PYY_{3-36} increases insulin sensitivity of glucose disposal in mice on a high fat diet

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Objective: PYY_{3-36} is released by the gut in response to nutrient ingestion. It inhibits food intake by modulation of the opposing activities of orexigenic neuropeptide Y (NPY) neurons and anorexigenic pro-opiomelanocortin (POMC) neurons in the hypothalamus. We wondered whether PYY_{3-36} can improve insulin sensitivity, because both NPY and POMC have been shown to impact insulin action.

Methods: to address this question, we examined the effect of intravenous PYY_{3-36} on glucose and free fatty acid (FFA) flux as well as muscle and adipose tissue specific glucose uptake during a hyperinsulinemic euglycemic clamp in mice maintained on a high fat diet.

Results: in basal conditions, none of the metabolic parameters was affected by PYY_{3-36}. In hyperinsulinemic conditions, glucose disposal was significantly increased in PYY_{3-36}-infused compared with vehicle-infused mice (103.8 ± 10.9 *vs.* 76.1 ± 11.4 µmol/min/kg, respectively, P=0.001). Accordingly, glucose uptake in muscle and adipose tissue was greater in PYY_{3-36}-treated animals, although the difference with controls did not reach statistical significance in adipose tissue (muscle: 2.1 ± 0.5 *vs.* 1.5 ± 0.5 µmol/ g tissue, P=0.049; adipose tissue: 0.8 ± 0.4 *vs.* 0.4 ± 0.3 µmol/ g tissue; P=0.08). In contrast, PYY_{3-36} did not impact insulin action on endogenous glucose production or FFA metabolism.

Conclusion: these data indicate that PYY_{3-36} independently of food intake reinforces insulin action on glucose disposal in mice fed a high fat diet.

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