Assessment of Neuropeptide Y Analogues As Feeding Antagonists

John A. Occhino UC II
PI: William T. Chance, Ph.D.

Introduction/Background:
Human obesity has been the cause of much morbidity and mortality, especially here in the United States. Form this has emerged a $20 billion/year weight loss industry. Also, research within the past 20 years has shown Neuropeptide Y (NPY) to be a primary mediator of food consumption. NPY is the most abundant peptide in the mammalian nervous system, and has been implicated in the pathophysiology of several diseases, including eating disorders, seizures, and cardiovascular disease.

Rationale/Hypothesis:
We believe further understanding of the NPY system will lead to a variety therapeutic opportunities. This past summer I tested to see if compounds that bind well to in vitro systems expressing NPY Y1 or Y5 receptors and decrease cAMP production will inhibit NPY-induced feeding.

Methods:
Stainless steel cannulae were implanted into the perifornical hypothalamus of male Sprague-Dawley rats (275-325g) allowing for direct peptide administration. Four different peptides, VD-11, VD-21, VD-30, and VD-40 were tested as feeding antagonists of NPY. Animals were given 1μl injections of artificial CSF or antagonist peptide. A second injection followed five minutes later, controls received CSF and experimental animals received NPY (0.7μg/μl). Rat chow intake was monitored at 1, 2, and 4 hours. Data was analyzed using ANOVA and Tukey's Protected T Test.

Results:
NPY groups showed significant increase in food intake versus CSF control groups ($p<0.010$). Peptide VD-11 significantly reduced NPY-induced feeding at the1 hour interval ($p<0.05$).

Conclusions/Significance/Future Work:
We determined that the NPY analog, VD-11, significant feeding antagonist of NPY. This opens the future for further analysis of VD-11, including dose response and specificity of feeding antagonism. Different delivery methods will also be studied in the future, all in hopes of developing anti-obesity compounds

Acknowledgments:
W.T. Chance, Ph.D.
A. Balasubramaniam, Ph.D.
University of Cincinnati