

Circulating GLP-1 and CCK-8 reduce food intake by non-vagal mechanisms.

J. Zhang and R. C. Ritter. Programs in Neuroscience, Dept. of VCAPP, Washington State University, Pullman, WA 99164

CCK and GLP-1 are secreted by intestinal endocrine cells in response to luminal nutrients. Consequently, plasma concentrations of both peptides increase postprandially. Reduction of food intake by intraperitoneal (IP) CCK injection is abolished or attenuated by vagotomy, and at least one report suggests that reduction of food intake by IP GLP-1 also is vagally mediated. However, endogenous secretion or IP CCK or GLP-1 injection likely produce much higher local peptide concentrations than are achieved in the systemic circulation. Though vagal mediation of food intake reduction by IP peptide injection is established, vagal participation in feeding reductions in response to elevated plasma CCK and GLP-1 is uncertain. Here we report that intravenous infusion of GLP-1 (1.25, 2.5, 5.0 or 10.0 $\mu\text{g}/\text{rat}$) or CCK-8 (1.4 or 2.8 $\mu\text{g}/\text{rat}$) reduced 30 min intake of 15% sucrose of intact rats. Reductions of intake by intravenous CCK and GLP-1 were not attenuated either by bilateral subdiaphragmatic vagotomy or systemic capsaicin treatment. Further, at the 10 $\mu\text{g}/\text{rat}$ dose, GLP-1 reduced food intake more in vagotomized and capsaicin-treated rats than in controls. On the other hand, reduction of food intake by IP CCK was abolished in these same groups of vagotomized and capsaicin-treated rats. We conclude that abdominal vagal afferents mediate reduction of food intake by IP CCK, but are not required for feeding effects of circulating CCK or GLP-1. Furthermore, it appears that vagal lesions increase responsiveness of non-vagal substrates mediating reduction of food intake by circulating GLP-1.