Ghrelin, hyperphagia and adipose tissue content and distribution

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INTRODUCTION

Obesity is a modern epidemic, which still has no effective medical treatment. In order to understand the pathophysiology of obesity it is necessary to investigate the physiology of normal body weight regulation [1]. Ghrelin, a circulating gastric hormone, stimulates food intake in rodents and humans and hyperphagia, weight gain and adiposity on chronic administration in rodents [2]. Here we investigated the effect of chronic subcutaneous ghrelin on fat volume and distribution using magnetic resonance imaging (MRI).

METHODS

Male Wistar rats were implanted with subcutaneous osmotic mini-pumps (Alzet, USA) containing either saline (n=10) or ghrelin (n=18), set to deliver 30nmol in 24μl per 24h for 7 days. The ghrelin treated animals were subdivided into freely fed rats (G) and rats pair fed to the median food intake of the saline control group (GPF). Food intake and body weight were measured daily for 7 days. A subgroup (G n=6, GPF n=5, S n=5) from each treatment allocation was randomly selected for measurement of adipose tissue content and distribution by magnetic resonance imaging (MRI), using a quadrature bird-cage coil. Transverse T1-weighted MR images (TR 600 ms, TE 16 ms) were acquired, with a slice thickness of 2 mm and a 2 mm gap between slices, a 10 cm field of view and a 256x256 matrix. MR images were analysed using an in-house image segmentation software programme that employs a threshold range and a contour following algorithm with an interactive image editing facility [3].

RESULTS

Ghrelin-treated rats were hyperphagic (cumulative 7-day food intake G 192.8 ± 5.5g vs S 169.8 ± 3.9g, $p<0.01$) and gained more weight (54.6 ± 3.8g, $p<0.001$) than saline-treated (32.0 ± 2.3g) or GPF rats (33.6 ±1.5g). However, both ghrelin-treated groups had increased adipose tissue volume compared to saline-treated controls. Freely-fed ghrelin treated rats had significantly increased total (G 39.3 ± 2.5ml/rat vs S 31.2 ± 1.8ml/rat) and visceral (G 13.6 ± 1.3ml/rat vs S 9.7 ± 0.7ml/rat) adipose tissue volume ($p<0.05$) with a trend towards increased subcutaneous adipose tissue volume (G 25.7 ± 1.6ml/rat vs S 21.5 ± 1.2ml/rat) whilst ghrelin pair-fed rats had significantly increased visceral adipose tissue volume (12.7 ± 0.7ml/rat, $p<0.05$ vs S) with a trend towards increased total (37.2 ± 2.1ml/rat) and subcutaneous (24.4 ± 1.5ml/rat) adipose tissue volume. These differences were unaltered by correction for total body weight.

DISCUSSION

Continuous subcutaneous ghrelin administration promotes ongoing hyperphagia and weight loss. Whilst there was no increase in body weight in ghrelin treated rats pair fed to saline control, these rats did have significantly increased visceral fat. Thus ghrelin appears to favour adipose tissue deposition independently from its effect on food intake.

REFERENCES

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