Impacts of GLP-1, GLP-2, Glucagon, Oxytomodulin, and Glicentin on Food Intake

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INTRODUCTION

- Overeating reflects dysregulation of neural and hormonal satiety pathways.
- Obesity and metabolic diseases are strongly linked to the Western Diet (WD).

The Western diet (WD): a highly palatable, calorically dense diet that is relatively high in fat and sugar, and relatively low in protein.

The glucagon gene (*Gcg*): encodes preproglucagon, which is processed into several peptides including GLP-1.

Glucagon-like-peptide-1 (GLP-1): an endogenous intestinal hormone and neuropeptide, produced in the caudal brainstem.

- Regulates appetite and energy balance.
- Reduces food intake and limits consumption of highly palatable foods like WD.

Genetic knockdown (KD): the genetic reduction of *Gcg* expression was used to disrupt preproglucagon-derived peptide signaling.

Objective: To determine whether *Gcg* gene expression influences total caloric intake and WD preference in male and female rats.

Hypothesis: Rats with *Gcg* knockdown will consume more total calories and show increased preference for WD relative to chow, with potential sex-dependent effects.

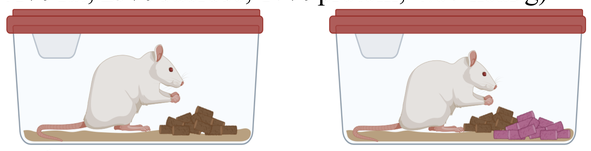
METHODS

Subjects: 6-week-old male and female rats with *Gcg* knockdown (KD), developed and validated by our lab, and wild-type (WT) controls.

- Housing: Group-housed with 2-3 rats per cage

Diet conditions (8 weeks):

- Chow only: (14% fat, 0% sucrose, 29% protein; 3.35 kcal/g)
- Choice diet: Chow + WD (41% fat, 29% sucrose, 17% protein; 4.67 kcal/g)



Groups:

- Chow only: 5 cages per sex and genotype
- Choice diet: 5 cages of females and 6 cages of males per genotype

Measures:

- Total caloric intake (in kcals)
- WD caloric intake and preference for the choice group

Data Analysis:

- Average intake per rat was calculated by dividing the total cage intake by the number of rats per cage.
- Statistical analyses were conducted using mixed-ANOVAs in RStudio, with sex, genotype, diet, and week as factors.

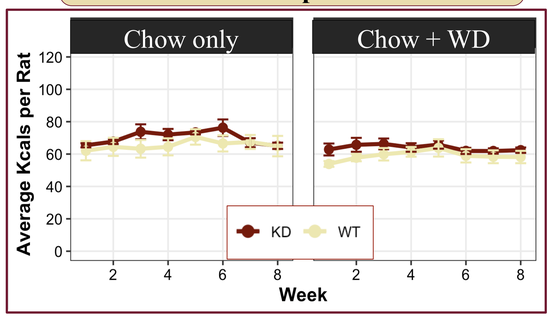
FUNDING

Funded by: NIH MH059911 T32MH093311 McKnight Doctoral Fellowship

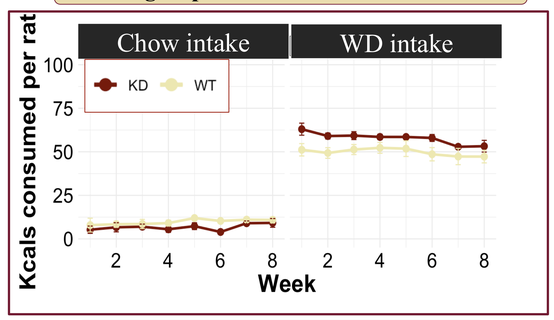
RESULTS

Female

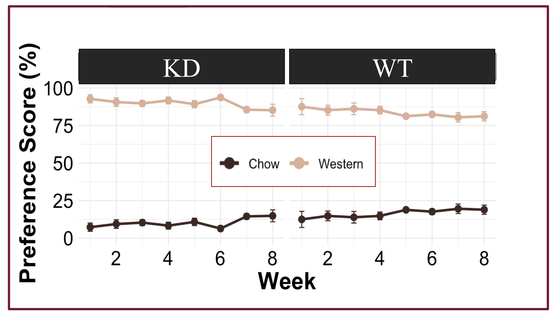
Chow only + choice group total kcal consumption:



Choice group kcal intake of WD and Chow:

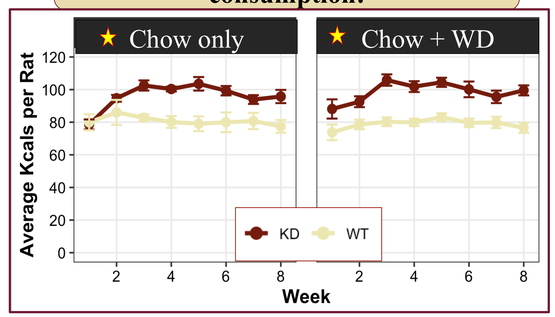


Choice group preference for WD:

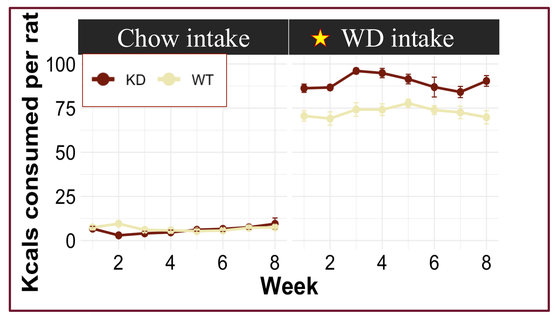


Male

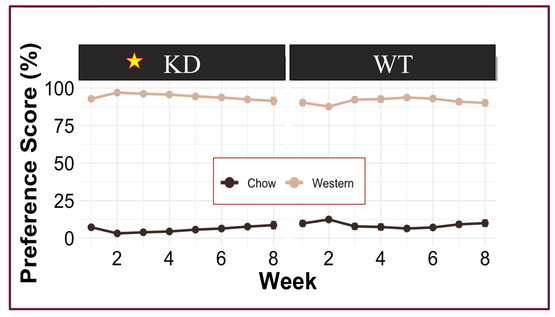
Chow only + choice group total kcal consumption:



Choice group kcal intake of WD and Chow:



Choice group preference for WD:



DISCUSSION

- The results from this study indicate that suppression of the *Gcg* gene alters satiety and diet preferences in rats. Reduced *Gcg* signaling produced a sex-dependent increase in caloric intake in male rats.
- When *Gcg*-encoded peptide signaling is reduced, males may be more likely to overconsume high-fat, high-sugar foods than female rats.
- These findings highlight *Gcg* as a crucial regulator of food intake and preference, as well as sex being an important biological factor.

Future research:

- Examining the relationship between female hormones and signaling of peptides such as GLP-1.
- Examining if *Gcg* KD alters motivation for palatable foods such as WD.

REFERENCES