Appetite, food intake and ageing: The role of the gut

A thesis submitted by
Barbara Parker

For the degree of Doctor of Philosophy
Department of Medicine
University of Adelaide

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Dedication

I dedicate this thesis to my darling husband and children, Lyndon, Lucy and Callum Parker. This would not have been possible without you.

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Thesis summary

This thesis is concerned with gastrointestinal mechanisms and the changes that occur with age that may affect food intake and appetite. Studies are presented that evaluate the contribution of these mechanisms to the control of appetite in older persons. In particular, the use and validation of visual analogue scales in these studies and gastrointestinal aspects of appetite control, the effects of intraduodenal and gastric infusions of fat versus carbohydrate, relationships between gastric antral area and appetite (using ultrasound measurements) and the effect of accelerating gastric emptying (with domperidone) on appetite and food intake are addressed.

Life expectancy is increasing both in Australia and overseas. Many health initiatives focus on decreasing food intake due to the increasing prevalence of obesity in our society, however reduced nutritional intake can also contribute to illness and death in older people. Ageing is associated with changes in gastrointestinal function affecting food intake. The spiralling costs of healthcare highlight the need for promotion and maintenance of healthy lifestyle choices, especially adequate nutritional intake, in older persons.

Healthy ageing is associated with decreased appetite and food intake, the so-called 'anorexia of ageing'. This anorexia of ageing is a part of the normal process of ageing in people who do not suffer physical, psychiatric or social disorders. From young to old adult (18-70 years) the average daily food intake falls by approximately 30%. This reduction is probably in response to a normal decline in activity, however, when our food intake decreases more than our exercise levels weight loss, usually muscle, occurs. Unlike fat, loss of muscle has adverse effects including decreases in strength and increases in falls and fractures, loss of independence and increased risk of protein energy malnutrition, which in turn increases acute and chronic illness, hospitalisation and death. There are many explanations for changes in appetite and food intake in older people including sensory (taste and smell changes, dental abnormalities) and social (poverty, loneliness, institutionalisation) factors.

Appetite regulation in humans is complex. Although many of the mechanisms are unclear, alterations in gastrointestinal responses to food ingestion are important in appetite (how hungry or full we feel) and food intake changes with age. Changes occur with increasing age in functions of the stomach and small intestine, including how quickly food and fluids leave the stomach and enter the small intestine to begin digestion, and changes in the way food is distributed and retained within the three sections of the stomach. These changes can influence appetite by increasing fullness and decreasing hunger. In addition, small intestinal hormones associated with appetite regulation increase with age and there is a greater sensitivity to their effects. The interaction of nutrients with gastrointestinal tract receptors stimulates the release of satiety hormones, including cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), gastric inhibitory peptide (GIP) and amylin, and inhibits the release of ghrelin, which stimulates feeding.

Visual analogue scales (VAS) are widely used in appetite research involving adults of all ages, yet the reproducibility and validity of these scales to evaluate appetite has not been assessed in older subjects. In two studies discussed in Chapter 4, retrospective (to determine the relation of appetite sensations to food intake) and prospective (to determine reproducibility), VAS were evaluated as a measurement of appetite in healthy older subjects. The retrospective study was a combined analysis of four single-blind, randomised, controlled appetite studies undertaken in young and older subjects and the prospective study was an assessment in healthy older men and women aged 65-85 years. Perceptions of appetite (i.e. hunger and fullness) were assessed by 100mm visual analogue scales administered at regular intervals. Food intake was quantified from food intake at a test meal.

In the retrospective study, food intake at the test meal was positively related to perceptions of hunger, drowsiness, and calmness and inversely related to ratings of fullness taken immediately before the meal in both older and young subjects. In the prospective study, VAS measures of appetite were found to have comparable reproducibility and validity in older subjects to reported values in young adults. These observations confirm that food intake is related to perceptions of hunger and fullness as assessed by VAS in healthy older and young subjects, and suggest that sensations, not obviously associated with appetite, including 'drowsiness' and 'calmness', are also associated with food intake.

Gastric distension reduces food intake, and antral rather than proximal, gastric distension may be the dominant mechanism in the initiation of appetite-related sensations. To evaluate the age-related changes in appetite, food intake, gastrointestinal hormone concentrations and antral area healthy young and older subjects were administered oral yoghurt preloads and water (control) 60 minutes prior to a buffet meal (Chapter 5). Antral area was greater after the nutrient preloads than after water ($P = 0.001$) and larger in the older than young subjects ($P = 0.005$). Hunger ($r = -0.59$, $P < 0.001$) and food intake ($r = - 0.90$, $P < 0.001$) were inversely, and fullness directly ($r = 0.66$, $P < 0.001$), related to antral area in both age groups. In healthy older and young subjects the suppression of subsequent food intake was nutrient-dependent and both satiation (meal termination) and satiety (time to subsequent meal consumption) were related to antral area, and antral distension.

The effect of intragastric and intraduodenal administration of macronutrients, such as fat and carbohydrate, on appetite and food intake may be influenced by age. In Chapter 6, intragastric infusions of water (0 kcal), carbohydrate and fat (both 343 kcal), were delivered over 5 minutes to older and young men. Food intake was assessed at a buffet meal. Carbohydrate infusion suppressed food intake significantly more than the fat infusion (23 v 10%, $P = 0.005$), and this was so in both young (25 v 14%, $P = 0.03$) and older (21 v 7%, $P = 0.05$) men. These results were compared to equienergetic, equivolaemic fat and carbohydrate solutions delivered into the small intestine of older and young men. Fat inhibited food intake significantly more than carbohydrate in the young men (26 v 5%, $P < 0.001$) whilst the suppressive effects of fat and carbohydrate were similar in the older men (21 v 22%, $P = 0.05$). This suggests that with increasing age regional differences in the gastrointestinal tract play both distinct and interacting roles in appetite regulation.

Ghrelin is a recently identified peptide hormone secreted primarily from the gastric mucosa. It plays a role in energy balance by stimulating appetite, thereby increasing food intake and enhancing weight gain and fat mass deposition. Plasma ghrelin concentrations increase with fasting and are suppressed by nutrient intake. In Chapter 7, the contribution of both the stomach and small intestine in postprandial suppression of ghrelin was assessed. On three separate days, glucose (300 kcal) and water (C, 0 kcal) were infused slowly over 150 minutes into the stomach (IG), and an equienergetic infusion of glucose was infused into the small intestine (ID) of older men and women. Ghrelin was suppressed following both glucose infusions compared to control (ID 25% and IG 19% v C, $P < .00001$). There was no difference in the degree of suppression between the two glucose infusions ($P = 0.2$). These results suggest that although the primary source of ghrelin is the gastric mucosa, small intestinal exposure is largely responsible for ghrelin suppression in humans. The effect of age on the suppression of ghrelin in response to nutrient intake is unclear.

Domperidone, a prokinetic drug, is a predominantly peripheral acting dopamine2-receptor antagonist known to accelerate gastric emptying. It has been reported to be effective in the treatment of gastrointestinal symptoms associated with non-ulcer dyspepsia, Parkinson's disease and diabetic gastroparesis. The acute effects of domperidone on perceptions of appetite and food intake in healthy older people may include a reduction in antral distension (as a result of more rapid gastric emptying and pharmacologically-induced gastric 'relaxation') and meal-related symptoms, and increases food intake at a subsequent meal.

In Chapter 8, 10 older men were treated with either domperidone or placebo and food intake, appetite and antral area assessed after a yoghurt preload. There were no differences in appetite scores of food intake between the study days. There was a decrease in antral area and an increase in blood glucose concentrations on the domperidone day, suggesting an increase in gastric emptying, although this difference was not significant. Further studies are required to evaluate the effects of this prokinetic agent on gastric emptying and food intake in older subjects.

As the causes of the anorexia of ageing are still largely unknown, the aim of this research was to examine the effects of ageing on appetite, food intake and gastrointestinal function. This research will provide further insight into the 'physiological' anorexia of ageing and management of the frail elderly, whether resident at home, in acute or long-term care.

Declaration of originality

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university, and to the best of my knowledge and belief contains no material previously published or written by another person, except where due reference is made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Barbara Parker
December 2004

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Dr Kerstin Sturm (based at the Department of Medicine, Royal Adelaide Hospital; 2000-2002) co-conducted the work in Chapter 5 and provided instruction in the use of the ultrasound machine.

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Mrs Selena Doran (Department of Medicine, Royal Adelaide Hospital) provided instruction and assistance in the studies presented in Chapters 7 and 8.

Ms Judith Wishart (Department of Medicine, Royal Adelaide Hospital) conducted the plasma insulin, cholecystokinin, glucagon-like peptide-1 and ghrelin assays reported in Chapters 5, 6 and 7.

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Publications

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Parker BA, Ludher AK, Khai Loon, Tan, Horowitz M, Chapman IM (2004). Reproducibility and validity of visual analogue scales in assessment of appetite sensations and food intake in healthy older subjects. *Appetite* 43,227-233.

Parker BA, Chapman, I (2004). Food intake and ageing- the role of the gut. Review. *Mechanisms of Development and Ageing* 125, 859-866.

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Sturm K, **Parker BA**, Feinle C, Jones KJ, Wishart J, Chapman IM, Horowitz M (2004). Energy intake and appetite are related to antral area in healthy young and older subjects. *Am J Clin Nutr*. 80(3),656-667.

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