Society for Endocrinology media release

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Hormone combination shows promise in the treatment of obesity and diabetes

A new treatment combining two hormones can reduce appetite, according to new research presented today at the Society for Endocrinology annual conference in Harrogate, UK. This early study from an internationally-renowned team at Imperial College London provides 'first in man' evidence that a combined therapy using the hormones glucagon and glucagon-like peptide 1 (GLP-1) may form the basis for a new treatment for obesity and diabetes in the future.

Previous results from in animal studies showed that glucagon/GLP-1 combination might be an effective lead to combat obesity and diabetes. The hormones play key roles in regulating blood sugar. Glucagon works in opposition to insulin, preventing the storage of glucose in fat deposits and the liver, and raising blood sugar levels. GLP-1 stimulates the release of insulin to lower blood sugar and also acts at the brain to reduce appetite.

The research team, led by Professor Stephen Bloom, set out to identify whether glucagon and GLP-1 given in combination might work together to reduce appetite. In this small study, 16 human volunteers were randomly allocated to a sequence of four treatment infusions for 120 minutes, separated by at least three days, each: 1) glucagon, 2) GLP-1, 3) glucagon and GLP-1 in combination and 4) a saline infusion as a control. Double-blind crossover experiments such as these are used across clinical research to reliably identify cause and effect in a series of interventions.

The team provided the subjects with a meal at 90 minutes into each infusion, measured the amount of oxygen consumed, took blood samples to measure blood sugar and metabolic hormone levels, and took readings for pulse, blood pressure and nausea, all both at baseline and during the infusions. This provided data on energy intake (amount of food consumed), energy expenditure (oxygen used), blood sugar control, and the safety of and tolerance to the treatment.

The energy intake during the meal was 1086+/-110.1kcal for the control group vs. 879+/-94.2kcal for the hormone combination group: **a significant reduction of 13% ($p<0.05$)** which was also not seen when either hormone was given alone (glucagon: 1086+/-96.9kcal, GLP-1: 1052+/-81.3kcal; $p>0.05$). A non-significant trend toward increased energy expenditure was also observed in the combination and glucagon-alone groups. The infusions were tolerated safely.

The data show that the promising findings using a glucagon/GLP-1 combination in mice can be replicated in man. Appetite was significantly reduced during the combination treatment compared to the glucagon, GLP-1 alone or saline infusions. The group must now test this glucagon/GLP-1 combination treatment in more people and for longer periods of time to see if the effects can be sustained in the long term.

Professor Stephen Bloom, Head of Division of Diabetes, Endocrinology and Metabolism at Imperial College London said:

"*The hormones glucagon and GLP-1 are both used by the body to control blood sugar and metabolism, so there is great interest in utilising them to find new treatments for obesity and type 2 diabetes.*

"*We found that volunteers treated with a glucagon/GLP-1 combination consumed significantly less food. These data replicate our findings in animals, suggesting that a glucagon/GLP-1 combination may be a promising lead from which to develop a new treatment for obesity and diabetes.*

"13% is a big reduction in food intake by anyone's standards, but our experiment is only an appetiser. An effective future treatment will need to suppress appetite in the long term, so we next aim to establish whether the effects can be sustained to lead to real weight loss."

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Notes for Editors:

This research will be presented as a lecture (OC4.5) at the Society for Endocrinology BES meeting, on Tuesday 19 March 2013. The abstract for this lecture is reproduced at *Endocrine Abstracts*.

The Society for Endocrinology BES 2013 conference is Britain's biggest scientific meeting on hormones, and is taking place at the Harrogate International Centre from 18-21 March 2013. For the full programme, please click here.

Please mention the Society for Endocrinology meeting in any story

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The Society for Endocrinology is Britain's national organisation promoting endocrinology and hormone awareness. For general information, please visit our website: http://www.endocrinology.org

For more information on diabetes, obesity, endocrinology and hormones please visit You & Your Hormones (www.yourhormones.info), the Society for Endocrinology's public information website.

Consistently rated amongst the world's best universities, Imperial College London is a science-based institution with a reputation for excellence in teaching and research that attracts 14,000 students and 6,000 staff of the highest international quality. Innovative research at the College explores the interface between science, medicine, engineering and business, delivering practical solutions that improve quality of life and the environment - underpinned by a dynamic enterprise culture.

ABSTRACT

Energy intake following infusion of glucagon and GLP-1: a double-blind crossover study

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Obesity is a growing global epidemic and current medical therapies have proven inadequate. Endogenous satiety hormones provide an attractive target for the development of drugs which aim to cause effective weight loss with minimal side effects. Two related peptide hormones, glucagon and glucagon-like peptide 1 (GLP-1), are the subject of this investigation. Both have been found to reduce appetite and cause weight loss. Additionally, glucagon increases energy expenditure. It is proposed that co-administration of both peptides will have an additive effect on appetite reduction, while GLP-1 will protect against the hyperglycaemic effect of glucagon.

In this double-blind crossover study, a weight-adjusted dose of each peptide, alone or in combination, or placebo, was infused into 12 human volunteers for 120 minutes. An ad libitum meal was provided after 90 minutes and calorie intake determined. Resting energy expenditure was measured by indirect calorimetry at baseline and during the infusion. At regular time points blood samples were taken for assay of glucose, insulin, GLP-1 and glucagon. Pulse, blood pressure and self-perceived nausea levels were also recorded at each time point.

Co-infusion of glucagon with GLP-1 led to a reduction in food intake of 17.9%. Furthermore, the addition of GLP-1 protected against glucagon-induced hyperglycaemia and a trend of increased energy expenditure was seen on co-infusion of glucagon with GLP-1. This was achieved in the absence of negative effects on cardiovascular parameters.

This study therefore supports the concept of GLP-1 and glucagon dual agonism as a possible treatment for obesity.