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Increased proximal gastric volume induced by gastric ballon therapy for weight control

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Objectives: To investigate the effect of intravenously administered PYY 1-36, PYY 3-36 and saline on gastric emptying and short-term metabolic control.

Methods: The study involved eight healthy adult volunteers. At three separate occasions, infusions of saline, synthetic human PYY 1-36 or PYY 3-36 ($0.8 \text{ pmol kg}^{-1} \times \text{min}$) were given together with a radio-labelled omelette in a single-blinded design. Outcome measures included gastric emptying of solids (scintigraphy), appetite ratings (VAS), and plasma concentrations of insulin, glucose, GLP-1 and PYY.

Results: PYY 3-36 inhibited gastric emptying. Half emptying time was thus prolonged from 63.1 ± 5.2 to 87.0 ± 11.5 min. PYY 1-36 had no effect on gastric emptying. Neither forms influenced plasma concentrations of glucose, insulin or GLP-1. PYY 3-36 induced nausea with an increase in VAS rating of 47.5 ± 22.6 and decreased prospective consumption [VAS change of 39.5 ± 7.7].

Conclusion: The ability of PYY 3-36 to reduce food intake might be mediated by nausea and decreased gastric emptying rate.

Conflict of Interest: None declared.

FRI034

Intestinal serotonin signalling measured in high-fat diet rats using electrochemical techniques

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Introduction: A high fat diet is associated with subtle changes in gastrointestinal function and in the levels of intestinal hormones secreted. Enterochromaffin (EC) cells containing serotonin (5-HT) do not directly detect fat in the intestinal lumen, but they may respond in a compensatory fashion to altered gut function such as occurs during obesity.

Objectives: Our aim was to characterize real-time uptake and release of 5-HT in a rat model of diet-induced obesity.

Methods: Real-time electrochemical methods using a carbon fibre electrode were used to determine the effect of a 'cafeteria-style' diet on 5-HT availability. Peak and steady state (SS) 5-HT concentrations (calculated from the oxidation current at +300 mV, amperometry mode) were measured with or without the serotonin reuptake transporter (SERT) blocker, fluoxetine ($1 \mu\text{mol L}^{-1}$), in control (age matched, chow-fed; $508 \pm 16 \text{ g}$, $n = 6$) and high-fat diet rats (HFD; $740 \pm 26 \text{ g}$, $n = 11$). Paired and unpaired data were compared with a one way ANOVA ($P < 0.05$) using a Tukey-Kramer *post-hoc* test.

Results: In control rat ileum, SS levels of 5-HT were $12.3 \pm 3.4 \mu\text{mol L}^{-1}$ and peak compression-evoked release was significantly higher at $22.3 \pm 4.2 \mu\text{mol L}^{-1}$ ($P < 0.05$; $n = 6$; each sampled from three positions on the mucosa). In HFD rats, the levels of 5-HT were significantly increased (SS: $23.8 \pm 3.4 \mu\text{mol L}^{-1}$; peak: $66.8 \pm 13.4 \mu\text{mol L}^{-1}$; $P < 0.05$, $n = 11$). In control rats, fluoxetine doubled the peak and SS 5-HT release (180% of control, $n = 3$), while in HFD rats fluoxetine caused no significant changes. Run-down for compression-evoked release was similar in both control ($n = 3$) and HFD rats ($n = 4$; $P > 0.05$) with peak release reduced by ~50% during a second response.

Conclusion: A high fat diet alters the release of 5-HT from the EC cells of the rat ileum. Our electrochemical data show that both peak and steady state levels are increased and predict that a high fat 'cafeteria-style' diet will be associated with an increased 5-HT availability. Further investigation into levels of tryptophan hydroxylase 1, SERT, and EC cell numbers will serve to test the accuracy of this prediction.

Conflict of Interest: None declared.

FRI035

Selective changes in vagal afferent receptor expression in fasting and obesity

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Introduction: Vagal afferents mediate satiety signals from the gut in response to mechanical and enteroendocrine derived stimuli.

Objectives: Since there is evidence for dampening of satiety signalling in fasting and in obesity, we investigated if the molecular and functional expression of key receptors for enteroendocrine cell mediators is changed with alteration of food intake.

Methods: C57BL6 mice were either fasted for 18 h or fed *ad libitum*. Preliminary studies were also performed on mice made obese by consumption of a 60% fat diet for 12 weeks compared with normally fed controls. Quantitative RT-PCR of receptor mRNA in nodose ganglia was performed relative to total RNA or beta-tubulin. Single-fibre electrophysiological recordings were made of mechanosensitive vagal afferents in the stomach *in vitro*.

Results: Fasting decreased the expression of the leptin receptor (ObR) in nodose ganglia by 87% ($n > 5$ each), and increased the expression of CCK1R by sevenfold. Expression of total RNA, beta-tubulin, 5-HT3R, GLP-1R, P2X2R, and P2X3R was unchanged. Changes in leptin receptor expression were also investigated functionally. In fed mice, leptin ($0.1\text{--}10 \text{ nmol L}^{-1}$) more than doubled mucosal receptor mechanosensory responses to mucosal stroking with calibrated von Frey hairs ($10\text{--}1000 \text{ mg}$) ($P < 0.01$, $n = 5$). In fasted mice, leptin had no effect on mucosal receptor responses. Leptin receptor levels were reduced by 50% in obese mouse nodose ($n = 5$, $P < 0.05$). The changes in CCK1R expression in obesity and the functional correlates of these changes are currently under investigation.

Conclusion: The marked down-regulation of leptin receptors in nodose ganglia after an overnight fast correlated with leptin-mediated effects on function of vagal mucosal afferents. Vagal leptin receptor expression in obesity is reduced as it is in fasting, suggesting the acquisition of a 'fasted' phenotype favouring increased food intake. How the up-regulation of CCK1-receptor expression can be reconciled with leptin receptor changes remains elusive for the time being.

Conflict of Interest: Funded by the University of Adelaide and the Hanson Institute.

FRI036

Increased proximal gastric volume induced by gastric balloon therapy for weight control

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Introduction: The intra-gastric balloon, filled with air or liquid, is used in the treatment of morbid obesity. Randomized controlled studies comparing balloon vs diet exclusively report heterogeneous data without true consensus on the actual efficacy of this therapy. Modifications of gastric wall properties, secondary to the presence of the balloon, could explain treatment failure.

Objectives: We aimed at assessing gastric volume variations induced by an intra-gastric balloon filled with air and inserted during 5 months in the stomach of mini-pigs.

Methods: Gastric volumes were measured by single photon emission computed tomography (SPECT) in animals with and without a gastric balloon. Ten Gottingen minipigs were randomly allocated into two groups: five pigs had a balloon, five belonged to the control group. Balloons were inserted during an upper endoscopy, under anaesthesia and were filled with 350 mL of air at 20 mmHg. Using SPECT imaging, gastric volumes were measured before, 2 weeks after insertion and every 3 weeks until balloon extraction. Tomographic acquisition was performed after ingestion of a ^{99m}Tc-labelled meal. Cholestyramine, which has mucoadhesive properties on the gastric mucus, was incorporated to the mixture to underline the gastric mucosa. Three-dimensional gastric reconstructions and measurements were performed with OSIRIX software. Furthermore, the exact volume of the balloon was measured by abdominal CT every month.

Results: The balloon volume was unaltered during the entire experimental period ($342 \pm 8.7 \text{ cm}^3$). Two weeks after balloon insertion, gastric volume was significantly increased ($2047 \pm 256.8 \text{ cm}^3$ after vs $1674 \pm 318.7 \text{ cm}^3$ before insertion, $P < 0.05$) whereas it remained stable in the control group ($1632 \pm 121.0 \text{ cm}^3$ vs $1652 \pm 243.9 \text{ cm}^3$). This increase was entirely related to a larger volume of the proximal stomach ($1107 \pm 36.5 \text{ cm}^3$ vs $795 \pm 116.3 \text{ cm}^3$, $P < 0.01$) while the volume of the distal stomach remained unchanged. Afterwards gastric volume remained enlarged without significant difference compared to the first measurement following balloon placement.

Conclusion: The insertion of an intra-gastric balloon during several months, in conditions similar those used in clinical practice for obesity treatment, is followed by a significant increase in proximal but not distal gastric volume. The increase in proximal gastric volume is larger than the volume of the gastric balloon indicating that it is due to an active rather than a pure mechanical phenomenon. This enlargement is probably causative for a reduced balloon efficacy towards food intake. Its origin is still putative but might be related to an increased compliance of the gastric wall.

Conflict of Interest: None declared.

FRI037

The role of gender in the sensation of hunger

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Introduction: Early research showed that men appear to experience hunger in a physical way (gastric sensations) whereas women appear to experience hunger in a diffuse and cerebral way (negative moods, urge to eat and preoccupation with food).^{1,2} Data previously collected by the principal investigator appeared to support this hypothesis. It was found that hunger positively correlated with a gastric myoelectrical rhythm that is associated with a fed stomach (3 cycle per minute activity) in women, but negatively correlated with this same activity in men. This finding seems to indicate that men associate hunger with an empty stomach, but that women associate hunger with a fed stomach, indicating that women's hunger may be primarily motivated by non-gastric cues. A recently developed questionnaire, the Intuitive Eating Scale (IES)³ examines eating patterns from an adaptive perspective (i.e., eating to satisfy hunger) and hence is useful for examining these gender differences on a large scale.

Objectives: The purpose of the current study was to examine the relationships between the IES, body mass index (BMI) and gender.