Investigating the GLP-1 Receptor Pools Responsible for Mediating the Weight Loss and Glucose Lowering Effects of Oral Exendin-4



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BACKGROUND

Oral formulations of Glucagon Like Peptide 1 (GLP-1) demonstrate comparable weight loss and glucose lowering effects to injectables. Women show greater weight loss on GLP-1 analogs than men, underscoring the need to understand the sex specific responses for personalized treatments.

HYPOTHESIS

GLP1R pools within in the intestine are responsible for the glucose lowering and weight loss effects of orally administered exendin-4.

METHODS

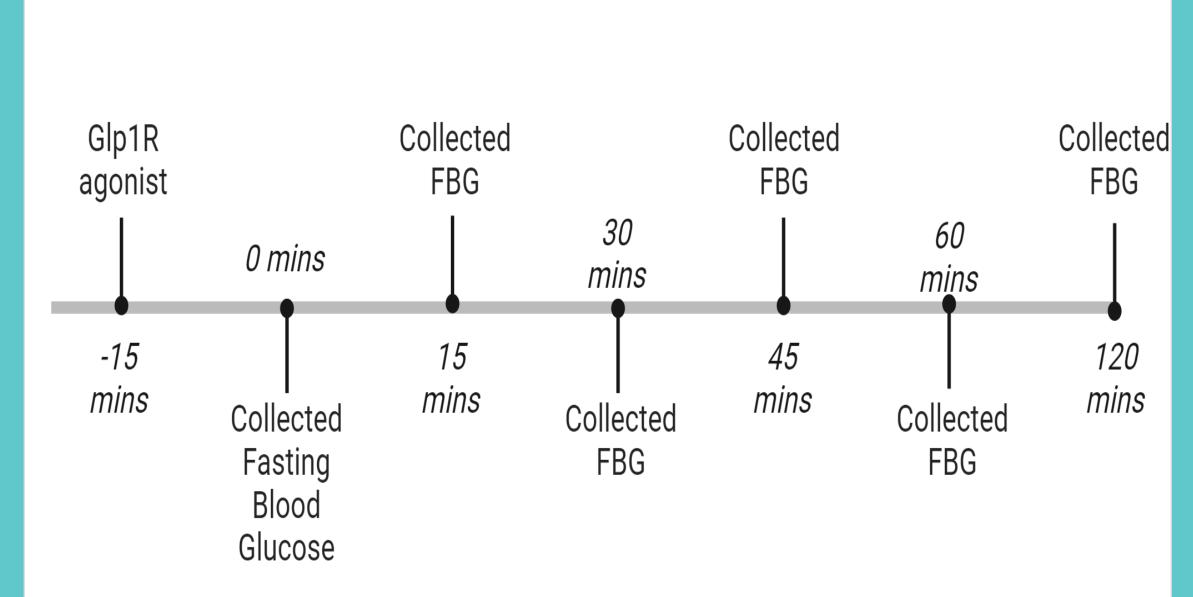


Figure 1. Schematic of Methods

RESULTS

Orally administered exendin-4 lowers blood glucose

Figure 2: Intraperitoneal glucose tolerance test in male and female 8wk old mice after oral and systemic Figure 3: Interval food intake of male and female 8wk old mice after oral and systemic administration of exendin-4 administration of exendin-4 (A-B) Gastric emptying (C). Plasma levels of GLP1 and Exendin-4 after (A-B) after a 16 hour fast * p < 0.05, ** p < 0.005, *** p < 0.01, **** p < 0.001. administration(D). Responders versus non responders glucose curves (E)

A)

GLP1R within the intestinal epithelium and enteric nervous system are not needed for the glucose lowering effects of administered exendin-4

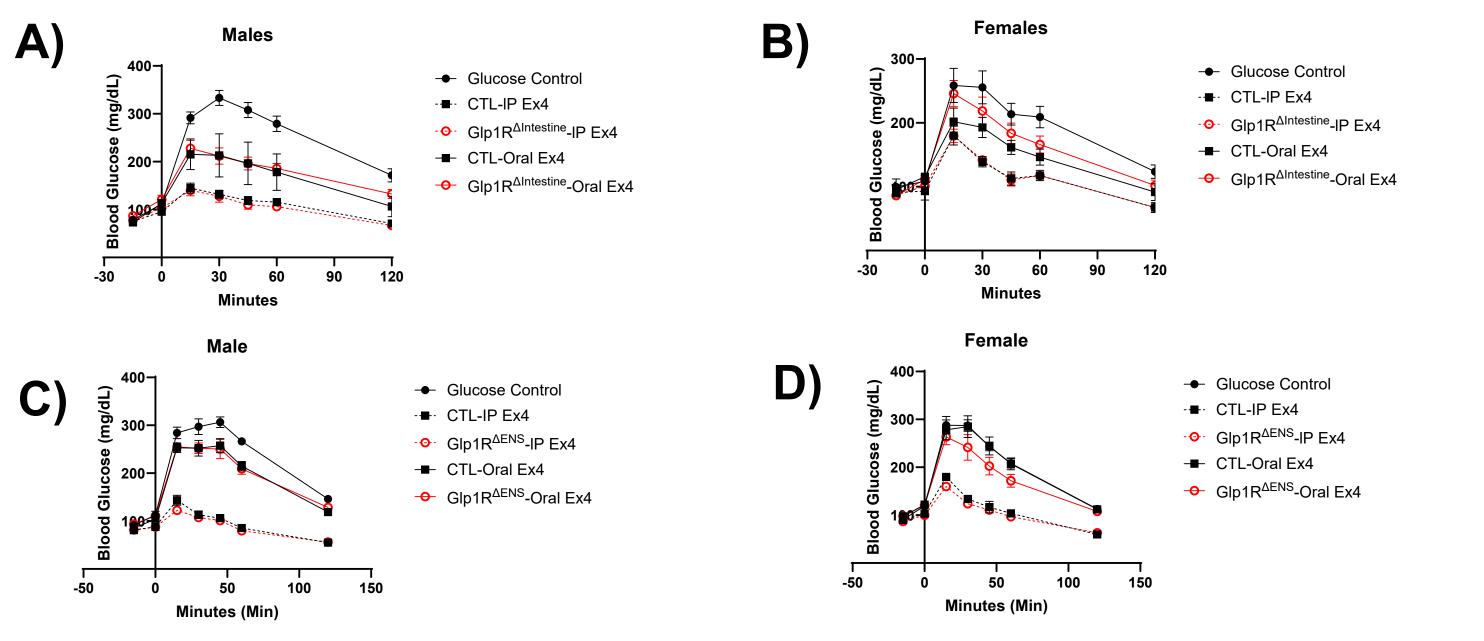
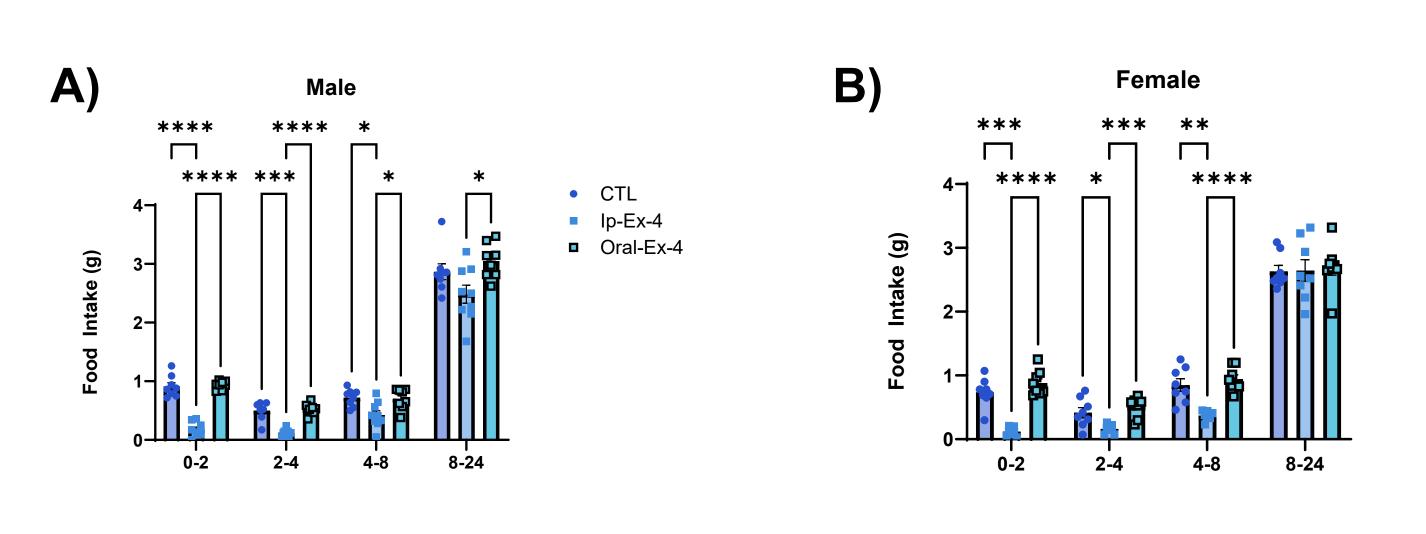


Figure 4: Intraperitoneal glucose tolerance test in male and female 8wk old GLP1R villin cre mice(A & B) and GLP1R wnt Cre male and female mice (C & D).

Orally administered exendin-4 does not impact food intake



GLP1R within the vagus nerve are needed for the glucose lowering effects of administered exendin-4 in males but not females

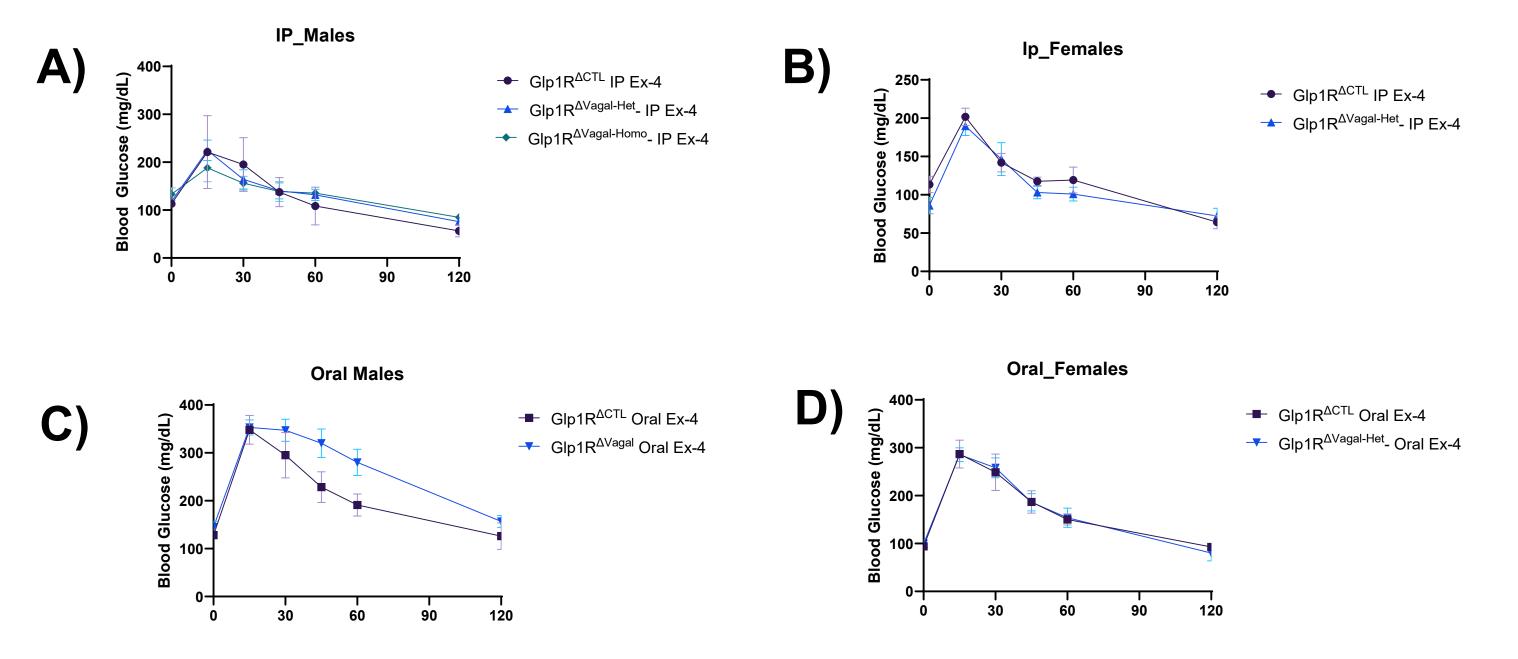
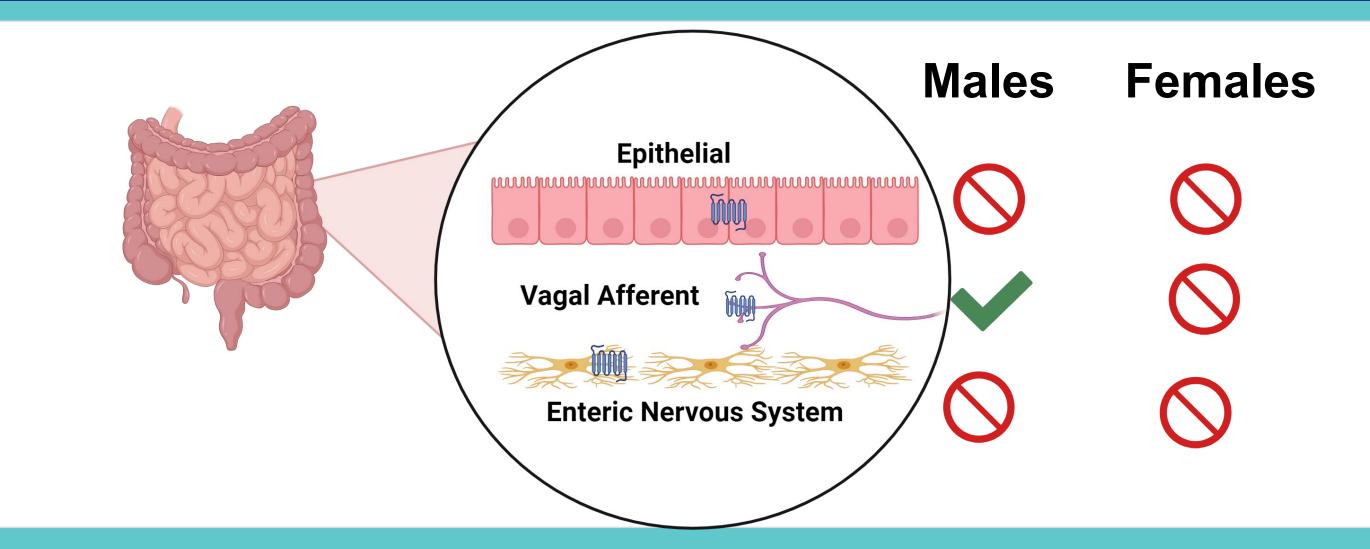


Figure 4: Intraperitoneal glucose tolerance test in male and female 8wk old GLP1R vagal mice after IP administration of exendin-4 (A & B) and oral administration(C & D).

CONCLUSION



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