

Peripheral administration of PYY[3-36] reduces food intake, body weight, and glycemic indices in rodent models of obesity and diabetes. *Pittner et al. Int J Obesity 2004; 28:963-971*

Peptide YY (PYY) is a 36 amino-acid peptide secreted from intestinal cells following meals. The cleaved subpeptide PYY[3-36] represents the majority of the circulating PYY-like peptide present after meals. Previous research demonstrated an orexigenic effect (increase in food intake) following intracerebroventricular administration of pancreatic polypeptide, neuropeptide Y and PYY. A study by Pittner et al. at Amylin Pharmaceuticals found PYY[3-36] to elicit a satiogenic response (decreased food intake) following peripheral administration in various rodent models of obesity and type II diabetes.

Pittner et al. used ALZET Osmotic Pumps (models 2004 and 2ML4) to study the chronic effects of different concentrations of PYY[3-36] in various obese and diabetic rodent models. Intraperitoneal (IP) injections were used to study the acute effects in normal mice. Experimental parameters included measurements of food intake, body weight and glycemic indices. The Amylin research study showed that IP injections of PYY[3-36] elicited a potent and dose-dependent reduction in food consumption over 60 minutes in fasted, nonobese mice. A 4-week

infusion of PYY[3-36] in diet-induced obese male mice led to reductions in body weight, cumulative food intake, and adiposity. Similar treatments in genetically obese ob/ob mice led to a dose-dependent decrease in body weight devoid of changes in cumulative food intake and glycemic indexes. Furthermore, infusion of PYY[3-36] for 8 weeks in genetically obese fatty Zucker rats also resulted in reductions in body weights and food consumption. In diabetic rodent models, chronic administration of PYY[3-36] induced similar beneficial effects, where a 4-week infusion of PYY[3-36] in diabetic fatty Zucker rats was associated with changes in body weight and a dose-dependent reduction in food consumption. Additionally, both glycemic indicators measured (HbA1c and fructosamine) were reduced in a dose-dependent manner. In contrast, PYY[3-36] had no acute glucose lowering effect in obese and diabetic mice.

Results from this study have prompted further investigation into the physiological and therapeutic roles of PYY[3-36]. A phase-1 clinical study is currently underway at Amylin Pharmaceuticals as a potential treatment for obesity.