Peripheral Administration of Human CRH Increases Energy Expenditure and Decreases Adiposity

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INTRODUCTION

Central administration of CRH increases energy expenditure and decreases food intake in rodents. Humans, on the other hand, have a peripherally circulating binding protein and measurable levels of CRH in blood. The source of this circulating CRH is unknown. Human CRH (hCRH), but not ovine CRH (oCRH) binds to the circulating binding protein (CRH-BP). We proposed the hypothesis that peripheral administration of CRH would increase energy expenditure and decrease food intake in human subjects.

METHODS

Four men and four women (age 19 - 39 y) entered in a three period, cross-over, double blind trial to test the effect of hCRH, oCRH, and placebo (PL) on resting energy expenditure (REE) as measured by indirect calorimetry (Deltatrac II). CRH was administered by intranasal continuous infusion at progressively increasing doses of 0.5, 1.0, and 2.0 μg/kg/hour (2 each).

RESULTS

hCRH, but not oCRH, increased REE ( % increase over placebo in PL: 1.7% at 0.5 μg/kg/hour, 2.3% at 1.0 μg/kg/hour, and 2.6% at 2.0 μg/kg/hour, p < 0.05 for hCRH vs. placebo). hCRH increased EE at the 1.0 μg/kg/hour dose, with a larger increase in energy expenditure at the 2.0 μg/kg/hour dose. REE fell from 0.268 to 0.768 during the hCRH infusion, from 0.643 to 0.794 during oCRH, and from 0.833 to 0.857 during PL. Heart rate increased from 66.3 ± 9.4 bpm to 78.5 ± 5.4 bpm after 2.0 μg/kg/hour hCRH. There were no effects on hunger ratings or food intake.

CONCLUSIONS

Short-term peripheral infusion of hCRH increases REE. Since hCRH, which binds to CRH-BP, was able to increase REE, CRH-BP does not inhibit this effect. Activation of peripheral CRH receptors may offer a novel strategy to increase REE.


The aim of this study was to evaluate the specific interrelationships among changes in weight, glycemic control, and CV risk factors using clinical trial data from obese DM treated with antioxidants who completed 13 mo of a double-blind trial with a hyperosmotic diet plus antioxidants (HODA) and placebo (PL). Weight loss was greater in OBL and PL (6.2 ± 2.0 vs. 4.0 ± 0.4 kg, P < 0.05). AUC HbA1c was also greater in OBL vs. PL (7.5 ± 0.3 vs. 7.1 ± 0.3; P < 0.05). Insulin, triglycerides, cholesterol, and glycemic control (HbA1c) were measured before and after treatment. Simple correlations coefficients of change in each of 12 CV risk factors from initial to 12 mo were calculated in HbA1c (AUC HbA1c) and change in weight (A Weight) were calculated. These correlations were re-examined by partial correlation analysis to assess the association of A HbA1c with these CV variables after statistically removing weight gain.

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Departments of Psychiatry, University of California, San Francisco, Institute of Vertebrate Physiology, University of Zurich.

Salmon calcitonin is a 32-amino acid peptide hormone that is involved in the treatment of bone diseases such as Paget's disease, hypercalcemia and osteoporosis. The hormone has also been reported to potentially reduce food intake. The present work sought to determine the effect of repeated peripheral administration of SC on food intake, body weight and adiposity. Thirty-two adult male Long Evans rats were maintained on a diet of laboratory chow and tap water throughout the experiment. After being weight-matched into 4 equal groups, rats received one single daily intraperitoneal (IP) injection of saline vehicle or one of three doses of SC (100, 400, and 800 pmol/kg) over a 7-day period.

Substantial reductions of 24-h food intake were observed over the first two days, with the 2 higher doses (400 and 800 pmol/kg) producing significant reductions of about 25 and 50%, respectively. The reduction of food intake tended to persist over the subsequent 5 injection days, however, the effect was appropriately attenuated. Significant reductions of body weight were also observed after SC treatment. While the control animals gained about 14 g over the 7-day injection period, the group that received 800 pmol/kg SC lost 10.4 g of body weight. Upon sacrifice after 5 injections, the group that received 800 pmol/kg SC for 5 days, did not differ from controls, but the other 2 SC groups had significantly reduced body weights. These data suggest that the administration of calcitonin reduces food intake, body weight and body fat after repeated treatment with SC.