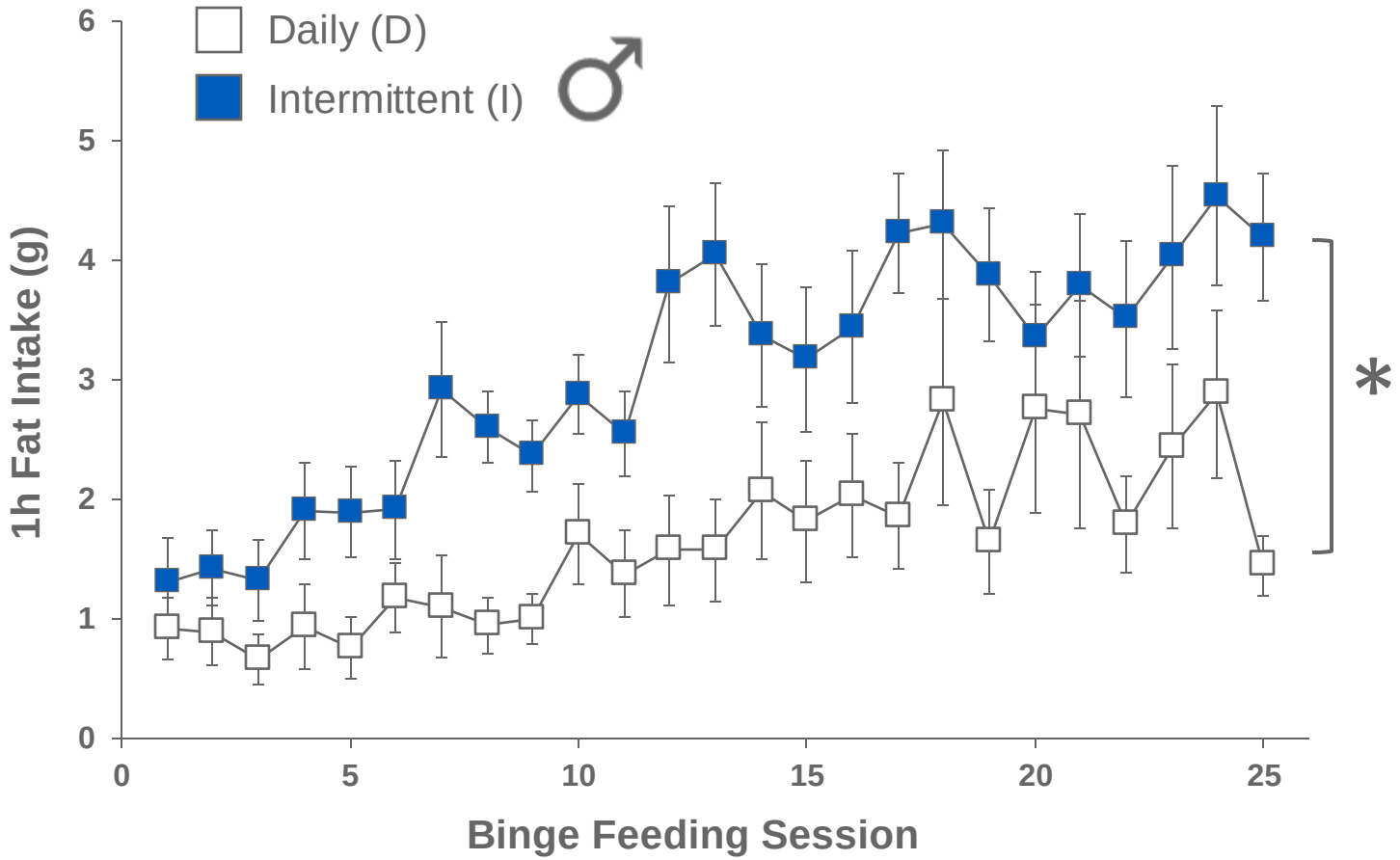
Corwin (2004), Puhl et al. (2011), Wojnicki et al. (2008)

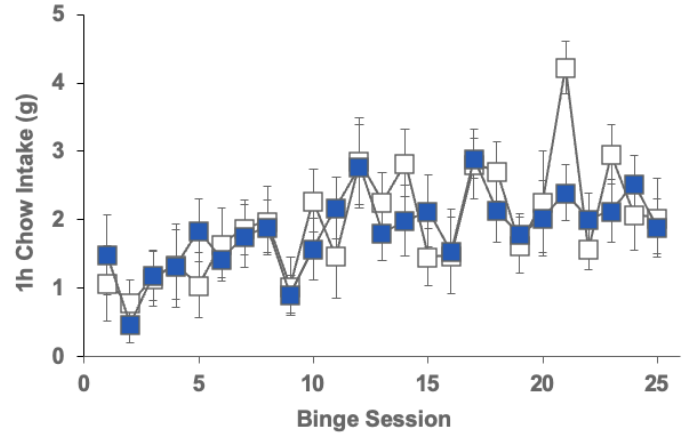
Does binge-like eating affect NTS GLP-1 in male rats?

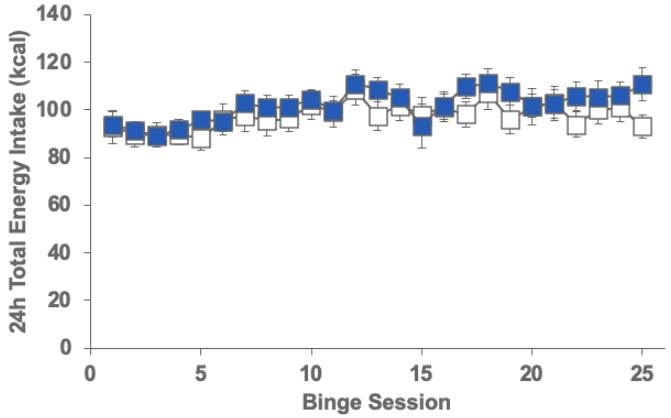
Mukherjee, Hum, et al. (2020)



- No differences in baseline measures
  - Daily average chow intake
  - Overnight vegetable shortening (fat) intake
  - Body weight at baseline

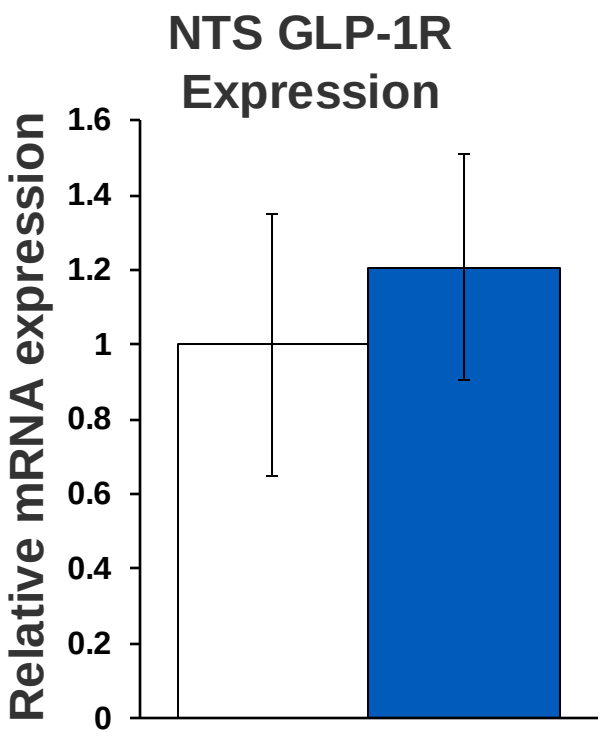


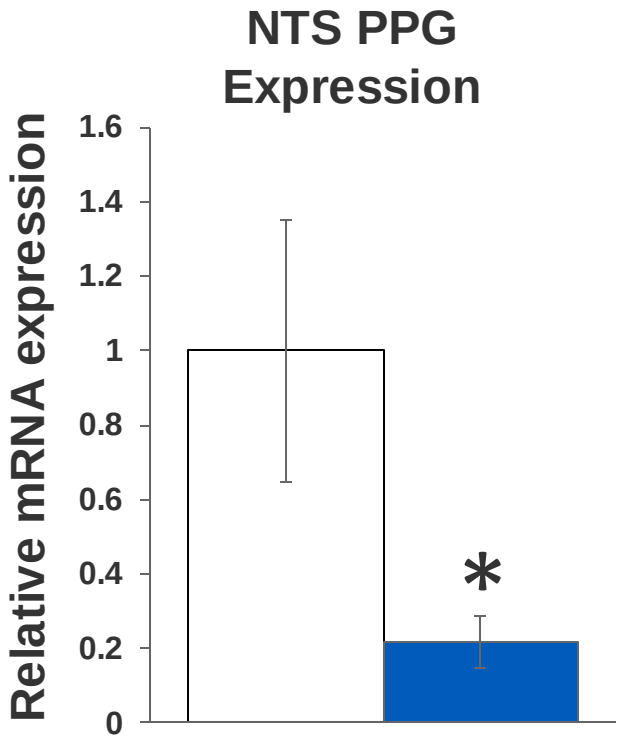


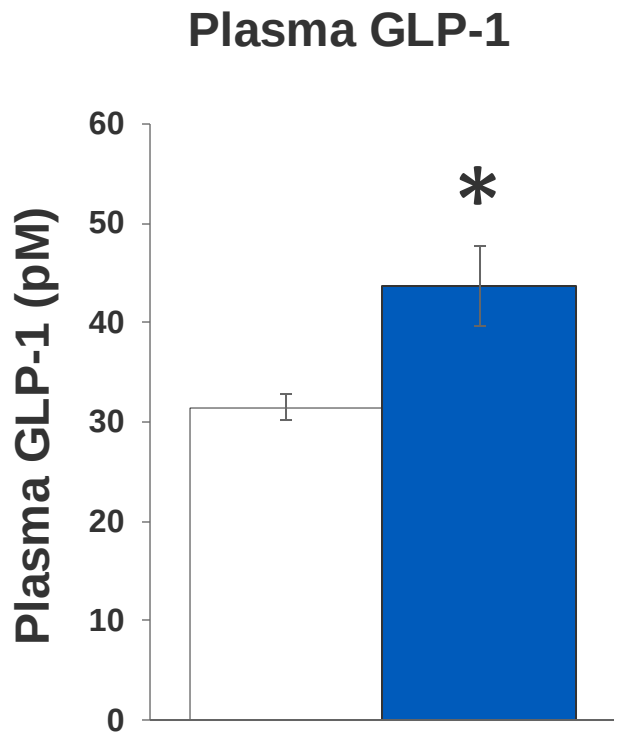


No significant differences in body weight throughout experiment (p>0.05)

Mukherjee, Hum, et al. (2020)

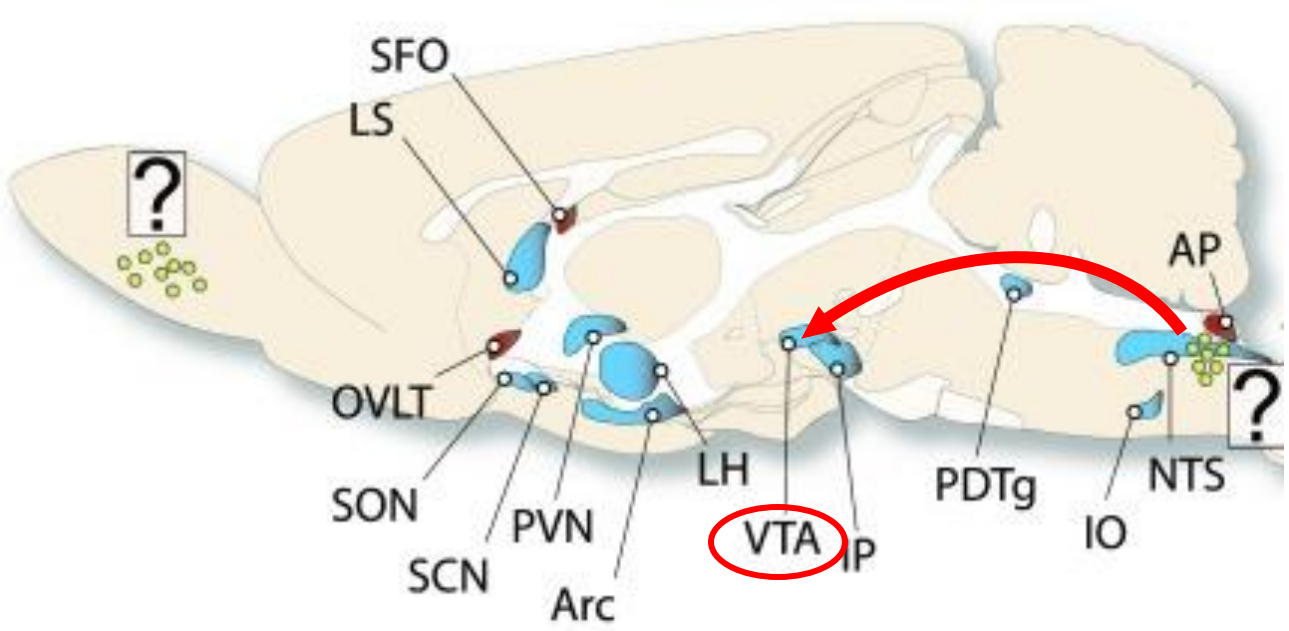






Daily Intermittent

Mukherjee, Hum, et al. (2020)



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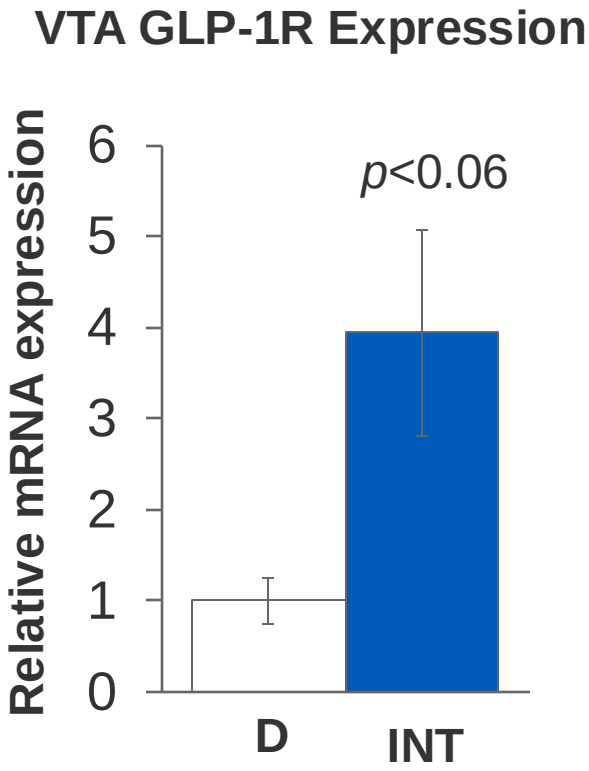


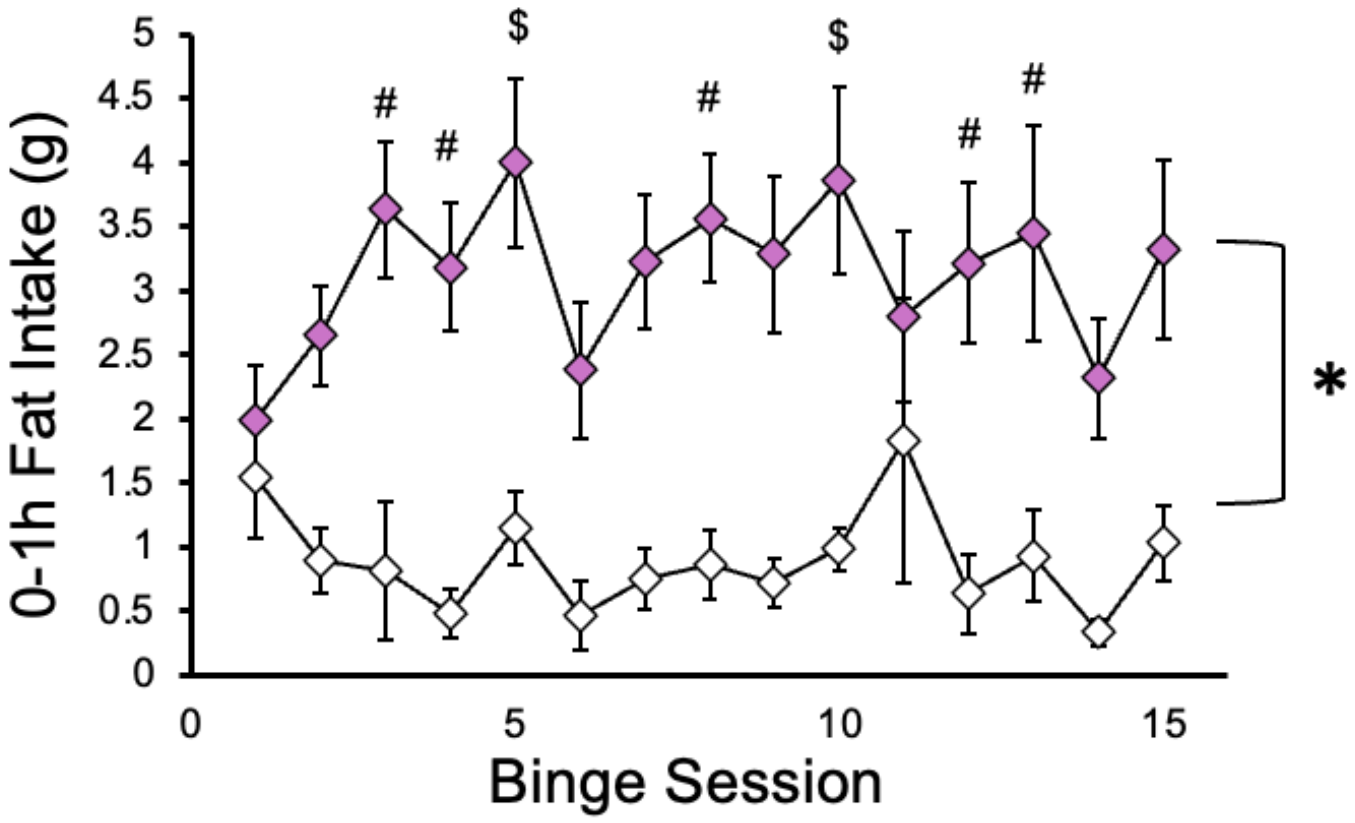
Could increasing central GLP-1 signaling be a strategy to ameliorate binge eating?

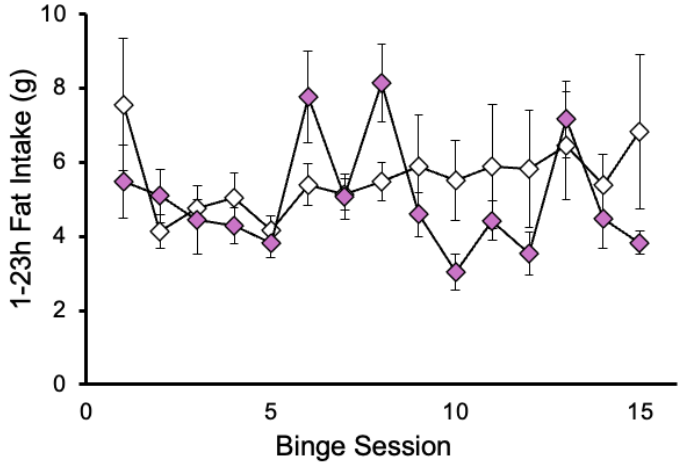
Are there sex differences in these effects?

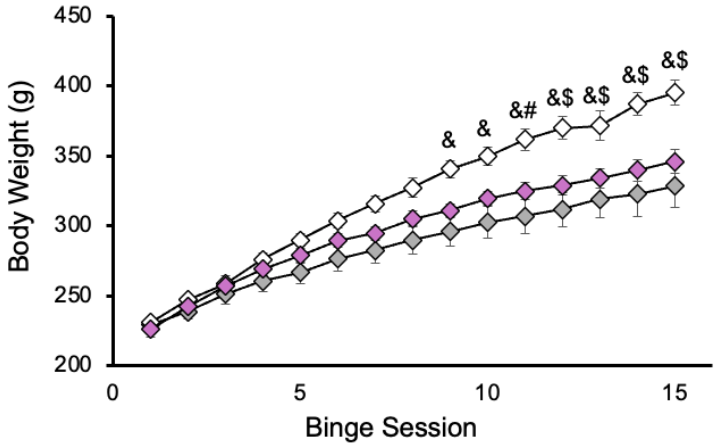
Mukherjee, Schottenfeld, et al. (unpublished)

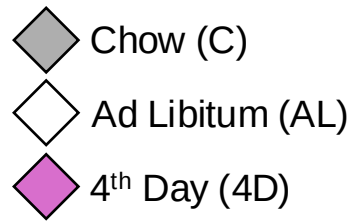
Does binge-like eating affect NTS GLP-1 in *female* rats?

- Fat access either ad libitum (AL) or every 4th day (4D); chow only as control

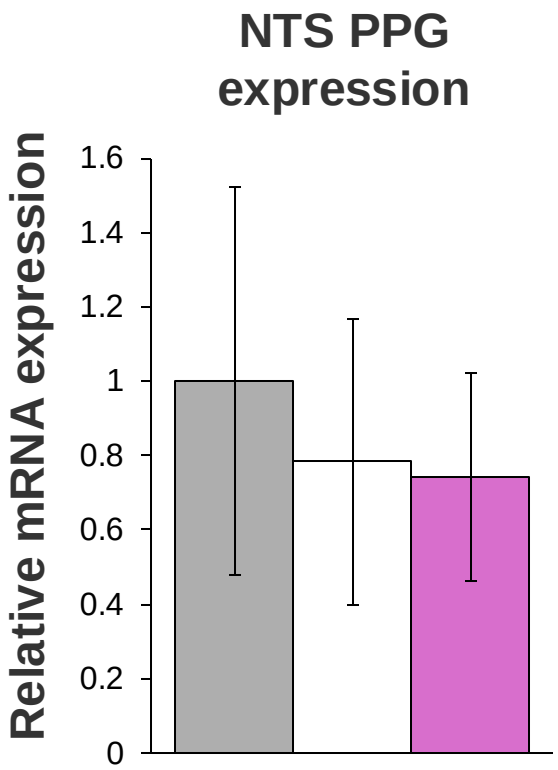


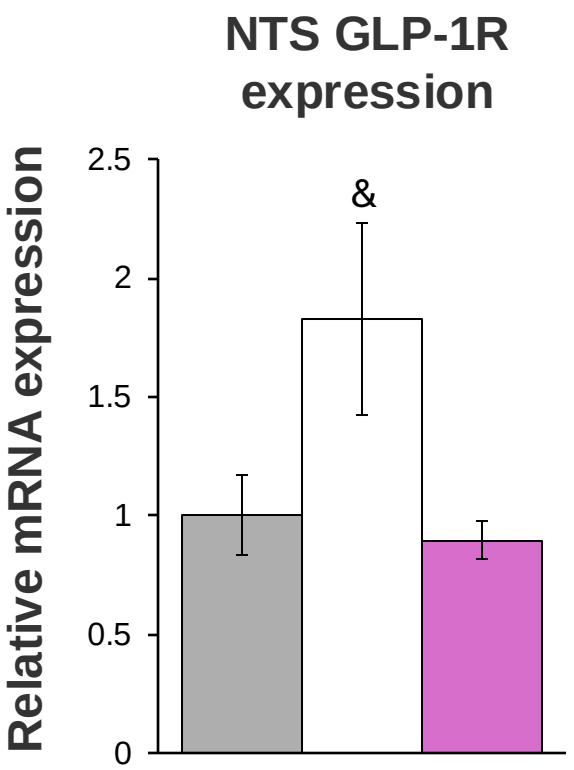


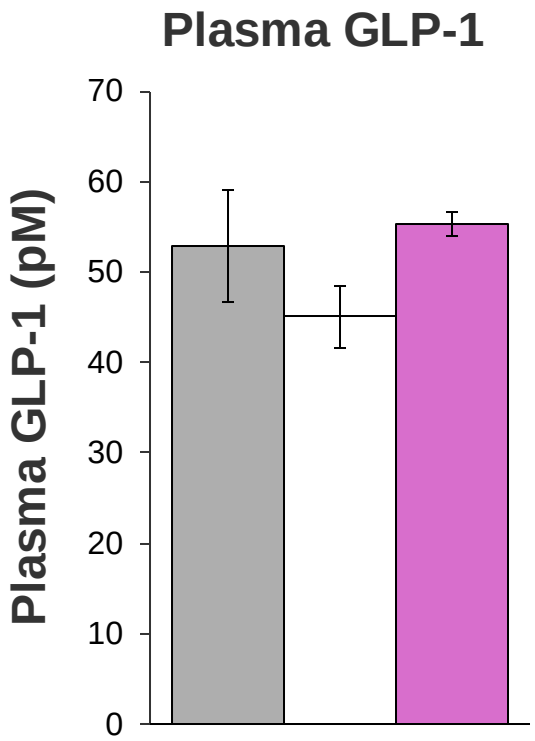




Mukherjee et al. (2022)





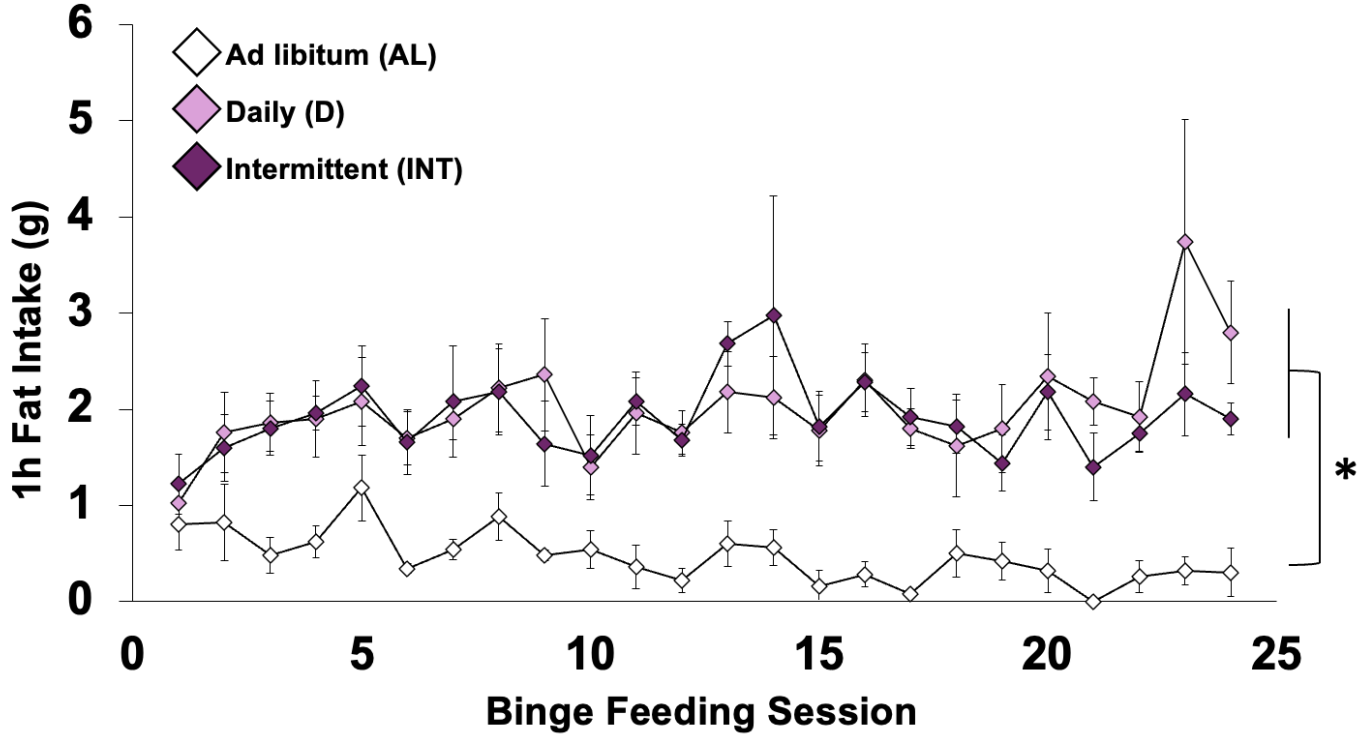


Chow Ad Libitum (AL) 4th Day (4D)

Mukherjee et al. (2022)

Future directions and challenges

- Sex differences in binge eating / effects on the GLP-1 system?
  - Different effects on central PPG / GLP-1R and circulating GLP-1



Future directions and challenges

- Sex differences in binge eating / effects on the GLP-1 system?
  - Different effects on central PPG / GLP-1R and circulating GLP-1
- Funding – understanding essential changes in GLP-1 signaling that occur in the context of binge eating
  - Timing of effects
- Potential effects of other hormonal systems?
  - Most effective drug / combination therapy?

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