DISSERTATIONS IN
HEALTH
SCIENCES

Kristiina Juvonen

Appetite Control

The Role of Food Composition and Structure

Publications of the University of Eastern Finland
Dissertations in Health Sciences

UNIVERSITY OF
EASTERN FINLAND

KRISTIINA JUVONEN

Appetite control – the role of food composition and structure

To be presented by permission of the Faculty of Health Sciences, University of Eastern Finland
for public examination in Auditorium ML3, Medistudia building, Kuopio,
on Friday, October 5th 2012, at 12 noon

Publications of the University of Eastern Finland
Dissertations in Health Sciences
Number 129

Department of Clinical Nutrition,
Institute of Public Health and Clinical Nutrition,
Faculty of Health Sciences, University of Eastern Finland
Kuopio
2012

Kopijyvä Ltd
Kuopio, 2012

Distributor:

University of Eastern Finland
Kuopio Campus Library
P.O. Box 1627
FI-70211 Kuopio, Finland
http://www.uef.fi/kirjasto

ISBN (print): 978-952-61-0886-5
ISBN (pdf): 978-952-61-0887-2
ISSN (print): 1798-5706
ISSN (pdf): 1798-5714
ISSN-L: 1798-5706

Author's address: Department of Clinical Nutrition
Institute of Public Health and Clinical Nutrition
University of Eastern Finland
KUOPIO, FINLAND

Supervisors: Adjunct Professor Leila Karhunen, Ph.D.
Department of Clinical Nutrition
Institute of Public Health and Clinical Nutrition
University of Eastern Finland
KUOPIO, FINLAND

Academy Professor Kaisa Poutanen, D.Tech.
VTT Technical Research Centre of Finland and
Department of Clinical Nutrition
Institute of Public Health and Clinical Nutrition
University of Eastern Finland
KUOPIO, FINLAND

Professor Karl-Heinz Herzig, M.D., Ph.D.
Institute of Biomedicine
Division of Physiology and Biocenter of Oulu
University of Oulu
OULU, FINLAND

Reviewers: Alan R Mackie, Ph.D.
Institute of Food Research
NORWICH, UNITED KINGDOM

Adjunct Professor Liisa Valsta, Ph.D.
University of Helsinki, Faculty of Agriculture and Forestry
Department of Food and Environmental Sciences
HELSINKI, FINLAND

Current position:
Senior Scientific Officer
European Food Safety Authority (EFSA)
Dietary and Chemical Monitoring Unit
PARMA, ITALY

Opponent: Professor Margriet Westerterp-Plantenga, Ph.D.
Department of Human Biology
Maastricht University
MAASTRICHT, THE NETHERLANDS

Juvonen, Kristiina
Appetite control – the role of food composition and structure.
University of Eastern Finland, Faculty of Health Sciences, 2012
Publications of the University of Eastern Finland. Dissertations in Health Sciences 129. 2012. 109 p.

ISBN (print): 978-952-61-0886-5
ISBN (pdf): 978-952-61-0887-2
ISSN (print): 1798-5706
ISSN (pdf): 1798-5714
ISSN-L: 1798-5706

ABSTRACT

In the current situation where obesity has reached pandemic proportions, it is important to understand dietary factors that affect appetite and food intake both in short- and long-term. Besides the dietary composition the structure and physical form of food play an important role in the regulation of appetite and food intake. The synergetic effects of food properties modulate the postprandial systemic functions and affect ultimately energy balance.

Gut-brain cross-talk, the core of appetite control, coordinates short- and long-term signals that serve energy balance. In this process the neuroendocrine system in the gastrointestinal (GI) tract plays a major role by adjusting digestion through the release of several peptide hormones in response to energy status and various food-related stimuli. The intrinsic characteristics of dietary components are known to modulate postprandial physiology including GI peptide release which in turn modulates GI functions and metabolism.

The aim of this work was to investigate the postprandial effects of dietary fibres and proteins and their structural modification on postprandial appetite and appetite-related GI responses in healthy normal-weight individuals.

Psyllium fibre enrichment of vegetable patties suppressed postprandial metabolic and GI peptide responses. The effects of simultaneous soy protein enrichment were less evident. Oat bran enrichment of the semisolid porridge lowered glucose and insulin responses, whereas GI peptide responses were comparable among oat and wheat bran containing products. Oat bran-enriched beverage with lowered viscosity stimulated postprandial metabolic and GI peptide responses, accelerated gastric emptying and increased satiety, which was not the case when viscosity of the oat bran beta-glucan was maintained. Caseinate and whey protein produced different, protein-specific postprandial amino acid profile and cholecystokinin response. Enzymatically crosslinked caseinate consumed in beverage form did not affect postprandial responses, whereas crosslinked caseinate in gel form suppressed metabolic and GI peptide responses and increased fullness.

In conclusion, viscous dietary fibre both in solid and liquid food matrix and the physical form of food modifies gastric emptying, GI peptide responses and appetite ratings. These data emphasize the importance of dietary fibre and food form in modifying the short-term physiological and appetite responses.

National Library of Medicine Classification: WI 102, QU 50, QT 235, WK 170
Medical Subject Headings: Appetite; Appetite Regulation; Gastric Emptying; Postprandial Period; Food; Molecular Structure; Enzymes; Viscosity; Gastrointestinal Hormones; Blood Glucose; Insulin; Dietary Fiber; Psyllium; beta-Glucans; Dietary Proteins; Soybean Proteins; Milk Proteins

Juvonen, Kristiina
Elintarvikkeiden koostumuksen ja rakenteen merkitys ruokahalun säätelyssä.
Itä-Suomen yliopisto, terveystieteiden tiedekunta, 2012
Publications of the University of Eastern Finland. Dissertations in Health Sciences 129. 2012. 109 s.

ISBN (print): 978-952-61-0886-5
ISBN (pdf): 978-952-61-0887-2
ISSN (print): 1798-5706
ISSN (pdf): 1798-5714
ISSN-L: 1798-5706

TIIVISTELMÄ

Lihavuuden yleistyessä maailmanlaajuisesti ruoan ominaisuuksien merkitys ruokahalun ja energiatasapainon lyhyt- ja pitkäaikaissäätelyssä korostuu. Ravintoainekoostumuksen lisäksi ruoan rakenteella ja olomuodolla on huomattava vaikutus ruokahaluun ja syömiseen. Näiden ominaisuuksien yhteisvaikutukset säätelevät elimistön aterianjälkeistä toimintaa ja vaikuttavat keskeisesti energiatasapainoon.

Ruokahalua ja syömistä säädellään keskushermoston ja perifeerisen elimistön yhteistyönä. Säätelyjärjestelmän keskeinen osa, ruoansulatuskanavan neuroendokriininen järjestelmä säätelee ruoansulatuksen lisäksi suolistosta vapautuvien peptidihormonien eritystä. Energiaravintoaineet ja ruoan rakenne vaikuttavat näiden peptidien eritykseen, mikä puolestaan muuttaa ruoansulatuskanavan toimintaa ja aterianjälkeistä aineenvaihduntaa.

Tämän tutkimuksen tarkoituksena oli selvittää erilaisten ravintokuitujen ja proteiinien sekä niiden rakenteen muokkauksen vaikutusta aterianjälkeisiin metabolisiin ja hormonaalisiin vasteisiin sekä ruokahaluun nuorilla normaalipainoisilla henkilöillä.

Kasvispihvien psyllium-kuitulisä vaimensi aterianjälkeisiä metabolisia ja hormonaalisia vasteita, kun taas soijaproteiinilisän vaikutukset olivat vähäisiä. Runsaasti beetaglukaania sisältäneen kauraleseen lisäys puuromatriisiin madalsi glukoosi- ja insuliinivasteita, mutta kuitulisä ei vaikuttanut hormonivasteisiin. Kauralesejuomien matala viskositeetti stimuloi sekä aterianjälkeisiä metabolisia ja hormonivasteita että mahalaukun tyhjenemistä ja lisäsi kylläisyyden tunnetta. Kaseinaatin entsymaattinen ristisilloitus ei vaikuttanut aterianjälkeisiin metabolisiin vasteisiin tai ruokahaluun, kun rakennemuokattu kaseinaatti nautittiin juomana. Geelimäisenä tuotteena rakennemuokattu kaseinaatti sen sijaan vaimensi aterianjälkeisiä metabolisia ja hormonaalisia vasteita sekä lisäsi täyden olon tunnetta.

Tämä tutkimus osoitti, että liukoiset ravintokuidut, viskositeetti ja ruoan olomuoto muokkaavat aterianjälkeisiä fysiologisia vasteita ja ruokahalua. Nämä tulokset korostavat ravintokuidun ja ruoan rakenteen vaikutuksia aterianjälkeisissä fysiologisissa vasteissa ja ruokahalun säätelyssä.

Luokitus: WI 102, QU 50, QT 235, WK 170
Yleinen suomalainen asiasanasto: ruokahalu; kylläisyys; aterianjälkeinen jakso; ruoka; rakenne; ruoansulatuskanavan hormonit; verensokeri; insuliini; ravintokuitu; leseet; beetaglukaani; proteiinit; soija; hera; viskositeetti; entsyymit

Acknowledgements

This study was conducted at the Department of Clinical Nutrition, University of Eastern Finland, Kuopio campus and at the Department of Physiology, University of Oulu. I would like to sincerely acknowledge all the people whose contribution made this work possible.

I am deeply grateful to all my supervisors, Adjunct Professor Leila Karhunen, Academy Professor Kaisa Poutanen and Professor Karl-Heinz Herzig for their excellent guidance, patience and encouragement which were priceless and carried me through the whole process. I owe my sincere gratitude to my principle supervisor, Adjunct Professor Leila Karhunen for her never failing optimism, empathy and invaluable scientific and personal support during these years. You always had time for me, unconditionally also outside the office hours. I equally appreciate the generous support of my co-supervisors, Academy Professor Kaisa Poutanen and Professor Karl-Heinz Herzig whose enthusiasm, dedication and innovativeness in the realm of science are admirable. It has been a privilege to work under your impressive expertise.

I sincerely thank the official pre-examiners of the thesis, Adjunct Professor Liisa Valsta, from the European Food Safety Authority, Italy and Alan Mackie Ph.D., from the Institute of Food Research, United Kingdom for their great effort and critical review of the thesis. The thesis was significantly improved by their valuable comments and constructive criticism. I feel deeply honoured that Professor Margriet Westerterp-Plantenga, from the University of Maastricht, The Netherlands accepted the invitation to act as an official opponent in the public examination of my doctoral dissertation.

I wish to thank Professor Hannu Mykkänen, Professor Emerita Helena Gylling, Academy Professor Kaisa Poutanen and Professor Karl-Heinz Herzig for the opportunity to use the department facilities.

All my co-authors of the original publications are warmly acknowledged for their support and scientific contribution including Professor Matti Uusitupa M.D., Professor Leo Niskanen M.D., Professor Hannu Mykkänen Ph.D., David Laaksonen M.D., Ph.D., Martina Lille M.Sc., Anna-Kaisa Purhonen Ph.D., Maritta Siloaho Ph.D., Marjatta Salmenkallio-Marttila Ph.D., Professor Liisa Lähteenmäki Ph.D., Marika Lyly Ph.D., Kirsi-Helena Kanninen D.Tech., Sanna Flander M.Sc., Elisa Vuori B.M., Toni Karhu M.Sc. and Alicia Jurado-Acosta M.Sc. In addition, I would like to thank Vesa Kiviniemi Ph.Lic. and Marja-Leena Hannila M.Sc. for their valuable support in statistical issues.

All the former and present young researchers are thanked for the pleasant working atmosphere. Especially I wish to thank Kaisa R for peer-support and great discussions. I would also like to thank Tiina, Anna-Maija, Liisa, Maija, Maria, Anne, Niina, Jenni, Jenna, Taisa and Otto M for inspiring colleagueship.

I wish to express my gratitude to Eeva Lajunen for her guidance and diligent work with all the myriad of samples. You patiently familiarized me with the challenging laboratory work and supported me whenever needed. I warmly thank also Erja Kinnunen for all the help, cooperation and thoughtful discussions over the years. I deeply appreciate the expertise and assistance from Maritta Siloaho with all the laboratory analysis. My sincere thanks are

given to Martina Lille for her invaluable help with the ingredients and protocol for the test products. I would also like to thank Päivi Turunen, Kaija Kettunen and Tuomas Onnukka for their expert laboratory assistance.

The secretaries of the department, Maarit Närhi, Irma Pääkkönen and Anja Laine, are warmly thanked for their patience and kind help with the administrative and practical issues. I would also like to express my warm thanks to all the colleagues for the very pleasant atmosphere at the Department of Clinical Nutrition.

My dear friend Marketta Puttonen deserves my warmest gratitude. Your friendship – it is truly special!

All participants of the postprandial studies are warmly acknowledged. Without your contribution these studies would not have succeeded.

In appreciation of their financial support for this work, I would like to thank Academy of Finland (The Research Programme on Nutrition, Food and Health, ELVIRA), The Finnish Graduate School on Applied Bioscience: Bioengineering, Food & Nutrition, Environment, The EVO funding of Kuopio University Hospital, Tekes – the Finnish Funding Agency for Technology and Innovation, The Finnish Cultural Foundation, Raisio Oyj, Atria Suomi Oy, Fazer Bakeries Oy, VAASAN Oy, Valio Oy, Arla Ingman Oy Ab, Oy Sinebrychoff Ab, Apetit Pakaste Oy and Suomen Viljava Oy.

Kuopio, September 2012

Kristiina Juvonen

List of the original publications

This dissertation is based on the following original publications which will be referred to their Roman numerals *I–V* in the text:

I Karhunen LJ, Juvonen KR, Flander SM, Liukkonen KH, Lähteenmäki L, Siloaho M, Laaksonen DE, Herzig KH, Uusitupa MI, Poutanen KS. A psyllium fiber-enriched meal strongly attenuates postprandial gastrointestinal peptide release in healthy young adults. *J Nutr. 2010; 140: 737-744.*

II Juvonen KR, Salmenkallio-Marttila M, Lyly M, Liukkonen KH, Lähteenmäki L, Laaksonen DE, Uusitupa MI, Herzig KH, Poutanen KS, Karhunen LJ. Semisolid meal enriched in oat bran decreases plasma glucose and insulin levels, but does not change gastrointestinal peptide responses or short-term appetite in healthy subjects. *Nutr Metab Cardiovasc Dis. 2011; 21: 748-756.*

III Juvonen KR, Purhonen AK, Salmenkallio-Marttila M, Lähteenmäki L, Laaksonen DE, Herzig KH, Uusitupa MI, Poutanen KS, Karhunen LJ. Viscosity of oat bran-enriched beverages influences gastrointestinal hormonal responses in healthy humans. *J Nutr. 2009; 139: 461-466.*

IV Juvonen KR, Karhunen LJ, Vuori E, Lille ME, Karhu T, Jurado-Acosta A, Laaksonen DE, Mykkänen HM, Niskanen LK, Poutanen KS, Herzig KH. Structure modification of a milk protein-based model food affects postprandial intestinal peptide release and fullness in healthy young men. *Br J Nutr. 2011; 21: 1-9.*

V Juvonen KR, Lille ME, Laaksonen DE, Mykkänen HM, Niskanen LK, Herzig KH, Poutanen KS, Karhunen LJ. Crosslinking with transglutaminase does not change metabolic effects of sodium caseinate in model beverage in healthy young individuals. *Nutr J. 2012; 11: 35.*

Contents

Abbreviations

AgRP	Agouti-related peptide
ARC	Arcuate nucleus
AUC	Area under the curve
BITE	Bulimic Investigatory Test Edinburgh
BMI	Body mass index
CART	Cocaine- and amphetamine-stimulated transcript
Cas	Caseinate
Cas-TG	Caseinate crosslinked by transglutaminase
CCK	Cholecystokinin
CCK1R	Cholecystokinin receptor 1
CCK2R	Cholecystokinin receptor 2
CHO	Carbohydrate
CNS	Central nervous system
DF	Dietary fibre
DPP IV	Dipeptidyl peptidase
E%	Percentage of total energy
FFA	Free fatty acid
GHS-R	Growth hormone secretagogue receptor
CNS	Central nervous system
GE	Gastric emptying
GI	Gastrointestinal
GIP	Glucose-dependent insulinotropic polypeptide, gastric inhibitory polypeptide
GLP-1	Glucagon-like peptide 1
GLP-1R	GLP-1 receptor
LCT	Long-chain triacylglycerol
MCFA	Medium-chain fatty acid
MCT	Medium-chain triacylglycerol
NPY	Neuropeptide Y
NTS	Nucleus of the solitary tract
OGTT	Oral glucose tolerance test
POMC	Pro-opiomelanocortin
PP	Pancreatic polypeptide
PYY	Peptide tyrosine-tyrosine
TFEQ	Three-Factor Eating Questionnaire
TG	Transglutaminase
VAS	Visual analogue scale
Wh	Whey protein

1 Introduction

The prevalence of obesity has reached pandemic proportions with associated significant health problems and economical burdens for the societies (Swinburn et al., 2011). Therefore it is essential to find dietary factors that have favourable effects on appetite and food intake regulation. The regulation of appetite and food intake is, however, a complex system, influenced strongly by not only the food and its various attributes, but also a range of individual (internal) characteristics and social, cultural and environmental (external) factors (Schwartz et al., 2000; Lenard and Berthoud, 2008; Zheng et al., 2009). In this system, the external factors may markedly interfere with the internal homeostatic control. Nonetheless, food is an integral part of these "outer" and "inner" systems and the attributes of foods that support the bodily system towards energy balance should be identified.

Although quantitative dietary factors (i.e. amount of food and energy consumed) are important contributors to appetite and energy balance, consideration of the qualitative factors, e.g. macronutrient composition and type, food structure and physical state, are of equal importance. Previous data demonstrate that dietary fibre (DF) and protein are essential elements of a healthy diet, and they affect a variety of physiological factors underlying and determining the overall health status (Anderson et al., 2009; Jahan-Mihan et al., 2011). Consequently, dietary guidelines commonly recommend high DF intake as a part of a weight management strategy in the overall health promotion and disease prevention. Furthermore, dietary protein has recently received considerable attention in regard to appetite control and weight management. Besides being an essential structural and functional component, proteins serve as a distinctive and beneficial source of energy (Paddon-Jones et al., 2008b; Westerterp-Plantenga et al., 2009).

Based on previous evidence, also food structure and physical state influence postprandial physiology and appetite regulation although underlying mechanisms are incompletely understood (Norton et al., 2007; Lundin et al., 2008). This is due to the fact that foods are multicomponent matrices with complex structural arrangements which in turn determine the physicochemical and sensory properties of foods. DF and proteins along with carbohydrates and fats are the main components affecting the structural properties and energy content of foods, and therefore the characteristic of the major components govern also the properties of individual foods. Individual and synergistic properties of these elements in turn modify postprandial physiology and subsequent food intake. However, to differentiate the individual effects of these elements they should be studied separately.

Due to the complex nature of appetite regulation, several methods and techniques are used to identify the different determinants of appetite and food intake control. Gastrointestinal (GI) motility (e.g. gastric emptying, GE), GI peptide responses and metabolic indicators in addition to the assessment of appetite sensation and food intake are the classical ways to demonstrate the responses of different parts of the GI tract to various food stimuli in relation to food intake control (Blundell et al., 2010; Delzenne et al., 2010). However, all these methods are a mere reflection of the actual mechanisms that orchestrate the sophisticated and highly coordinated system. Therefore, it is important to recognize the limitations of all the methods used in the studies and their ability to reflect the complexity of the phenomenon.

In this study the aim was to determine the postprandial effects of selected dietary fibres and protein ingredients and their enzymatically induced structure modification on

postprandial metabolic and GI hormone responses and GE together with appetite responses and food intake in healthy normal-weight subjects.

2 Review of the literature

2.1 PROCESSED FOODS AND EVOLUTION OF THE MODERN DIET

The evolution of the human diet can be divided into distinct periods passing through the Miocene to early Pleistocene era, the Paleolithic era, the Neolithic era and the Industrial Revolution (Jew et al., 2009) and ending up in the technology-driven "Information Era". During the period of millions of years the evolution of the human diet has been striking – from the very early preagricultural "table" of hunter-gatherers to the affluent buffets of postagricultural Western societies (O'Keefe and Cordain, 2004; Jew et al., 2009; Kuipers et al., 2010). Thus, the dietary choices of *hominin* populations have developed through the diets of ancient foragers consuming minimally processed, wild plant- and animal-based foods to the functional and processed foods of the space-age man produced by advanced technology. In this transition the introduction of agriculture and animal husbandry (~10 000 y ago) and the Industrial Revolution (200 y ago) (Cordain et al., 2005) together with the remarkable technological advances in food production, delivery and storage during recent decades have been crucial.

In support of the evolutionary discordance theory, it has been proposed that the modern diet has evolved too soon and too far away from the diet which our ancestors adapted to and survived with, which in turn conditioned our ancient genetic makeup and physiology (Eaton and Konner, 1985; Eaton et al., 1988). This evolutionary mismatch between our primeval genome and the dietary quality of recently introduced foods, in addition to the effects of other environmental factors, may underlie the so-called diseases of civilization (Cordain et al., 2005). Unfavourable nutritional changes are reflected in particular in glycaemic load, fatty acid and macronutrient composition, micronutrient density, acid-base balance, sodium-potassium ratio, and fibre content (Cordain et al., 2005). The listing of the nutritional characteristics mentioned above should also include the physicochemical structure of foods. That is to emphasize the importance of the physical state of foods and different structural levels of food items, which has often been overlooked in understanding the metabolic responses and long-term health consequences of various diets (Schneeman, 2002).

Even though several characteristics of staple foods created by the increased industrialized affluence and modern food technology have changed from the past, the development of food science and food industry has undoubtedly benefited human nutrition and overall health and well-being (Eaton, 2006). Obviously, remarkable scientific and technological advances in food production, processing, distribution and storage have radically improved food safety in addition to the extensive availability and affordability of variety of foods especially in the developed societies. Consequently, it has been argued that these achievements are much more important contributors to increasing life expectancy than nutritional advances relative to chronic disease prevention could ever be (Eaton, 2006). However, the industrialized food production seems to have also disadvantages. The increasing variety of refined, energy dense, affordable and highly palatable food products manufactured and intensively advertised by the modern food industry is gradually undermining the health benefits achieved by improved food safety and availability, and therefore corrective actions are urgently required (Gortmaker et al., 2011; Swinburn et al., 2011).

Nevertheless, we still have the considerable challenges of disease prevention and health promotion as it relates to the non-communicable diseases of adulthood (e.g. cardiovascular diseases, non-insulin dependent diabetes mellitus, metabolic syndrome, hypertension, cancer) in Westernized and Westernizing populations (WHO, 2003). Although it is neither appropriate nor possible to adopt solely the diet of our early ancestors, it may be advantageous to utilize the health-supporting characteristic of the early diets, i.e. the food and food ingredients from our ancestral era that have been demonstrated to possess health benefits, even in the form of tailored and functional foods (Jew et al., 2009; Lindeberg, 2012). This could be performed by modifying and supplementing the modern diet with these favourable attributes with the aid of modern food technology. However, to formulate optimally health-benefiting foods, it is crucial to have a clear understanding of the manner with which food will achieve these desired effects (Lentle and Janssen, 2010). This requires a detailed knowledge of the gut physiology and the physicochemical properties of foods that influence the physiology and efficiency of digestion and absorption both at the organ and the cellular level (Lentle and Janssen, 2010). Ultimately, this process might entail reintroduction of the essential elements from the diet and lifestyle of our early ancestors. The remodeling of the dietary elements may not affect our life expectancy radically, but rather affect the years in good health and alleviate the burden of the public health care costs (Eaton et al., 1988; Jew et al., 2009; Kuipers et al., 2010).

2.2 REGULATION OF FOOD INTAKE

Despite considerable variation in our daily food consumption, many of us are able to adjust the overall energy intake to energy expenditure which is indicated by relatively stable body weight over longer periods of time. The mechanism is termed energy homeostasis which is a dynamic regulatory process controlling short-term and long-term energy balance in the body (Schwartz et al., 2000; Badman and Flier, 2005; Murphy and Bloom, 2006). However, an escalating number of overweight and obese individuals worldwide (Finucane et al., 2011) indicates that this highly coordinated mechanism is not functioning adequately any more in our modern environment with westernized dietary habits and lifestyle (Murphy and Bloom, 2006; Zheng et al., 2009). The reason for this "malfunction" may be found in the inherent asymmetry in the adaptive responses to famine and feast. The early "designing" of the system was set to defend adequate nutrient intake and optimal adiposity level and/or body weight. Thus, in nutritionally unfavourable conditions a strong defense was set against too low adiposity and/or body weight. Instead, in the opposite conditions, e.g. in the westernized food environment, the homeostatic defense of the upper limits of adiposity and/or body weight is weak (Zheng et al., 2009). Consequently, overweight and obesity are considered as a normal physiological response to a changed environment (Zheng et al., 2009; Swinburn et al., 2011).

The regulation of food intake is a complex process where energy homeostasis is the ultimate target. It is fine-tuned according to the internal (homeostatic), i.e. neural, hormonal and metabolic signals, and external (non-homeostatic; environment and lifestyle, physical activity, cognition, reward, stress, mood etc.) factors (Berthoud, 2004; Lenard and Berthoud, 2008; Shin et al., 2009; Zheng et al., 2009) (Figure 1). Therefore, it has been suggested that food intake itself is not a regulated factor but rather assists the homeostatic maintenance of other regulated variables, such as blood glucose and body fat (Woods, 2009). Consequently, in environmentally favourable conditions individuals have the luxury of adopting regular consumption patterns that mirror a balance among various factors, such as food availability, social context, lifestyle, and others. However, if restrictions are set on food

intake, individuals readily abandon the preferred eating habits and adopt a strategy more suitable to maintain energy balance in the altered conditions (Woods, 2009).

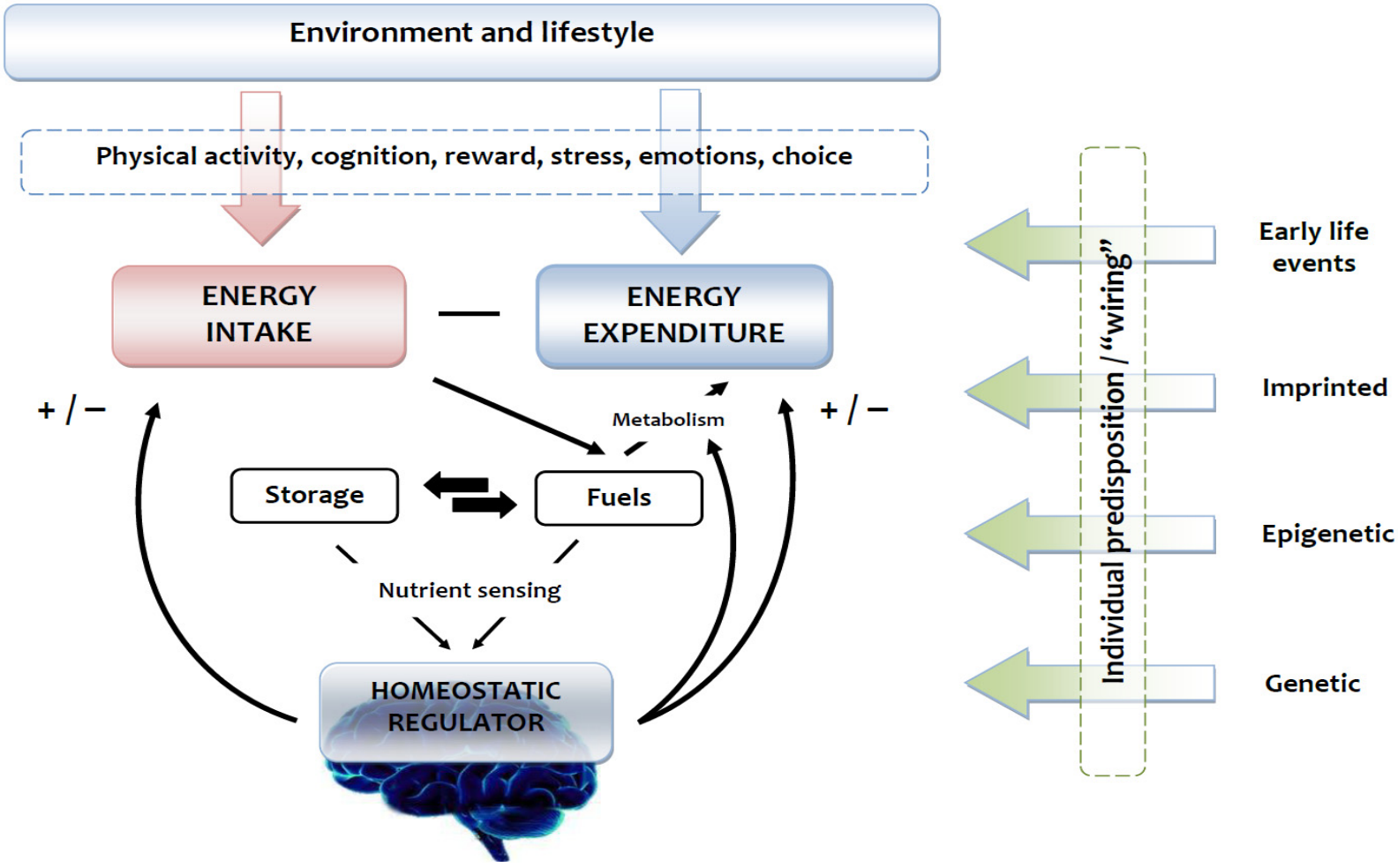

Figure 1. Major mechanisms and factors determining energy balance. Modified from Lenard and Berthoud, 2008.

The organ cross-talk, i.e. the communication among numerous organs (brain, gut, liver, adipose tissue, pancreas and muscle) is a fundamental mechanism underlying the regulation of appetite and food intake. However, the continuous cross-talk between the two players, the gut and the central nervous system (CNS) is considered the major axis in this homeostatic process in short-term (Figure 2) (Badman and Flier, 2005; Field et al., 2010). Enteroendocrine cells in the intestinal mucosa sense the luminal content pre- and postprandially, and release cell-specific peptides which control the crucial GI functions such as motility, secretion and absorption (Cummings and Overduin, 2007). Moreover, recent discoveries have indicated that various "taste receptors" on the enteroendocrine cells play an important role in GI peptide secretion (Kokrashvili et al., 2009; Gerspach et al., 2011; Steinert and Beglinger, 2011; Steinert et al., 2011b). This peptide-specific signalling mechanism reports the peripheral short-term energy status to the CNS via circulation and/or neural activation. Reciprocally, the CNS responses to these signals and coordinates adaptive responses via negative or positive feedback to the peripheral targets affecting ultimately energy intake and expenditure and body fat stores (Schwartz et al., 2000; Wynne et al., 2005). Thus, the highly interrelated gut-brain-axis is the core of the appetite control and energy balance, where the endocrinological capacity of the GI tract plays a key role under the modulatory control of the brain.

Peripheral signals involved in the regulation of food intake and energy balance operate in two different time dimensions. Classically, they are categorized as short- and long-term operators (Badman and Flier, 2005; Wren and Bloom, 2007). In general, the long-term signals such as leptin mirror the amount of adiposity stored in the body, and regulate body weight over longer periods of time (Schwartz et al., 2000; Wynne et al., 2005). The short-term signals arise from the GI tract. These gut hormones such as ghrelin, cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1) and peptide YY (PYY) regulate not only appetite but also a wide range of intestinal and other vital physiological functions (Chaudhri et al., 2006). Despite the difference in the time dimensions of their actions the two systems overlap considerably, albeit the long-term system having control over the short-term (Schwartz et al., 2000; Morton et al., 2006). Nevertheless, recent studies indicate that the categorization between long- and short-term signals is more or less artificial, since many of the regulators, such as orexigenic ghrelin and anorexigenic PYY have been identified as regulators both in the short- and long-term energy homeostasis (Wren and Bloom, 2007; Karra et al., 2009; Castaneda et al., 2010).

The short-term regulation of food intake is discussed in more detail below.

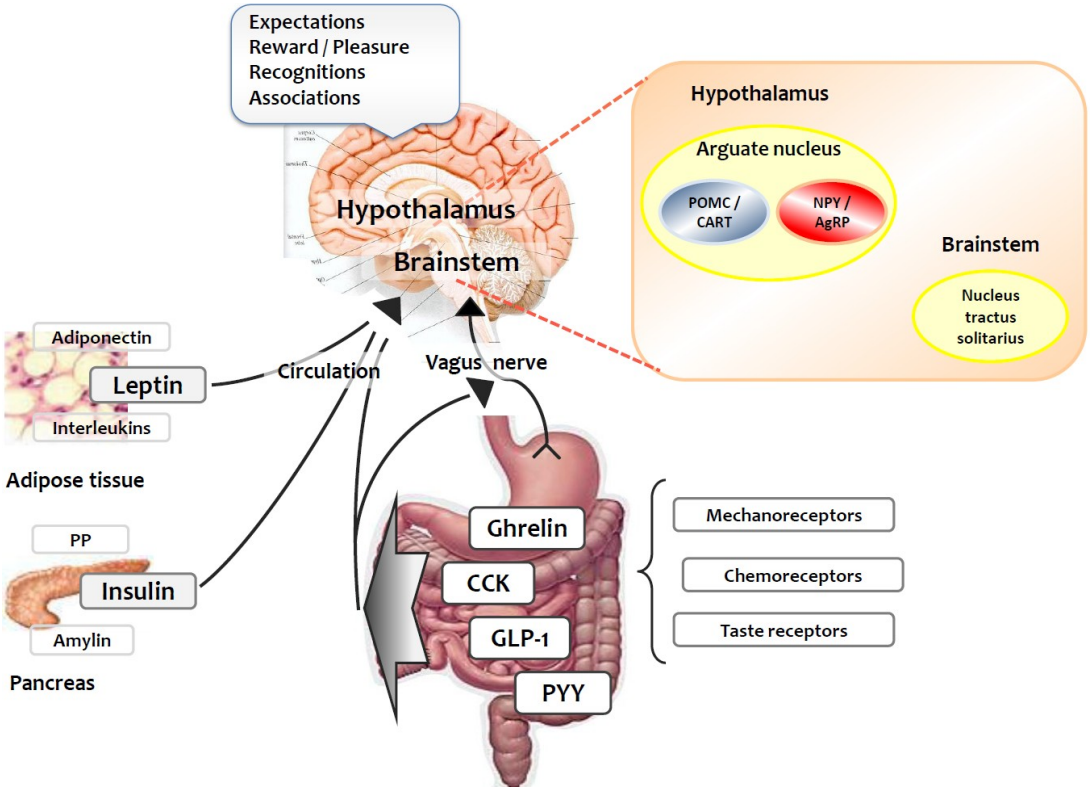

Figure 2. Simplified illustration of the factors participating in the regulation of appetite and food intake. AgRP, agouti-related peptide; CART, cocaine- and amphetamine-stimulated transcript; CCK, cholecystokinin; GLP-1, glucagon-like peptide 1; NPY, neuropeptide Y; POMC, pro-opiomelanocortin; PP, pancreatic polypeptide; PYY, peptide YY. Modified from Badman and Flier, 2005.

2.3 SHORT-TERM REGULATION OF FOOD INTAKE

2.3.1 Appetite

The concept

The concept of "appetite" can be defined in two ways; first, it covers the whole field of food selection, consumption, motivation and preference, and secondly, it refers especially to the qualitative aspects of eating, sensory aspects or responsiveness to environmental stimulation in contrast to the homeostatic control of eating (Blundell et al., 2010). As a perception or feeling, appetite is also described as a desire to consume food, often something specific, and is perceived as sensations of hunger, desire to eat, urge to eat, and/or prospective food consumption (Leidy and Campbell, 2011). In sum, it has been stated that appetite control is the summary of the perceived appetite and satiety sensations which ultimately lead to whether food is or is not consumed (Leidy and Campbell, 2011).

In this thesis, the term "appetite" is used as a general expression referring to the overall sensations associated with food intake, if not otherwise stated.

Appetite sensations

Hunger and desire to eat. "Hunger" is commonly described as a conscious sensation reflecting an urge to eat which may be indicated as changes in the physical sensations in

different body parts, e.g. stomach (emptiness, rumbling feeling), limbs or head (Blundell et al., 2010). It is not directly measurable, but can be subjectively rated in magnitude. Although hunger is associated with food deprivation, it is not always determined by it, and it can be seen as a step between the physiological state and food consumption (de Castro and Elmore, 1988). Furthermore, hunger is an important but not the only factor in determining food intake (de Castro and Elmore, 1988).

"Desire to eat" is difficult to determine, since this concept is frequently used as synonym for hunger in the current literature. Even so, this feeling refers to willingness to accept food primarily because of the rewarding and pleasurable characteristics of food (Kissileff and Van Itallie, 1982). Desire to eat can be stimulated even when an individual is highly satiated, and it can be considered as an important determinant of subsequent food consumption (Cornell et al., 1989).

Satiety and fullness. The general concept of "satiety" consists of sensory, cognitive, post-ingestive and post-absorptive aspects. It can be divided into two distinct functions, "satiation" and "satiety". "Satiation" or "intra-meal satiety" refers to a process that promotes the termination of a meal (eating) restricting thus energy intake within a meal. "Satiety", "inter-meal satiety" or "post-ingestive satiety" consists of events that inhibit eating, indicated as declined postprandial hunger and/or increased fullness and lengthened intermeal interval and/or decreased meal frequency (Blundell et al., 2010). Satiation likely results from synchronized neural and hormonal signals that originate from the mouth and upper GI tract in response to the physicochemical properties of ingested food while satiety may result more from the post-absorptive metabolic processes and their metabolites which operate inter-meal basis (Figure 3) (Cummings and Overduin, 2007). Since satiation and satiety are closely connected to the sensory aspects of food and learning process through their association with environmental cues and through physiological, psychological and social consequences during and after eating, they can be defined also on these bases (Blundell et al., 2010). Thus, metabolic satiation and satiety refers to all postprandial physiological mechanisms (e.g. hormonal and neural signals, GI motility) between the gut and brain being closely related to energy homeostasis. Sensory specific satiation, in turn, refers to the decrease of reward value of food during consumption, and it is responsible for variation in food choice. Lastly, sensory mediated satiation/satiety refers to learned satiety and is seen as a conditioned response based on the experiences with foods (Blundell et al., 2010).

The term "fullness" can be defined as a sensation reflecting the degree of stomach filling (Sorensen et al., 2003).

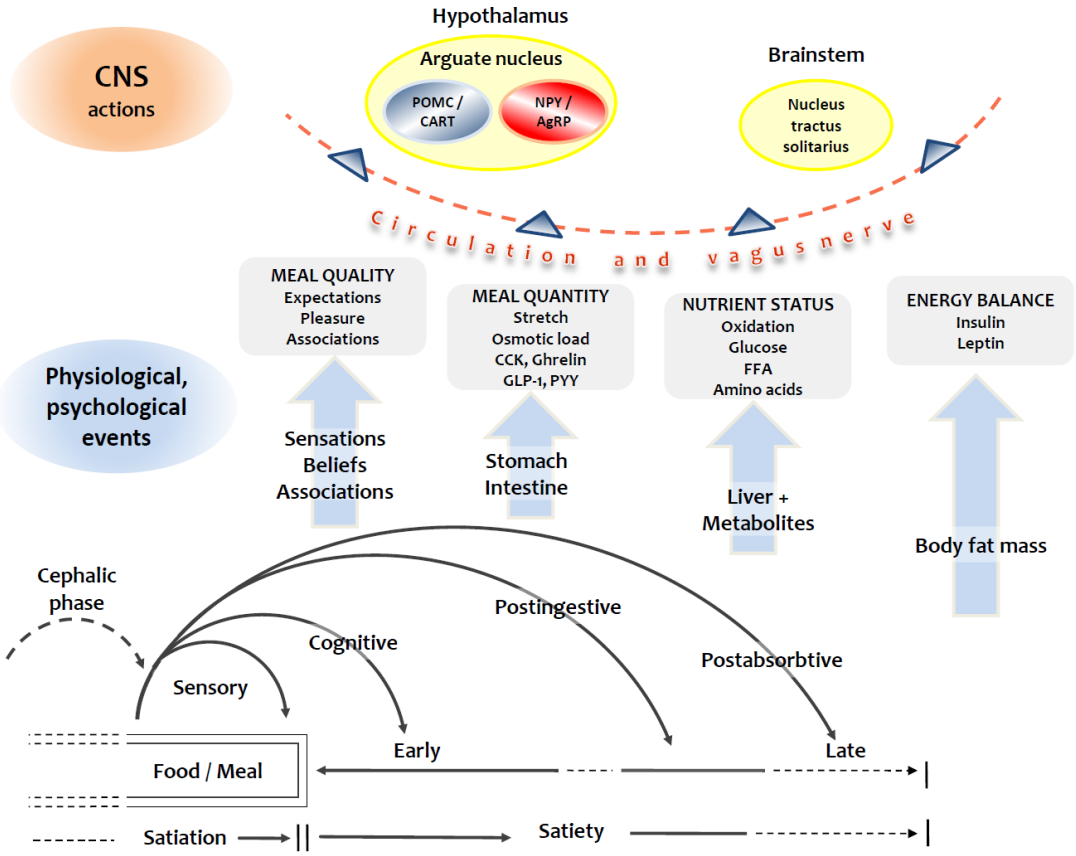

Figure 3. Satiety cascade associated with cognitive and physiological responses. AgRP, agouti-related peptide; CART, cocaine- and amphetamine-stimulated transcript; CCK, cholecystokinin; CNS, central nervous system; FFA, free fatty acid; GLP-1, glucagon-like peptide 1; NPY, neuropeptide Y; POMC, pro-opiomelanocortin. PYY, peptide YY. Modified from Blundell et al., 2010.

Measurement of appetite

There are several frequently used ways to measure and quantify appetite. Self-report scales are widely used to assess various appetite-related subjective sensations, such as feelings, thoughts and somatic sensations (Blundell et al., 2010). The most commonly used visual analogue scale questionnaires (VAS) typically consist of an unstructured horizontal line with verbal anchors of a unipolar question at either end describing the weakest or strongest statement (Hill et al., 1995; Flint et al., 2000; Stubbs et al., 2000). Subjects are instructed to make a mark on the horizontal axis corresponding to their sensation at the time of assessment. Ratings are quantified by measuring the distance between the left end of the horizontal line and the mark.

Subsequent food/energy intake has also been utilized to quantify the effect of dietary manipulations. In this method, an *ad libitum* meal is served after the test meal under standardized conditions at predetermined time points or when requested. Subjects are instructed to eat until comfortable full after which the amount of food consumed is recorded (Blundell et al., 2010).

Appetite and appetite-related gastrointestinal hormones

A whole branch of research has focused on the relationship between appetite and the key GI hormones related to appetite (e.g. de Graaf et al., 2004; Wynne et al., 2005; Wren and Bloom, 2007; Delzenne et al., 2010; Mars et al., 2012). One of the initial objectives of these studies has been to discover reliable biomarkers for appetite (de Graaf et al., 2004). A lot of progress has been made in this area, but due to the complexity of appetite regulation, it has been rather challenging to restrain the entire concept to the assessment of few measurable biomarkers (Delzenne et al., 2010). However, it is important to understand the mechanism underlying food-related appetite and food consumption, and therefore the search for these biomarkers is still very active.

2.3.2 Gastric motility

To identify the postprandial metabolic and hormonal effects of food and its components, it is crucial to understand the physiological functions of the GI tract in the digestion process, where food undergoes major transformation from undigested food items to absorbable nutrients during mechanical and chemical breakdown processes (Kong and Singh, 2008). After mastication and ingestion, the food bolus enters the stomach which is the next site after oral cavity to strongly stimulate the physiological signals related to food consumption (Delzenne et al., 2010; Janssen et al., 2011). The stomach not only stores the undigested food but also actively processes it participating considerably in the disintegration of foods, and finally empties the processed fluid content with relatively homogenous properties into the duodenum for further degradation by digestive enzymes (Hellstrom et al., 2006).

GE is a critical step in the regulation of postprandial digestion and absorption processes to achieve long-term metabolic stability and control (Rayner et al., 2001; Hellstrom et al., 2006). Gastric functions initially reduce the size of solid food particles and fat globules, and adjust the pH, osmolality, caloric density and the viscosity of liquids (Schulze, 2006). GE is controlled by several interrelated and complex factors including neural regulatory mechanisms, hormonal influences and dietary factors (Hellstrom et al., 2006; Kong and Singh, 2008).

Among the dietary factors, the physical state of food, i.e. liquid vs. solid, affects markedly the integrated function of different gastric compartments resulting in a distinctive GE pattern. In general, liquids are emptied relatively rapidly while the GE rate is slower for solid foods (Schulze, 2006). In addition, several other intrinsic attributes of food, such as meal size, density, food structure, caloric content, viscosity, osmolality, pH, temperature and even molecular structure (microstructure) have been demonstrated to affect the GE rate and/ or profile (Hunt and Knox, 1972; Camilleri et al., 1985; Marciani et al., 2001; Hellstrom et al., 2006; Goetze et al., 2007; Kong and Singh, 2008; Kwiatek et al., 2009; Mishima et al., 2009; Little et al., 2010). Overall, GE rate is decreased more after digestion-resistant foods structures (Marciani et al., 2001; Willis et al., 2011) and after more viscous, energy dense and hypertonic test meals (Marciani et al., 2001; Kwiatek et al., 2009; Kristek et al., 2010). Furthermore, body posture modulates physical intragastric conditions and the dynamic GE process. This in turn is affected by the various properties of the test meals that affect the chemical environment of the gastric lumen (Hunt et al., 1965; Horowitz et al., 1993; Spiegel et al., 2000).

The enteroendocrine and nervous system has a major impact on the control of the GE and intestinal motility which subsequently affect appetite sensations and control of food intake (Hellstrom et al., 2006; Delzenne et al., 2010; Janssen et al., 2011). Both gastric and postgastric mechanisms are involved. For example, gastric distension activates GLP-1 containing neurons in the nucleus of the solitary tract (NTS) which suggests that GLP-1 is involved in the gastric distension-induced regulation of appetite (Vrang et al., 2003).

Moreover, suppression of food intake by CCK is enhanced when the stomach is distended (Kissileff et al., 2003). Several GI-derived peptides including CCK, GLP-1 and PYY as well as ghrelin affect also GE (Moran, 2000; le Roux and Bloom, 2005; Baggio and Drucker, 2007; Castaneda et al., 2010), where the former peptides reduce the GE rate and ghrelin has the opposite effect. The postgastric feedback mechanisms, especially the ileal brake mechanism (via PYY), adjust the gastric outflow rate to meet the digestion and absorption capacity of the upper small intestine (Van Citters and Lin, 1999; Maljaars et al., 2008).

Gastric motility affects also appetite sensations. The main determinant underlying gastric satiation and satiety is based on mechanosensitivity in which gastric distension and accommodation are the major determinants (Janssen et al., 2011). It has also been suggested that reduction of gastric distension may play a role in the development of postprandial hunger (Sepple and Read, 1989). At the same time, nutrient sensing *per se*, i.e. the detection of the energy and nutrient content of a meal by the stomach most likely play a minor role in controlling of appetite (Powley and Phillips, 2004; Goetze et al., 2007). However, if the gastric phase is bypassed, the effects are likely to be negative on short-term control of appetite, i.e. hunger is less suppressed and satiety and fullness less increased when nutrients are administered directly to the duodenum (Steinert et al., 2012). Moreover, GE modulates appetite sensations; decreased GE rate has been linked with augmented satiety and/or fullness (Di Lorenzo et al., 1988; Carbonnel et al., 1994; Hveem et al., 1996; Jones et al., 1997) and decreased hunger after a test meal (Horowitz et al., 1993).

Thus, gastric motility is an important determinant for hunger, satiation and satiety. Mechanisms related to different sensations of appetite depend on the site of the gut exposed to nutrients. Gastric satiation seems to be more volumetric and intestinal satiation nutritive (Powley and Phillips, 2004; Janssen et al., 2011). Both gastric motility and intestinal nutrient exposure are required for the regulation of appetite sensations, but the role of intestinal exposure is emphasized as the stomach empties (Janssen et al., 2011).

2.3.3 Gastrointestinal hormones in appetite regulation

The enteric nervous and enteroendocrine systems are integral parts of the GI tract. The enteroendocrine system produces a large number of appetite-controlling hormones and other regulatory factors, which are released from the different parts of the GI tract in response to ingested food (Karhunen et al., 2008; Juvonen et al., 2009). In the following sections the key GI hormones known to participate in the regulation of appetite and food intake are discussed, focusing mainly on studies performed on healthy normal-weight individuals ingesting test foods.

2.3.3.1 Ghrelin

Ghrelin, a 28-amino-acid peptide first discovered in 1999, is unique among the biologically active GI peptides, since it is one of the major peripheral orexigenic (appetite-stimulating) hormones (Cummings, 2006), others would be PYY_{1-36} and orexin-A. It is therefore also called a "hunger hormone" (Wren and Bloom, 2007). Initially, ghrelin was characterized as an endogenous ligand for the growth hormone secretagogue receptor, GHS-R1a (Kojima et al., 1999). However, subsequent studies demonstrated its powerful effects on short-term appetite and food intake and long-term energy homeostasis (Cummings et al., 2005; Cummings, 2006). Hence its role in the regulation of energy balance is widely considered as its most important function, besides its multiple other physiological actions (Cummings, 2006).

Release and molecular forms

Similar to several other GI peptide hormones, ghrelin is cleaved from a precursor protein and is further subjected to posttranslational modification where a medium-chain fatty acid (MCFA), typically octanoic acid, is covalently attached to the molecule (on serine-3 residue) (Chen et al., 2009; Romero et al., 2010). This type of modification is entirely unique to ghrelin, and acylation is prerequisite for ghrelin to bind its receptor and for the most of its biological actions (Wren and Bloom, 2007). Furthermore, the stomach is the only place where the posttranslational octanoylation of ghrelin with MCFA can occur (Nishi et al., 2005). Consequently, a bioactive peptide, acyl-ghrelin is formed and ready for signalling its actions via the classical ghrelin receptor, GHS-R1a (Kojima et al., 1999). GHS-R1a is widely expressed in the periphery, but also in the CNS where it is expressed in neurons involved in appetite control and energy balance, such as hypothalamic arcuate neuropeptide Y (NPY)/agouti-related peptide (AgRP) neurons (Figure 2). The other major molecular form of ghrelin is unacylated ghrelin (des-acyl ghrelin), which is considered the main circulating form of ghrelin in plasma (Cummings and Overduin, 2007). The orexigenic effects of ghrelin are signalled via systemic circulation by which it reaches the hypothalamic sites and by neuronal signalling via vagus nerve with projections to NTS in the brainstem and further to the arcuate nucleus (ARC) in the hypothalamus (Wynne et al., 2005).

The major site of ghrelin release is the stomach (Kojima et al., 1999), especially the fundus area. The mucosal enteroendocrine X/A-like cells, which synthesize and secrete ghrelin, can also be found throughout the GI tract with decreasing density towards the distal parts of the intestine (Sakata et al., 2002). Furthermore, the type of ghrelin cells vary within the GI tract; closed type cells are found in the upper part of the GI tract while the ghrelin cells become gradually more open more distally in the intestine. Interestingly, a recent study showed that the closed type gastric cells contain acylated ghrelin, des-acyl ghrelin, and obestatin, whereas the open type cells contain only des-acyl ghrelin (Fujimiya et al., 2010). Thus, the regulatory mechanisms of ghrelin secretion could also be different in the stomach and subsequent parts of the GI tract (Sakata and Sakai, 2010).

Actions and modulatory factors

A wide spectrum of physiological actions has been attributed to circulating ghrelin (Chen et al., 2009; Castaneda et al., 2010). Major endogenous effects are related to the hypotalamic stimulation of growth hormone secretion, adipogenic and orexigenic effects. Exogenous effects cover a range of peripheral targets including glucose and lipid metabolism, gastric acid secretion and GI motility, endocrine and exocrine pancreatic secretion, cardiovascular, immunologic and inflammatory functions (Chen et al., 2009; Castaneda et al., 2010). The majority of these biological effects are ascribed to acylated ghrelin. However, the physiological role and significance of the des-acyl ghrelin remain for the most part unidentified.

Several internal and external factors modulate plasma ghrelin levels in the body. In general, ghrelin concentration follows an endogenous distinct pattern oscillating according to the circadian rhythm (Cummings et al., 2001). The relationship between ghrelin and insulin remains unclear, however it is believed that insulin has most likely a negative impact on ghrelin secretion (Castaneda et al., 2010). Ghrelin may also function as an appetite-stimulating counterpart to insulin and leptin in overall energy balance (Cummings, 2006). In addition, the anorexigenic GI hormones CCK, GLP-1 and PYY may suppress ghrelin secretion (Brennan et al., 2007). Circulating ghrelin levels are also affected by the body energy stores. Individuals in chronic negative energy balance (e.g. anorexia nervosa) have elevated plasma ghrelin levels whereas in obesity the levels are reduced (Shiiya et al., 2002; Tolle et al., 2003). Moreover, ghrelin secretion in obese individuals is

impaired so that the postprandial reduction in ghrelin concentration may be blunted (English et al., 2002; Heinonen et al., 2007).

Even though it is obvious that ghrelin secretion is controlled partly by long-term nutritional status, increasing evidence indicates that pre- and postprandial factors such as short-term fasting/feeding status, anticipation of eating, meal pattern learning, hedonic and incentive responses, macronutrient content of ingested food and physiological factors contribute to ghrelin secretion (Cummings, 2006; Chen et al., 2009; Castaneda et al., 2010; Koliaki et al., 2010). Usually, an increase in ghrelin concentrations is observed during fasting and a decrease after food consumption or infusion of nutrients (Cummings et al., 2001; Murray et al., 2006). A peak in plasma ghrelin concentration can be observed immediately before a meal which has been considered as an indicator of meal initiation (Cummings et al., 2001). Plasma ghrelin levels may also partly reflect the preprandial responses of the body to the food-related cues. Frequently detected preprandial rise in ghrelin concentration have been shown to function as an anticipatory response preparing the body for food ingestion (Cummings et al., 2001; Drazen et al., 2006). Also vagal stimulation using modified sham feeding is able to enhance ghrelin suppression when used before an oral fat load (Heath et al., 2004) and mixed meal (Arosio et al., 2004), but stomach expansion as such, e.g. by ingestion of water, is not a sufficient stimulus to modify ghrelin secretion (Shiiya et al., 2002; Callahan et al., 2004; Blom et al., 2005). Recently, it was demonstrated using neuroimaging that ghrelin may favour food consumption by enhancing the hedonic and incentive responses to food-related cues (Malik et al., 2008).

Postprandial effects of dietary factors

Numerous studies have demonstrated that ghrelin secretion is affected by various dietary factors, such as energy content, individual macronutrients, DF and physicochemical attributes of foods (Karhunen et al., 2008; Juvonen et al., 2009; Koliaki et al., 2010). The postprandial inhibition of ghrelin secretion appears to be relative to the energy content of a meal; ghrelin release is dose-dependently suppressed by the number of ingested calories in normal-weight, however, but not in obese humans (Callahan et al., 2004; le Roux et al., 2005).

While all the macronutrients affect ghrelin secretion, there seems to be a macronutrient-specific effect on magnitude and pattern of postprandial ghrelin suppression. Dietary carbohydrates have the most suppressive effect on ghrelin release compared with protein- or fat-enriched test products (Erdmann et al., 2003; Monteleone et al., 2003; Erdmann et al., 2004; Tannous dit El Khoury et al., 2006; Foster-Schubert et al., 2008). A pattern effect has also been observed; after an initial decline ghrelin levels increased markedly above the preingestion level after the carbohydrate-based beverages during the second three hours of the study period, whereas no such upsurge was detected after protein- and fat-based beverages (Foster-Schubert et al., 2008). Carbohydrate type also modulates ghrelin response; glucose is more effective in suppressing ghrelin release than fructose (Teff et al., 2004; Steinert et al., 2011a), as are simple carbohydrates (maltodextrin) compared with complex carbohydrates (exopolysaccharide) (Blom et al., 2005).

The data on the effect of DF on ghrelin secretion are inconsistent. Nevertheless, increased fibre content in a meal has been shown to decrease (Nedvidkova et al., 2003; Gruendel et al., 2006; Gruendel et al., 2007; Vitaglione et al., 2009; Tarini and Wolever, 2010) or to inhibit the decrease (Mohlig et al., 2005; Weickert et al., 2006; Willis et al., 2010) or to have no clear effect on postprandial ghrelin concentration (Erdmann et al., 2003; Beck et al., 2009b). The discrepant findings could be explained by variations in the physicochemical properties of the various fibre types, different doses used, and the form of ghrelin measured in the circulation (El Khoury et al., 2012).

Although several studies have shown that high-protein meals reduce ghrelin secretion less than high-carbohydrate meals, postprandial levels tend to remain suppressed longer after protein-rich meals (Blom et al., 2006a; Bowen et al., 2006a; Bowen et al., 2006b; Tannous dit El Khoury et al., 2006; Boelsma et al., 2010), although this is not always detected (Lejeune et al., 2006). On the other hand, ghrelin suppression after high-protein meals is not obvious, and some studies have found ghrelin to actually increase after high-protein meals (Erdmann et al., 2003; Erdmann et al., 2004; Erdmann et al., 2006) or the levels were not affected (Greenman et al., 2004; Martens et al., 2011). Protein type may also modulate ghrelin levels; casein was more effective to suppress active ghrelin levels than soy protein (Veldhorst et al., 2009a), although the difference among the protein types on ghrelin release is not always demonstrated (Nieuwenhuizen et al., 2009; Veldhorst et al., 2009d; Charlton et al., 2011). In addition, protein level (high vs. low) may modulate postprandial ghrelin levels (Veldhorst et al., 2009d), but several other studies have not confirmed this (Hochstenbach-Waelen et al., 2009a; Veldhorst et al., 2009a; Veldhorst et al., 2009c; Veldhorst et al., 2009e).

In general, fat induces rather weak ghrelin suppression compared with carbohydrate or protein (Monteleone et al., 2003; Foster-Schubert et al., 2008). Reports on fat-rich meals on postprandial ghrelin have indicated decreased (Monteleone et al., 2003; Radulescu et al., 2010) and increased (Erdmann et al., 2004) concentrations. If decreased, the decrease is characterized by a slower return to baseline than after a high-carbohydrate meal (Foster-Schubert et al., 2008; Radulescu et al., 2010). Ghrelin secretion seems also be dependent on fatty acid chain length. Fatty acid with 12 carbons markedly suppressed ghrelin compared with 10 carbon fatty acid, which had no effect (Feltrin et al., 2006). Similarly, long-chain fatty acids (18 carbons) inhibited ghrelin release whereas MCFA (8 carbons) were ineffective (Degen et al., 2007).

Even though various studies have shown that macronutrients *per se* may regulate ghrelin secretion, it is still unclear which factors and mechanisms are the major determinants of postprandial ghrelin release. Both blood-borne signals and GI-based sensing system has been suggested. Currently, evidence suggests that ghrelin suppression is not mediated by nutrients in the stomach or duodenum as such, but requires postgastric and postabsorptive feedback mechanisms (Williams et al., 2003; Overduin et al., 2005; Steinert et al., 2012), possibly mediated by glucose, insulin (Broglio et al., 2004; Overduin et al., 2005; Cummings, 2006) and anorexigenic GI hormones (Brennan et al., 2007; Hagemann et al., 2007). Ghrelin secretion seems also depend upon the length of small intestine exposed since no postprandial decrease was observed when less than 60 cm from the upper isolated part of the small intestine was exposed to glucose (Little et al., 2006). Vagal activity (Berthoud et al., 2011b), GE rate (Blom et al., 2006b) and postprandial increases of intestinal osmolarity (Cummings, 2006) may also contribute to meal-induced ghrelin secretion.

2.3.3.2 Cholecystokinin

Release and molecular forms

Cholecystokinin (CCK) is the classical endogenous satiation peptide hormone, first described with such characteristics in 1973 (Gibbs et al., 1973). Although CCK cells are widely distributed along the GI tract, it is mainly synthesized and released from the duodenal and ileal endocrine I-cells into the circulation (Liddle, 1997). CCK is also produced in the CNS and enteric neurons (Larsson and Rehfeld, 1979; Rehfeld and Hansen, 1986). The posttranslational or extra-cellular processing of the pro-cholecystokinin polypeptide leads into a collection of bioactive fragments labelled according to the number of amino acids in the molecule, where CCK-58, -33, -22 and -8 are the predominant circulating forms in human plasma (Rehfeld, 1998; Rehfeld et al., 2001). CCK signalling is

transmitted via two receptor subtypes, CCK1R and CCK2R, of which the first predominates in the GI system including vagal afferents and enteric neurons, and the latter in the stomach and multiple areas in the CNS (Moran and Kinzig, 2004; Wynne et al., 2004). It is widely accepted that the satiation actions of CCK are mediated by the CCK1R on the vagus nerve (Ritter and Ladenheim, 1985; Kopin et al., 1999; Beglinger et al., 2001).

Actions and modulatory factors

CCK concentrations increase rapidly after a meal peaking within 15–30 minutes and return gradually towards basal levels within 3–5 hours (Liddle et al., 1985). However, its half-life is only 1–2 min and the action period is brief. Consequently, the inhibitory effect of CCK on food intake is short-lived, lasting less than 30 min. This is indicated as reduced meal size and duration but the onset of a next meal is not affected (Kissileff et al., 1981; Lieverse et al., 1995). Thus, it appears that CCK plays more important role in satiation than in satiety.

In addition to the suppressing effects on appetite and food intake (Kissileff et al., 1981; Muurahainen et al., 1988; Beglinger et al., 2001), CCK controls other vital actions related to the postprandial digestion process of nutrients such as inhibition of GE and stimulation of intestinal motility, exocrine pancreatic secretion and gall bladder contraction (Liddle et al., 1985; Liddle, 1989), all of which are coordinated to optimize the digestion process.

The satiating effect of CCK is mediated via activation of vagal afferent mechanosensitive fibres in the stomach and in the duodenum (Schwartz and Moran, 1994). Gastric distension augments the appetite suppressing effects of CCK in humans (Kissileff et al., 2003). Inhibition of GE rate is thus a crucial part of the CCK induced satiation mechanism. The vagus transmits the CCK signals to the NTS from which the information is conveyed to the hypothalamus (Rehfeld, 2004). The anorexigenic effects of CCK may also be mediated directly to the CNS, since the CCK1R have been found in the brainstem and hypothalamus. As a result, the hypothalamic NPY expression levels may be suppressed and indicated as reduced food intake (Bi et al., 2001; Moran and Kinzig, 2004).

As with many other gut peptides CCK levels are altered in obesity. A study by Zwirska-Korczala and colleagues (Zwirska-Korczala et al., 2007) showed that fasting CCK concentrations were lower in morbidly obese than obese or lean individuals. In the same study morbidly obese subjects exhibited also a blunted postprandial CCK response to meals. Nevertheless, these finding should to be confirmed in subsequent studies.

Postprandial effects of dietary factors

Proteins are potent stimulants for CCK release. CCK levels remain elevated longer after protein-rich than carbohydrate-rich test meals (Blom et al., 2006a; Bowen et al., 2006a; Bowen et al., 2006b). Protein type may also affect CCK response. Postprandial CCK release has been shown to be greater after whey than casein protein (Hall et al., 2003) and after milk protein than pea protein hydrolysate, whey protein or combination of these (Diepvens et al., 2008). However, the effect of protein type is not always observed (Bowen et al., 2006a; Bowen et al., 2006b; Charlton et al., 2011). For an effective CCK release in humans digestion of proteins is essential (Liddle, 1997). Proteins may stimulate CCK release via inhibition of trypsin induced digestion of the intestinal CCK releasing peptides (Herzig et al., 1996; Herzig, 1998).

Lipids stimulate CCK release significantly (Pilichiewicz et al., 2006; Feltrin et al., 2007). Triglycerides must be hydrolyzed in order to stimulate CCK secretion effectively (Feinle et al., 2003; Little et al., 2007). The nature of the fatty acids modifies CCK release. Long chain fatty acids, carbon chain length ≥ 12C, are potent stimulants for CCK release (Hopman et al., 1984; McLaughlin et al., 1999; Matzinger et al., 2000; Feltrin et al., 2004). Furthermore,

decreased fat droplet size (Seimon et al., 2009) and fat stability in stomach (Marciani et al., 2007) have been shown to stimulate CCK release.

In addition to macronutrients, DF affects postprandial CCK release. Different fibre types, such as hydrolyzed guar gum (Heini et al., 1998), beta-glucan in barley pasta (Bourdon et al., 1999), fibre mainly from oatmeal and oat bran (Burton-Freeman et al., 2002), oat beta-glucan in cereals (Beck et al., 2009b) and fibre in bean flakes (Bourdon et al., 2001) have been shown to produce greater postprandial CCK levels and/or prolonged elevations than low-fibre meals or placebo.

2.3.3.3 Glucagon-like peptide 1

Release and molecular forms

Glucagon-like peptide 1 (GLP-1) is one of the biologically important peptides cleaved from the preproglucagon polypeptide expressed in the gut, pancreas, and the brain (Mojsov et al., 1986; Drucker and Asa, 1988). The other major products after the posttranslational proglucagon processing are glucagon in pancreas and oxyntomodulin and glucagon-like peptide 2 together with GLP-1 in the brain and intestine.

Although endocrine GLP-1 expressing cells are found throughout the small intestine, GLP-1 is primarily secreted by L-cells in the distal small intestine and colon in response to nutrients, neural and endocrine factors (Baggio and Drucker, 2007). In L-cells GLP-1 is colocalized and released with oxyntomodulin and PYY (Mortensen et al., 2003; Wren and Bloom, 2007). The postprandial secretion of GLP-1 occurs in biphasic manner with initial rise seen within 10–15 min followed by a second larger period during 30–60 min after the low basal levels in the fasted state (Herrmann et al., 1995). In human plasma two equipotent bioactive forms of GLP-1 are detected; GLP-$1_{7\text{-}37}$ and GLP-$1_{7\text{-}36\text{amide}}$, of which the latter is the major circulating form (Orskov et al., 1994). Both peptides are rapidly inactivated in the circulation by N-terminal cleavage by dipeptidyl peptidase IV (DPP IV) yielding GLP-$1_{9\text{–}37}$ and GLP-$1_{9\text{–}36\text{amide}}$ (Deacon et al., 1995; Deacon, 2004). Due to rapid degradation of active GLP-1, i.e. within 2 min after the release (Kieffer et al., 1995), the plasma levels of the intact hormone are very low and therefore the effects on appetite and food intake are indicated as typical short-term effects.

GLP-1 receptor (GLP-1R) mediates the effects of the bioactive GLP-1 molecules (Baggio and Drucker, 2007). The receptors have been found in several sites in the periphery including small intestine and pancreas as well as in multiple areas in the CNS including hypothalamus.

Actions and modulatory factors

The biological actions of GLP-1 are widely distributed in the body (Baggio and Drucker, 2007; Holst, 2007). Direct or indirect actions are expressed in several peripheral tissues including pancreas, liver and stomach as well as the brain (Baggio and Drucker, 2007). GLP-1 is well recognized for its incretin actions (Kreymann et al., 1987; Nauck et al., 1993). Together with another GI-derived peptide, glucose dependent insulinotropic polypeptide (GIP), it enhances glucose-stimulated insulin secretion (Creutzfeldt et al., 1978; Kreymann et al., 1987). Together with PYY, GLP-1 is also involved in the "ileal brake" mechanism (Read et al., 1984; Spiller et al., 1984) which has an inhibiting effect on GE rate, upper intestinal motility, pancreatic exocrine and biliary secretion. Ileal brake mechanism is thought to control digestion with direct or indirect impact on satiety and food intake (Maljaars et al., 2008).

While several of the proglucagon peptides are implicated in satiation, the strongest evidence has been demonstrated for GLP-1 (Cummings and Overduin, 2007). However, the mechanisms underlying GLP-1-induced anorexia are not fully understood but are

suggested to involve vagal and possibly direct central pathways (Turton et al., 1996; Baggio et al., 2004; Abbott et al., 2005). The peptide can cross the blood brain barrier, but it seems unlikely that physiologically relevant quantities of endogenous peripheral GLP-1 evade peripheral DPP IV degradation and cross the blood brain barrier.

There are also data indicating that GLP-1 may play a role in the pathogenesis of obesity. Attenuated GLP-1 responses have been found in obese individuals compared with lean controls (Ranganath et al., 1996; Verdich et al., 2001; Adam and Westerterp-Plantenga, 2005). On the other hand, Näslund and colleagues (Naslund et al., 2004) demonstrated that subcutaneous injections of GLP-1 for 5 days reduced energy intake and body weight in obese individuals. These observations support the role of GLP-1 in the regulation of energy homeostasis.

Postprandial effects of dietary factors

Carbohydrates are strong stimulus for GLP-1 release consistent with it's role as incretin (Elliott et al., 1993; Herrmann et al., 1995; Gerspach et al., 2011). Nevertheless, GLP-1 responses differ among carbohydrate types; glucose is a stronger stimulus for GLP-1 release than fructose (Kong et al., 1999; Steinert et al., 2011a) or complex carbohydrates (Elliott et al., 1993).

Postprandial GLP-1 response is modified also by different dietary fibres. Elevated, inhibited and unaffected responses have been reported, possible related to the fibre types or amount consumed. Guar gum and inulin containing meals increased GLP-1 release (Adam and Westerterp-Plantenga, 2005; Tarini and Wolever, 2010) whereas resistant starch produced only slightly elevated GLP-1 response (Raben et al., 1994b) and the greatest amount of mixed fibres (12g) the lowest GLP-1 response (Willis et al., 2010). Rye bread containing oat beta-glucan concentrate and low-fibre wheat bread produced larger GLP-1 responses than whole-kernel whole-meal rye bread and dark durum pasta (Juntunen et al., 2002). A small amount of psyllium fibre did not modify postprandial GLP-1 response (Frost et al., 2003), nor did pea fibre (Raben et al., 1994a).

Protein stimulates GLP-1 release even more than carbohydrates (Raben et al., 2003; Lejeune et al., 2006). A high-protein protein meal has been shown to stimulate GLP-1 secretion more than a high-carbohydrate meal (Blom et al., 2006a), but this is not detected in every study (Karamanlis et al., 2007). On the other hand, although high-protein meals may stimulate GLP-1 release more than low-protein meals (Lejeune et al., 2006), several studies have not demonstrated this (Veldhorst et al., 2009a; Veldhorst et al., 2009c; Veldhorst et al., 2009d; Veldhorst et al., 2009e). High-protein meals may even lower the postprandial GLP-1 concentrations compared with lower protein meals (Smeets et al., 2008; Hochstenbach-Waelen et al., 2009a). Among different protein sources, whey protein has been shown to increase postprandial GLP-1 more than casein (Hall et al., 2003; Veldhorst et al., 2009a). Milk protein, in turn, increased GLP-1 more compared with whey protein, pea protein hydrolysate or combination of these (Diepvens et al., 2008). On the other hand, differences among various protein types are not demonstrated in all studies (Nieuwenhuizen et al., 2009; Veldhorst et al., 2009d).

GLP-1 concentration increases after fat ingestion (Elliott et al., 1993; Radulescu et al., 2010), although the increase is delayed when compared with carbohydrates (Herrmann et al., 1995). Fat hydrolysis seems to be a critical step for fat-induced GLP-1 stimulation (Beglinger et al., 2010). Monounsaturated fatty acids (olive oil, sodium oleate) induce higher GLP-1 concentrations than saturated fatty acids (butter, lard, sodium caprylate) (Thomsen et al., 1999; Beglinger et al., 2010; Radulescu et al., 2010). However, the effect of fatty acid saturation on GLP-1 release has not been observed in all studies (Brynes et al., 1998). The postprandial GLP-1 response to fats may also depend on the acyl chain length and fatty

acid composition. Fatty acid with 12 carbons (lauric acid) stimulated GLP-1, whereas the shorter ones (decanoic acid, C10) did not (Feltrin et al., 2004).

2.3.3.4 Peptide YY

The gut hormone peptide YY (PYY) was first extracted from the porcine small intestine and named as PYY after the tyrosine residues at the both ends of the molecule, Y being a single letter code for tyrosine (Tatemoto and Mutt, 1980). PYY is a 36-amino acid peptide, which belongs to the PP-fold peptide family together with pancreatic polypeptide (PP) and NPY, all of which share a common tertiary structure and significant amino acid homology (Conlon, 2002). However, these peptides have distinct effects on appetite. PYY and PP are well known anorexigenic peptides whereas NPY is considered the most potent short-term stimulus for appetite (Wynne et al., 2004; Badman and Flier, 2005).

Release and molecular forms

PYY is synthesized in and secreted predominantly from the open-type enteroendocrine L-cells which can be found throughout the GI tract but in particular in the distal segments of the intestine, i.e. ileum, colon and rectum (Adrian et al., 1985a). In addition to PYY, L-cells release preproglucagon-derived peptides, glicentin and oxyntomodulin (OXM) and especially GLP-1, with which PYY is co-secreted (le Roux and Bloom, 2005; Baggio and Drucker, 2007). Circulating PYY occurs in two active forms, $PYY_{1\text{-}36}$ and $PYY_{3\text{-}36}$, the latter being the major form in both the enteroendocrine cells and circulation (Eberlein et al., 1989; Grandt et al., 1994). The peripheral anorexigenic form $PYY_{3\text{-}36}$ results from the cleavage of two first amino acids from $PYY_{1\text{-}36}$ by the DPP IV (Eberlein et al., 1989), an action which subsequently affects receptor affinity and physiological actions of the peptide. PYY molecules mediate their actions via Y-receptors, which include five different subtypes (Y1, Y2, Y4, Y5, Y6) with diverse distribution and function in the body (Berglund et al., 2003; Wynne et al., 2004). The affinity of the full-length PYY is comparable for all Y-receptors, whereas $PYY_{3\text{–}36}$ shows high selectivity for the Y2 receptor and some affinity for Y1 and Y5 receptors (Larhammar, 1996). In addition to the intestinal locations, presynaptic Y2-receptors can be found on the vagal afferents and in the hypothalamic ARC. This indicates that the anorexigenic effects of $PYY_{3\text{–}36}$ may be mediated via vagal-brainstem-hypothalamic pathways and/or targeted directly to hypothalamus (Batterham et al., 2002; Koda et al., 2005). Interestingly, in contrast to the effects of peripheral $PYY_{3\text{–}36}$, centrally administered $PYY_{1\text{-}36}$ and $PYY_{3\text{-}36}$ have an orexigenic effect in rodents (Morley et al., 1985; Kanatani et al., 2000).

Actions and modulatory factors

$PYY_{1\text{-}36}$ is known to have numerous effects on GI tract and other body functions. Recent data show that endogenous PYY has a significant role in the regulation of energy homeostasis, controlling energy expenditure, lipid metabolism and ultimately fat stores in the body (Batterham et al., 2003; Guo et al., 2006; Sloth et al., 2007). In addition to its inhibitory effects on appetite and food intake, PYY inhibits gastric and exocrine pancreatic secretions, gallbladder contraction, and affects renal and vascular physiology (Adrian et al., 1985b; Ballantyne, 2006). Furthermore, PYY administration delays GE and intestinal transit time (Savage et al., 1987), an effect which indicates that PYY is involved in the postprandial intestinal feedback system facilitating digestion and absorption of nutrients. It is thus a potential stimulatory candidate of the ileal brake mechanism (Maljaars et al., 2008).

Typically circulating PYY levels increase in response to nutrient ingestion and decrease in fasting state (Batterham et al., 2006; Chan et al., 2006; Helou et al., 2008; Chandarana et al., 2009) consistent with a meal-related signal of energy balance. An initial rise in

postprandial PYY concentration can be detected within 15 min, well before nutrients reach the PYY releasing L-cells in the distal small intestine. This may be due to indirect neural reflex or hormonal factors affecting this initial secretion. Postprandially, PYY concentrations peak within 1 - 2 h and remain elevated for several hours there after (Adrian et al., 1985a). PYY levels are also affected by other satiety-enhancing gut peptides; CCK has been shown to increase (Brennan et al., 2007) and GLP-1 to decrease plasma PYY levels (Ballantyne, 2006). However, plasma PYY concentration is not altered by gastric distension (Oesch et al., 2006) or sham feeding (Soffer and Adrian, 1992).

Postprandial PYY concentrations differ according to the body energy stores. In patients with anorexia nervosa PYY levels are reported to be high (Misra et al., 2006) whereas in obesity PYY concentrations are attenuated (Batterham et al., 2003). Furthermore, postprandial rise in PYY appears to be blunted in obese individuals, which may result in impaired satiety and therefore increased food consumption (Batterham et al., 2006).

Postprandial effects of dietary factors

While the temporal PYY profile and postprandial peaks are clearly influenced by the amount of ingested calories, macronutrient composition and food consistency may also modulate circulating PYY levels (Degen et al., 2005; Batterham et al., 2006; Helou et al., 2008; Chandarana et al., 2009).

Dietary fat, protein and carbohydrates all stimulate PYY release but to different degrees and time-courses (Cox, 2007; Helou et al., 2008). In some studies, fat has been shown to have the strongest effect on postprandial PYY compared with protein and carbohydrate (Adrian et al., 1985a; MacIntosh et al., 1999; Essah et al., 2007). On the other hand, PYY concentration has also been shown to increase after proteins and carbohydrates while only a slight rise after a fat meal was observed (Pedersen-Bjergaard et al., 1996).

Different fats elicit different PYY release. Especially fat hydrolysis and acyl chain length seem to be essential (Degen et al., 2007). Increases in plasma PYY levels were greater after free fatty acids than triglycerides (Little et al., 2007). Fatty acids with 12 carbons or more stimulated PYY release, while fatty acids with 10 carbons or less stimulated PYY to a lesser extent (Maas et al., 1998) or had no effect (Feltrin et al., 2006; Degen et al., 2007). Fatty acid saturation of long chain fatty acids did not affect PYY secretion (Maljaars et al., 2009). Instead, physicochemical attributes of fat affect PYY release; increased droplet size was associated with the attenuation of the stimulation of plasma PYY (Seimon et al., 2009).

PYY release is stimulated also by dietary protein. Stimulatory effect of protein on PYY release has been observed after high-protein meals compared with high-fat and high-carbohydrate meals (Batterham et al., 2006) and after different protein solutions (whey or casein: whole protein versus hydrolysate) (Calbet and Holst, 2004). Higher dietary protein stimulates postprandial PYY more compared with lower protein consumption (El Khoury et al., 2010; Leidy et al., 2010b), although this is not observed in all studies (Smeets et al., 2008; Hochstenbach-Waelen et al., 2009a). Protein type may also modulate PYY response. Postprandial PYY was more increased after pork versus chicken meal (Charlton et al., 2011), and combination of whey protein and pea protein hydrolysate increased PYY more than milk protein or these proteins consumed separately (Diepvens et al., 2008).

DF has also been shown to modulate postprandial PYY response, although with differences between fibre types. Postprandial PYY release was greater after insoluble oat fibre-enriched bread than after insoluble wheat fibre bread (Weickert et al., 2006). Also beta-glucan-enriched bread (Vitaglione et al., 2009) and cereals (Beck et al., 2009a) increased postprandial PYY concentration more than control meal with no beta-glucan, whereas no effect on PYY levels was observed after increasing doses of mixed fibres in muffins (Willis et al., 2010).

Table 1 summarizes the major characteristics of the peripheral GI appetite-related hormones reviewed above.

Table 1. Summary of the attributes of the peripheral gastrointestinal appetite-related hormones.

Hormone	Identification and discovery	Active molecule	Primary site of production	Major target actions	Release	Half-life	Primary macronutrient stimulus	Effect on satiety	Effect on energy intake
Ghrelin	1999	Acyl ghrelin	Gastric fundus X/A -like cells	- GH release ↑ - gastric motility ↑	Rises before a meal	~10 min	CHO, protein	⇩	⇧
CCK	Late 1920s	CCK-58, -33, -22 and -8	I-cells, duodenum and jejunum	- gallbladder contraction ↑ - pancreatic enzyme and bicarbonate secretion ↑ - Gastric acid secretion and GE ↓	Rises rapidly after a meal	1–2 min	Fat, protein	⇧(*	⇩
GLP-1	1980	$GLP\text{-}1_{7\text{-}37}$, $GLP\text{-}1_{7\text{-}36amide}$	L-cells, small and large intestine	- incretin effect on insulin - glucagon release ↓ - gastric secretion and GE ↓ - small bowel motility ↓	Rises after a meal	1.5–5 min	CHO, fat	⇧	⇩
PYY	1980	$PYY_{1\text{-}36}$, $PYY_{3\text{-}36}$	L-cells, small and large intestine	- gastric acid , pancreatic and gallbladder secretion ↓ - GE and small bowel motility ↓	Rises after a meal	$PYY_{3\text{-}36}$ ~3 hours	Fat, protein	⇧	⇩

CCK, cholecystokinin; GH, growth hormone; GLP-1, glucagon-like peptide 1; PYY, peptide YY; GE, gastric emptying; CHO, carbohydrate; ⇧, increased; ⇩, decreased; (*, CCK's role more important in satiation than in satiety. Modified from Karhunen et al., 2008; Moss et al., 2012.

2.4 EFFECT OF FOOD CHARACTERISTICS ON REGULATION OF FOOD INTAKE

As reviewed in previous chapters, the control of appetite and energy intake is operated through redundant physiological functions to serve energy balance and ensure the operative system. Various food characteristics, such as energy and macronutrient composition, physical state of food and other physicochemical properties affect the system which is consequently reflected in appetite sensations and food intake. The following chapters will cover these issues.

2.4.1 Food volume, energy content and portion size

Under *ad libitum* conditions individuals tend to consume a fixed weight or volume of food (Lissner et al., 1987; Rolls and Bell, 1999; Bell and Rolls, 2001; Westerterp-Plantenga, 2001). This implies that these attributes are essential determinants for satiation and satiety regardless of energy density (van Dam and Seidell, 2007). On the other hand, energy density has been shown to modulate postprandial appetite-related responses also individually (Rolls, 2010).

Increased test meal volume has been related to reduced appetite (Gray et al., 2002) and decreased hunger and increased fullness (Rolls et al., 1999; Norton et al., 2006) independent of sensory properties, energy or macronutrient content (Rolls et al., 1998). Even a volume increased via incorporation of air or water in the test product reduced hunger and energy intake and increased fullness (Rolls et al., 1999; Rolls et al., 2000).

Appetite and energy intake are affected also by portion size and energy density (Westerterp-Plantenga, 2004a; Rolls, 2010). An increase in portion size leads to increased energy intake (Rolls et al., 2002; Rolls et al., 2004), an effect shown to apply nearly all types of foods (Rolls et al., 2007). It is also shown to persist over time without indication of compensation in intake (Jeffery et al., 2007; Rolls et al., 2007).

When the effect of energy density is considered, there seems to be an association between higher energy density and higher energy intake (Poppitt and Prentice, 1996; Drewnowski et al., 2004). Respectively, consumption of low-energy-density diet reduces energy intake (Ledikwe et al., 2006). In the short term, consumption of low-energy density foods can increase satiation and satiety despite reduced energy intake (Rolls and Bell, 1999; Ello-Martin et al., 2005; Rolls, 2010). Energy density affects satiety also when the macronutrient content and the palatability of the preloads are matched (Rolls, 2010).

In addition to their independent effects, portion size and energy density have combined effects on satiety and total energy intake. When combined, the reduction in energy intake is cumulated (Rolls et al., 2006). However, the effect of the energy-density manipulation is stronger than that of portion size (Rolls, 2010).

2.4.2 Composition

2.4.2.1 Dietary fat

The role of dietary fat in the human diet has been under a constant and vigorous debate (Shikany et al., 2010). The intensity of the discussion seems to be relative to the increasing prevalence of obesity. Even though dietary fat is an essential part of a healthy and balanced diet, it has also been related to the etiology of obesity due to its high energy density, high hedonic value, and relatively weak satiating-signaling properties (Bray et al., 2004). All these factors are likely to promote passive overconsumption in addition to an efficient storage capacity and a poor promotion of fat oxidation and diet-induced thermogenesis

(Westerterp-Plantenga, 2004b). Thus, both the behavioural responses and metabolic consequence of dietary fat increase the probability of positive energy balance and body fat gain (Peters, 2003).

The effects of dietary fat on appetite and food intake can be considered at least from two perspectives – from macronutrient and structural viewpoints. First, it appears to be generally accepted that dietary fat is the weakest macronutrient in the satiety hierarchy (Mann et al., 2007; Westerterp-Plantenga et al., 2009). Secondly, it is evident that not all fats and fatty acids are comparable in their effects on food intake, appetite and associated metabolic responses, even though studies investigating these effects are still limited. For example, studies associated with fat structure indicate that chain length and degree of saturation and esterification affect these responses (Samra 2010).

Medium-chain triacylglycerols (MCT, 8–12 carbons) are shown to be more satiating than long-chain triacylglycerols (LCT) (Rolls et al., 1988a; Stubbs and Harbron, 1996; Van Wymelbeke et al., 1998; St-Onge et al., 2003), but the effect is not always evident (Poppitt et al., 2010). However, the mode of administration (oral vs. gastrointestinal infusion) plays an essential role. MCT are more satiating than LCT when administered orally (Rolls et al., 1988a; Stubbs and Harbron, 1996; Van Wymelbeke et al., 1998; Van Wymelbeke et al., 2001; St-Onge et al., 2003). Instead, after intraduodenal infusion of long-chain fatty acids food intake was inhibited compared with medium-chain fatty acids, which had no effect (Matzinger et al., 2000). These responses are probable due to differential delivery routes of the lipids to the liver (Friedman et al., 1983) and the fatty acid oxidation level in the liver (Langhans, 1996). Furthermore, gut hormone secretion is affected by the fatty acid chain length (Maas et al., 1998). There is also evidence that the number of double bonds in fatty acid chains is associated with enhanced satiety (Samra 2010), although this has also been challenged (Strik et al., 2010). Additionally, the degree of esterification of dietary fats may influence appetite. Diacylglycerols have been reported to lower hunger, appetite, and desire to eat more than triacylglycerols when incorporated into foods (Kamphuis et al., 2003).

Two important functions, gut sensing and gut signaling should be considered when dietary fat and appetite and/or food intake regulation is considered (Maljaars et al., 2010). Proper satiety signaling by dietary fat is achieved only with complete fat digestion, since the digestion of triacylglycerols and the release of free fatty acids play a key role in the release of satiety hormones (Matzinger et al., 2000; Feinle-Bisset et al., 2005). Furthermore, for appropriate control of fat intake, it would be more beneficial to delay fat digestion and absorption in the gut without inhibiting it (Albertsson et al., 2007; Maljaars et al., 2008; Maljaars et al., 2010).

2.4.2.2 Dietary protein

The word “protein” originates from Greek words “prōteios” and “prōtos” which mean ‘of primary importance’ and ‘of first quality’ (Vickery, 1950). This is an apt description, since virtually all functions in the body are dependent on proteins. Unique properties and functionality of proteins are based on the amino acid sequence in the primary structure of the protein polypeptide chain. This in turn determines the unique 3-dimensional native conformation and biological functionality of proteins.

Physiological actions

The primary sources of dietary proteins are meat, fish, milk, egg and plant proteins, of which each source consists of a complex mixture of distinct proteins with specific amino acid composition (Jahan-Mihan et al., 2011). The effects of these proteins on postprandial physiology are determined by the food source, macronutrient composition, matrix and

processing as well as whether they are consumed as mixture or purified proteins alone (Jahan-Mihan et al., 2011). More specifically, the characteristics of different protein types, digestion products including bioactive peptides (BAP), digestion kinetics and non-protein bioactive components conjugated with them influence mechanical, hormonal and neuroendocrine functions within the GI tract. These functions include interacting with receptors releasing gut hormones, digestion and absorption process and neural signalling to the brain (Jahan-Mihan et al., 2011).

The signalling cascade of dietary protein begins from the oral cavity and terminates in the colon, but the critical events and effects originate from the small intestine. Therefore, pregastric, gastric, and post-gastric signals are important in determining the physiological outcomes after protein ingestion which in turn is markedly modulated by the mode of protein consumption, i.e. as purified or a mixture of proteins (Jahan-Mihan et al., 2011).

Nutritionally, the primary role of dietary protein is to provide amino acids, particularly essential amino acids for the protein synthesis and for other nitrogen-containing substances. Only secondarily proteins serve as a source of energy and other metabolic outcomes for the body requirements (Layman, 2009). Therefore, the traditional judgement on the function and quality of protein has been based on its capability to provide essential amino acids and support protein synthesis (Jahan-Mihan et al., 2011). Beyond their nutritional contribution dietary proteins and their digestion products, such as bioactive peptides encrypted in protein molecules, have a marked role in the regulation of glucose, insulin and lipid metabolism (Reynolds et al., 2006; Tremblay et al., 2007; Gannon and Nuttall, 2010), blood pressure (Altorf-van der Kuil et al., 2010), bone and muscle metabolism (Bonjour, 2005; Paddon-Jones et al., 2008a), immune function (Li et al., 2007) and food intake and energy balance (Paddon-Jones et al., 2008b; Soenen and Westerterp-Plantenga, 2008; Potier et al., 2009; Westerterp-Plantenga et al., 2009).

Postprandial effects of dietary proteins

The advances in recent research on dietary protein clearly demonstrate the beneficial role of dietary protein in the regulation of appetite and food intake (Paddon-Jones et al., 2008b; Soenen and Westerterp-Plantenga, 2008; Potier et al., 2009; Westerterp-Plantenga et al., 2009). The notion of dietary protein as having the greatest satiety value among the macronutrients in addition to the fact that protein provides the least energy per gram for the energy metabolism, is largely acknowledged (Paddon-Jones et al., 2008b; Westerterp-Plantenga et al., 2009). However, the source, quantity and quality (intact vs. hydrolyzed, different protein fractions) have a protein-specific effect on appetite, energy intake and GI peptide release (Appendix 1).

Effect of physical state of food

Recent studies indicate that the physical state of the protein-rich test meals plays an important role on postprandial physiology. Leidy and colleagues (Leidy et al., 2011) demonstrated that protein-rich solid breakfast led to a greater reduction in postprandial appetite (composite of perceived hunger, desire to eat and prospective food consumption) compared with protein-rich beverage, but fullness ratings were comparable between the meals. In addition, subsequent food intake was greater after the beverage compared with the solid meal. Equally, Martens and co-workers (Martens et al., 2011) showed that solid protein meal exerts a stronger post-lunch suppression of hunger and desire to eat than liquefied protein meal. In addition, Akhavan and co-workers (Akhavan et al., 2010) showed that satiety was greater after solid compared with liquid forms of gelatin and sweet, but not acid whey protein. Energy intake was not different between gelatin meals and control, but

both solid and liquid forms of whey protein suppressed energy intake compared with control.

Mechanisms regarding protein-induced satiety

Several mechanisms have been proposed to underlie the effects of dietary protein on appetite and food intake regulation affecting potentially body weight (Figure 4). These are increases in a) concentrations of satiety-related GI hormones, b) thermogenesis, c) amino acid concentrations and d) process of gluconeogenesis (Veldhorst et al., 2008; Westerterp-Plantenga et al., 2009). Various studies have shown that dietary protein stimulates the secretion of satiety-related GI hormones (CCK, GLP-1 and PYY) (e.g. Hall et al., 2003; Batterham et al., 2006; Blom et al., 2006a; Bowen et al., 2006a; Veldhorst et al., 2009a) and decreases hunger-stimulating ghrelin (Blom et al., 2006a; Bowen et al., 2006a). However, it has also been stated that the concentrations of appetite-related peptides may not be straightforward related to satiety, but rather reflect the nutrients studied (Diepvens et al., 2008; Smeets et al., 2008). Enhanced protein intake increases also thermogenesis (Westerterp et al., 1999; Lejeune et al., 2006; Hochstenbach-Waelen et al., 2009b), for which the plausible explanation is the increased metabolism due to the processing of the excess protein (nitrogen) load. Furthermore, the suggestion by Mellinkoff and colleagues already in mid 1950s indicated that excess amino acids not used for protein synthesis, serve as a satiety signal for mechanism controlling food intake and thus lead to suppressed food intake (Mellinkoff et al., 1956). The idea is supported by recent studies that suggest the relationship between satiating effect and kinetics of amino acid profiles, specific amino acid concentration and protein types (Diepvens et al., 2008; Veldhorst et al., 2009b; Veldhorst et al., 2009c; Veldhorst et al., 2009d; Veldhorst et al., 2009e). Finally, the process of gluconeogenesis may also be related to satiating effect. The excess glycogenic amino acids can be converted to glucose by the liver. Thus, satiety signalling may be transmitted through a modulation of glucose homeostasis and glucose signalling to the brain. Nevertheless, more evidence is required to establish the role of gluconeogenesis in the protein-related satiety.

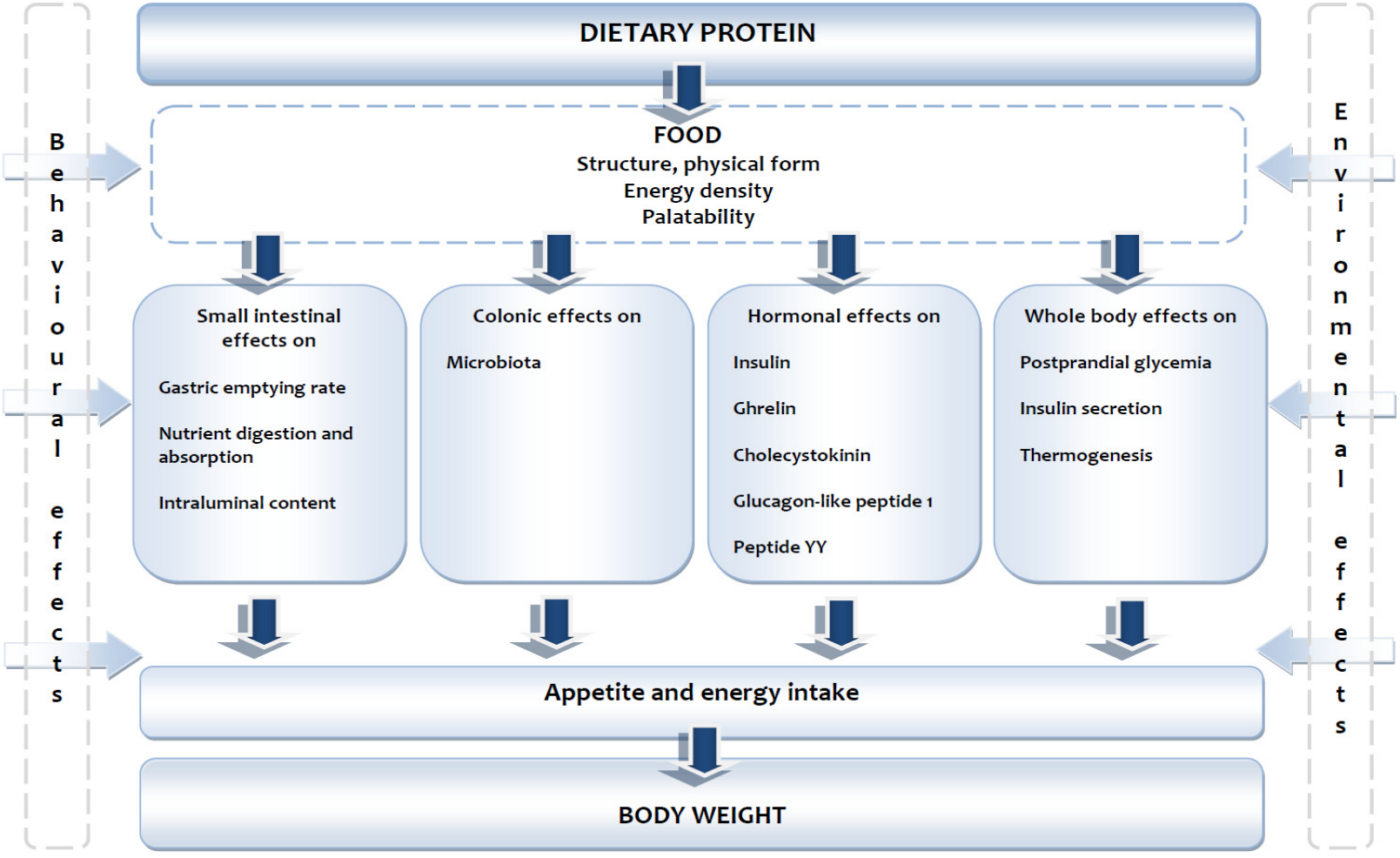

Figure 4. Physiological responses of dietary protein affecting body weight.

2.4.2.3 Dietary carbohydrate

The currently used, chemical (Cummings and Stephen, 2007) and nutritional (Englyst et al., 2007) classifications emphasize distinct characteristics of dietary carbohydrates (CHO). The chemical approach for dietary CHO is structure-based (i.e. nature of individual monomers, degree of polymerization and linkage type (α or β)) (Cummings and Stephen, 2007). The nutritional characterization, however, divides carbohydrates into two main categories, available and resistant CHO (Englyst et al., 2007). The former (such as starch) are digested and absorbed in the small intestine, and the latter (dietary fibre components, resistant starch) are non-digestible and as such potential substrates for the gut microbiota. Resistant, or non-digestible, CHO may be fermented producing short chain fatty acids which are absorbed from the large intestine. Consequently, the available and resistant CHO have quite different roles in energy balance and overall health.

CHO is the primary energy source in the diets of most populations. CHO has also a unique role as a controller of energy metabolism and homoeostasis (Mann et al., 2007). This role is due to the diverse nature of different CHO classes and their effects in the different parts of the GI tract. In the gut, digestibility (site, rate and extent) largely determines the postprandial effects of the specific types of CHO (Cummings and Stephen, 2007; Elia and Cummings, 2007; Englyst et al., 2007).

The role of CHO in the regulation of appetite and energy balance has been a focus of intensive research nearly 60 years. In the 1950s, Mayer proposed the original glucostatic theory. The theory suggests that short-term 'glucostatic' responses are involved in the regulation of energy balance, and it linked increased plasma glucose to increased satiety (Mayer, 1953; MAayer, 1955). Generally, among macronutrients CHO is considered more satiating than fat, but less satiating than protein (Mann et al., 2007; Paddon-Jones et al., 2008b; Potier et al., 2009; Westerterp-Plantenga et al., 2009), although this hierarchy has been challenged by some recent studies (Raben et al., 2003; Potier et al., 2010). The hierarchy could be explained by the macronutrient-specific effects on postprandial metabolism. CHO and protein, whose balance in the body is most tightly controlled, exerted greater suppressive effects on subsequent energy intake than fat, whose balance is more loosely regulated (Elia and Cummings, 2007).

Different types of CHO may affect appetite differently and these effects are closely related to CHO induced glycaemia, insulinaemia and CHO utilization (Mayer, 1953; Ludwig, 2000; Brand-Miller et al., 2002). For example, when the common hexose sugars glucose and fructose are compared, some studies suggest that glucose is more satiating than fructose whereas other studies propose the opposite (Moran, 2009). However, other factors (e.g. timing, volume, other food components) than the intrinsic dissimilarities in the ability of saccharides to induce satiety contribute to the many of the differential effects on food intake (Moran, 2009). When more complex CHO types are considered, whole grains tend to be more satiating than refined grains (Holt et al., 2001; Schroeder et al., 2009; Kristensen et al., 2010; Isaksson et al., 2011; Rosen et al., 2011). The role of glycaemic index is also important. It has been demonstrated that low glycaemic index foods increase satiety and decrease voluntary food intake (Ludwig, 2000). However, these benefits are not necessarily indicated in long-term studies (Bornet et al., 2007; Henry et al., 2007; Aston et al., 2008). On the other hand, high glycaemic index CHO has been concluded to suppress short-term (1-h) intake more effectively than low glycaemic index CHO, but the reverse to occur in long-term intake (Anderson and Woodend, 2003). Accordingly, as concluded in recent reviews the glycaemic index may have a favourable impact on short-term satiety and energy intake but the long-term effect remains inconclusive (Ford and Frost, 2010; Pan and Hu, 2011).

In addition to the CHO type, the food matrix appears to be essential when the satiation / satiety enhancing capacity of CHO is considered. In general, convincing evidence indicate that CHO consumed in liquid form (beverages) is less satiating than CHO consumed as solid foods (Mann et al., 2007; van Dam and Seidell, 2007; Mozaffarian et al., 2011; Pan and Hu, 2011).

2.4.2.4 Dietary fibre

Definitions

Since its early introduction by Hipsley (1953), the definition of dietary fibre (DF) has been under a constant debate, and the subsequent DF classifications have been a target of numerous amendments. The classical definition was formulated by Trowell and colleagues in the early 1970s based on a botanical-physiological viewpoint on edible plant cell material (Trowell et al., 1976). They defined DF as all the polysaccharides including lignin and associated substances that are indigestible by the human digestive enzymes in the small intestine. Currently four major definitions from different authorities are in use, all of which emphasize the physiological effects of DF together with the characterization of the accepted DF types (the Institute of Medicine of the National Academies (IOM, 2001), the American Association of Cereal Chemists (AACC, 2001), the European Union (EU, 2008), Codex Alimentarius Commission (Codex, 2009)) (Table 2). The overall uniformity of these definitions is still lacking due to some obvious differences among the definitions in the classification and physiological effects required of DF. However, it is largely recognized that the favourable physiological properties determine the significance of DF for human health.

Table 2. Dietary fibre definitions by the Codex Alimentarius Comission (Codex), the European Union (EU), the Institute of Medicine of the National Academies (IOM), and the American Association of Cereal Chemists (AACC).

Codex (2009)	EU (2008)	IOM (2001)	AACC (2001)
Dietary fibre means carbohydrate polymers* with ten or more monomeric units#, which are not hydrolysed by the endogenous enzymes in the human small intestine of humans and belong to the following categories:	**Fibre** means carbohydrate polymers with three or more monomeric units, which are neither digested nor absorbed in the human small intestine and belong to the following categories*:	**Dietary fibre** consists of nondigestible carbohydrates and lignin that are intrinsic and intact in plants.	**Dietary fibre** is the edible parts of plants or analogous carbohydrates that are resistant to digestion and absorption in the human small intestine with complete or partial fermentation in the large intestine.
Edible carbohydrate polymers naturally occurring in the food as consumed;	**Edible carbohydrate polymers** naturally occurring in the food as consumed;		
Carbohydrate polymers, which have been obtained from food raw material by physical, enzymatic or chemical means and which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities;	**Edible carbohydrate polymers** which have been obtained from food raw material by physical, enzymatic or chemical means and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence;	**Added fibre** consists of isolated, nondigestible carbohydrates that have beneficial physiological effects in humans.	**Dietary fibre** includes polysaccharides, oligosaccharides, lignin, and associated plant substances.
Synthetic carbohydrate polymers which have been shown to have a physiological effect of benefit to health as demonstrated by generally accepted scientific evidence to competent authorities	**Edible synthetic carbohydrate** polymers which have a beneficial physiological effect demonstrated by generally accepted scientific evidence.	**Total fibre** is the sum of dietary fibre and added fibre.	**Dietary fibres** promote beneficial physiological effects including laxation, and/or blood cholesterol attenuation, and/or blood glucose attenuation.

* Also lignin and other components such as phenolic compounds, waxes, saponins, phytates, cutin, and phytosterols are considered as fibre when closely associated with carbohydrate polymers of plant origin and extracted with the carbohydrate polymers for analysis of fibre.

Decision on whether to include carbohydrates from 3 to 9 monomeric units should be left to national authorities.

Classification

The large and heterogeneous group of DF possesses a wide array of fibre specific physicochemical properties including bulk/volume increasing capacity, viscosity and water holding property, adsorption and/or binding of organic molecules and bacterial degradation. These all have subsequent effects on postprandial physiology and metabolism (Dikeman and Fahey, 2006; Slavin, 2008; Anderson et al., 2009). Several classifications for the DF have been established according to the different DF characteristics which in turn are defined by chemical properties and analytical quantification (Slavin et al., 2009; Raninen et al., 2011).

The classification of DF has traditionally been based on water solubility resulting in categorization in soluble and insoluble fibre types (Table 3). Even though solubility is an apparent determinant of physiological responses, viscosity and fermentability have also been shown to exert significant beneficial effects on the physiological responses in humans. These indications may in fact restructure the traditional classification system of DF types (IOM, 2005). Moreover, DF types can be categorized between dietary fibres and functional fibres, in which the latter is defined as isolated (vs. intrinsic and intact plant derived fibres), non-digestible CHO with beneficial physiological effects.

Table 3. Four different ways to classify dietary fibres in relation to the physiological actions in the body.

Dietary fibres	**Functional fibres**
Cellulose (glucose polymer)	Resistant dextrins (indigestible polysaccharides)
Lignin (polyphenolic compound)	Psyllium (viscous mucilage)
Beta-glucans (glucose polymers)	Chitin and chitosan (glucosamine polymers)
Hemicellulose (polysaccharides)	Fructo-oligosaccharides (synthetic fructose)
Pectins (viscous polysaccharides)	Polydextroses and polyols (synthetic polysaccharides)
Gums (viscous polysaccharides)	
Inulin and oligofructose (fructose chain mixtures)	
Resistant starch (indigestible starch)	
Soluble fibres	**Insoluble fibres**
Wheat dextrin	Cellulose
Beta-glucans	Lignin
Gums (e.g. guar gum)	Some pectins
Mucilages (e.g. psyllium)	Some hemicelluloses
Pectins	
Fructo-oligosaccharides	
Some hemicelluloses	
Fermentable fibres	**Non-fermentable fibres**
Wheat dextrin	Cellulose
Pectins	Lignin
Beta-glucans	
Guar gum	
Inulin and oligofructose	
Viscous fibres	**Non-viscous fibres**
Beta-glucans	Cellulose
Pectins	Lignin
Some gums (e.g. guar gum)	Some hemicelluloses
Mucilages (e.g. psyllium)	

Adapted from Slavin et al., 2009.

Physiological effects of dietary fibre

Consumption of foods rich in DF provides a wide variety of health benefits, ranging from short-term effects on GI functions to long-term outcomes including glucose and lipid metabolism, immunomodulatory and prebiotic effects and body weight regulation. All of these may ultimately lead to reduced risk for certain diseases (Howarth et al., 2001; Pereira and Ludwig, 2001; Yao and Roberts, 2001; Slavin, 2005; Slavin, 2008; Weickert and Pfeiffer, 2008; Anderson et al., 2009) (Figure 5). However, DF may also have potential adverse dietary effects, such as reduced absorption of vitamins, minerals, proteins and energy as well as gastrointestinal side effects. This applies especially when DF is consumed in excess and within an inadequate period of time to allow the GI tract to adapt. However, it is unlikely that healthy, adult individuals who consume DF within the recommended range would have difficulties with nutrient absorption (Slavin 2008).

The quantitative analyses of the effects of DF show that higher DF intake is beneficial in terms of regulation of appetite, energy intake and body weight (Howarth et al., 2001; Pereira and Ludwig, 2001). However, the qualitative analyses on the effects of different DF types in respect of their physicochemical attributes, i.e. viscosity, solubility and fermentability, on these factors are still limited. Nevertheless, the existing data show that these attributes affect satiation, satiety and subsequent energy intake differently (Slavin and Green, 2007; Wanders et al., 2011). Viscous fibres are more effective in promoting satiety (Slavin and Green, 2007; Kristensen and Jensen, 2011; Wanders et al., 2011) and reducing acute energy intake (Wanders et al., 2011) than DF with lower viscosity, whereas the effects of solubility and fermentability on these measures appear less pronounced (Wanders et al., 2011).

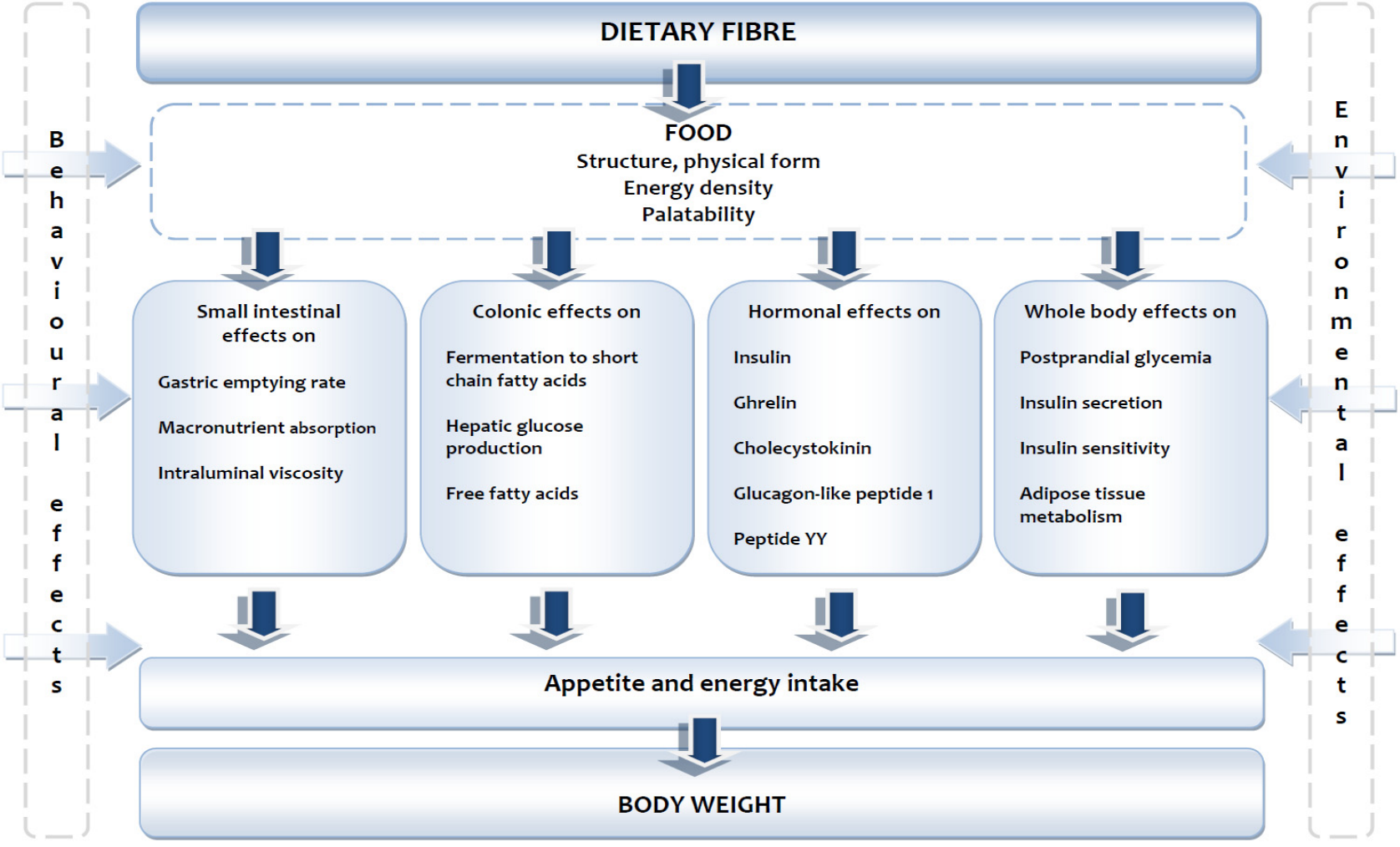

Figure 5. Physiological responses of dietary fibre affecting body weight.

Mechanisms regarding dietary fibre-induced satiety

Several explanations underlying the favourable effects of DF on appetite and subsequent energy intake have been proposed. Physicochemical factors of DF, especially bulk/volume increasing capacity, water holding properties and viscosity contribute to enhanced satiation and satiety (Slavin and Green, 2007). In addition to the fibre type, quantity and the food source of the fibre have a specific effect on appetite responses, food intake and GI peptide release (Appendix 2).

Satiety signals arise both pre- and post-absorptively (Blundell et al., 2010). Pre-absorptive factors, such as chewing effort and time, gastric motility and the early phase of nutrient absorption affect especially satiation. Foods rich in DF usually require more oral processing than low-fibre foods (Howarth et al., 2001). Chewing solid foods more promotes satiety signalling which is not stimulated by swallowing liquids (Haber et al., 1977) or when oral stimulation is bypassed (Cecil et al., 1998; Cecil et al., 1999; French and Cecil, 2001). These results can be explained by shorter orosensory exposure time (Zijlstra et al., 2009a).

Gastric distension and emptying may also contribute to DF-induced satiation. Increased production of saliva during mastication and postingestive secretion of gastric fluids, in addition to water-absorption capacity of certain DF, increases gastric volume and activates vagal afferent signalling for fullness. Moreover, DF affects GI function by delaying GE and small bowel transit time. This is due to the DF induced bulking and textural characteristics of the digesta. DF also slows down digestion and absorption of nutrients and affects GI hormone release (Benini et al., 1995; Burton-Freeman, 2000; Yao and Roberts, 2001; Schneeman, 2002; Karhunen et al., 2008). Especially viscous fibres have been shown to delay GE (Marciani et al., 2000; Marciani et al., 2001; Darwiche et al., 2003) and absorption of nutrients (Jenkins et al., 1978; Braaten et al., 1991; Burton-Freeman, 2000). These factors in addition to the fermentation process in the colon are likely reflected in satiety. Accordingly, all these mechanisms stimulate satiety by prolonging the contact of nutrients with different parts of the GI tract.

2.4.3 Food structure and physical state of food

Postprandial GI physiology is not governed solely by the macronutrient composition and / or energy content. Physicochemical factors, such as physical state, structure, rheology and breakdown, may also have a significant influence on the postprandial digestive and absorptive process and subsequent metabolic and hormonal responses in the body (Figure 6).

Food products are composed of multicomponent matrices with complex structures (microstructure) which is frequently reflected in the physical state (macrostructure, liquid to solid) of these foods (Norton et al., 2007; Lundin et al., 2008). While macronutrient composition clearly modulates the GI physiology, food structure and physical state may exert additional influence and play a significant role in the regulation of appetite sensations and food intake (Collier and O'Dea, 1982; Crapo and Henry, 1988; Tournier and Louis-Sylvestre, 1991; Hulshof et al., 1993; Santangelo et al., 1998; DiMeglio and Mattes, 2000; Peracchi et al., 2000; Mattes and Rothacker, 2001; Laboure et al., 2002; Mourao et al., 2007; Tieken et al., 2007; Lundin et al., 2008; Stull et al., 2008; Leidy et al., 2010a; Martens et al., 2011). In general, it appears that solid foods elicit stronger satiety and/or fullness or reduced hunger and/or desire to eat than more liquid foods (Haber et al., 1977; Bolton et al., 1981; Hulshof et al., 1993; de Graaf and Hulshof, 1996; Mattes and Rothacker, 2001; Tieken et al., 2007; Stull et al., 2008; Leidy et al., 2010a; Akhavan et al., 2011; Martens et al., 2011). They also elicit more pronounced compensatory response in energy intake (Tournier and Louis-Sylvestre, 1991; DiMeglio and Mattes, 2000; Mourao et al., 2007; Stull et al., 2008). This means that liquid calories seem to be less effective in suppressing appetite and often without energy intake compensation during subsequent meal (Mattes, 2006; de Graaf, 2011; Pan and Hu, 2011).

An interesting category within different physical states of foods is soups, i.e. a liquified food form, which appear to be more satiating or suppressing food intake more than more solid counterparts (Kissileff et al., 1984; Rolls et al., 1990; Spiegel et al., 1994; Spiegel et al., 1997; Himaya and Louis-Sylvestre, 1998; Santangelo et al., 1998; Rolls et al., 1999; Mattes, 2005). This is suggested to be a unique property of this food form (Mourao et al., 2007).

Several recent studies have demonstrated that food microstructure, i.e. the spatial arrangements of structural constituents, such as polymer strands, networks, crystals or droplets, and their interactions may affect postprandial GI physiology, too (Lundin et al., 2008). For example, the characteristics of fat emulsion, such as emulsification, stability, droplet size, hydrolysis level and fatty acid chain length (free fatty acids versus triglycerides) have been shown to modulate GE rate and lipolysis as well as subsequent GI hormone secretion and appetite (Marciani et al., 2006; Garaiova et al., 2007; Little et al., 2007; Marciani et al., 2007; Foltz et al., 2009; Marciani et al., 2009; Seimon et al., 2009). In the group of carbohydrates, the structural properties, especially those of high-molecular-weight CHO or non-starch polysaccharides have the capability to alter the GI functions and appetite responses (Marciani et al., 2001; Hoad et al., 2004; Dikeman and Fahey, 2006; Kristensen and Jensen, 2011; Wanders et al., 2011). Viscous dietary fibres and ingredients with intact botanical structure or physical attributes such as thickness, particle size and shape may slow down the GE rate, digestion and absorption of nutrients leading to delayed and blunted metabolic responses (Bjorck et al., 1994; Marciani et al., 2001; Dikeman and Fahey, 2006; Kristensen and Jensen, 2011). Moreover, dietary proteins possess diverse structural characteristics which are further reflected in postprandial GI functions, metabolism and appetite. For example, the intrinsic structural differences of the two main

milk proteins, casein and whey protein, and their diverse postprandial effects highlight this (Boirie et al., 1997; Hall et al., 2003; Veldhorst et al., 2009a).

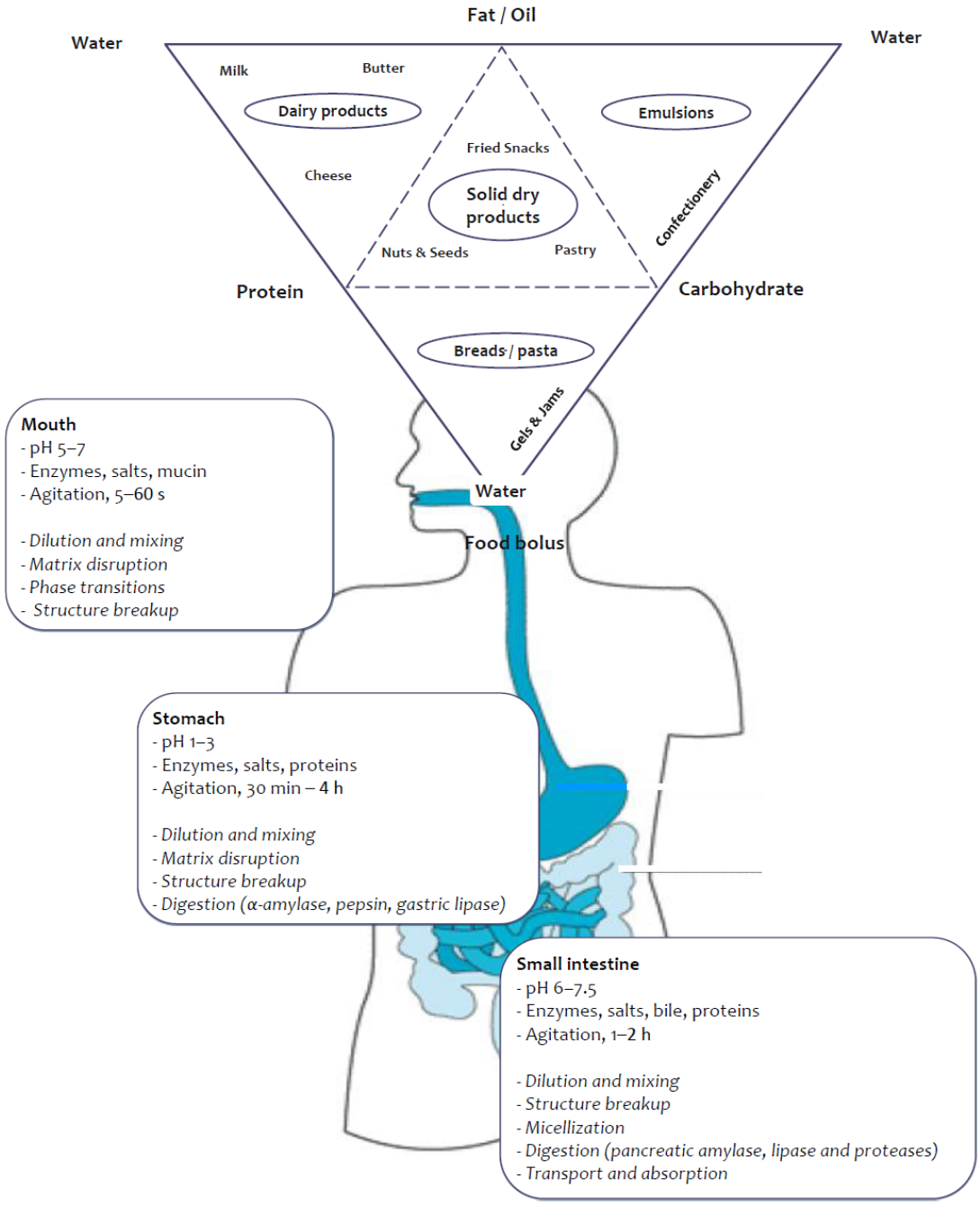

Figure 6. Simplified schematic presentation of the different structural levels of foods and human gastrointestinal system with various processes during digestion and absorption. Modified from McClements et al., 2009.

2.4.4 Sensory characteristics

Sensory characteristics, such as taste, odour, texture, temperature, visual appearance, sound and irritative perceptions (neural stimulation) are important attributes of food and influence food selection, appetite and food intake (Pollard et al., 2002; Sorensen et al., 2003; Smeets et al., 2010; Mattes, 2011). Sensory attributes are also essential determinants of palatability (Hyde and Witherly, 1993). Available evidence indicates that energy intake increases as palatability increases (Sorensen et al., 2003). Generally, sensory cues direct food choice; people choose foods they like and avoid foods they dislike (Smeets et al., 2010). Instead, studies on the influence of palatability on subjective appetite sensations have shown inconsistent results (Sorensen et al., 2003).

The olfacto-gustatory perception of food gives rise also to sensory-stimulated satiation and satiety, which is frequently referred to as sensory-specific satiety (Smeets et al., 2010). The concept is defined as a temporary and relative decline in pleasure or pleasantness originated from consuming a certain food relative to an unconsumed food (Rolls et al., 1981). A variety of sensory properties are capable of stimulating sensory-specific satiety, such as taste (de Graaf et al., 1993; Guinard and Brun, 1998), odour (Rolls and Rolls, 1997), texture (Guinard and Brun, 1998) and visual appearance (Rolls et al., 1982). However, it appears that energy content of food is not related to sensory-specific satiety (Rolls et al., 1988b; Bell et al., 2003). Additionally, studies on the role of macronutrients in sensory-specific satiety have given contradictory results. Yet, sensory-specific satiety may have an important influence on the amount of food eaten (Sorensen et al., 2003). The increasing variety of sensorily distinct foods postpone satiation, increase food and energy intake and in the short to medium term alter energy balance (Raynor and Epstein, 2001; Sorensen et al., 2003; Hetherington et al., 2006).

Finally, humans have expectations about satiety which different foods are expected to confer. These beliefs and expectations on food characteristics can have marked effects on satiety, a phenomenon termed “expected satiety” (Brunstrom, 2011). When expectations were compared across various commonly used foods (on a kJ-for-kJ basis), it was discovered that considerable mismatch occurred between expectations and the energy content of foods (Brunstrom et al., 2008). Foods high in energy and fat had significantly lower ratios of expected satiety than foods with lower energy and fat content (Brunstrom et al., 2008). In particular, expected satiety tends to increase when foods become familiar (Brunstrom et al., 2008), a phenomenon called “expected-satiation drift” (Brunstrom, 2011) and after they have been eaten to fullness. These observations suggest that expected satiety is also learned (Brunstrom et al., 2008; Brunstrom et al., 2010). Recently, it was also shown that the effect of expected satiety can persist well into the inter-meal interval (Brunstrom et al., 2011).

2.5 SUMMARY OF THE LITERATURE REVIEW

Appetite and food intake regulation is based on a set of elegant processes which aim ultimately at energy homeostasis. These processes are controlled by external (non-homeostatic) and internal (homeostatic) factors. In the internal homeostatic process, organ cross-talk including gut-brain-axis, is the fundamental mechanism operating in the system. In the GI tract, especially the neuroendocrinological system plays a major role in modulating the postprandial physiology in response to energy status and various food-related stimuli.

Food is an integral part of both the external and internal processes of food intake regulation. At the same time, foods are complex matrices with numerous physicochemical properties exerting diverse postprandial responses according to the attributes of their components. These responses are indicated in acute alterations in physiological and appetite responses as well as long-term outcomes at the level of metabolism and body composition. When interpreting the research findings of the effects of different dietary factors on postprandial appetite and physiology, it is important to note that a variety of individual (subject characteristics) and/or methodological aspects (e.g. variation in test products, study designs, sample collection and handling, assays used and peptide variants measured) considerably contribute to the available data. This in part explains the often quite heterogenous outcomes among different studies.

Dietary fibre and protein together with CHO and fat make up the bulk of food matrix. Moreover, recent studies have highlighted the importance of the physical state and structure of food on postprandial physiological responses. All these factors are also significant contributors to appetite and energy balance. Although it is important to reveal the synergistic effects of different foods and diets on the regulation of appetite and food intake, it is equally important to elucidate the individual dietary factors (components, attributes) that affect these variables.

3 Aims of the study

As shown, the physicochemical properties of dietary fibre and protein delineate their postprandial physiological and appetite responses. The structure and physical form of food also modulate these responses. However, the effect of various dietary fibres, proteins and food structure on postprandial gastrointestinal physiology in relation to appetite control is still incompletely understood.

This study aimed to determine the postprandial physiological and appetitive responses of selected dietary fibres and proteins in healthy normal-weight subjects. The ingredients used in different food models were chosen based on their physicochemical properties and suitability for structure modification.

The specific aims were to investigate the postprandial effects of the following ingredients and factors in different food models:

- psyllium fibre and soy protein (*Study I)*
- oat and wheat bran (*Study II*)
- sodium caseinate and whey protein (*Studies IV* and *V*)
- viscosity of oat beta-glucan (*Study III*)
- structure modification of sodium caseinate (*Studies IV* and *V*)

on plasma or serum glucose, insulin and gastrointestinal peptide responses, gastric emptying, appetite sensations and short-term energy intake in healthy normal-weight subjects.

It was hypothesized that increased amount of dietary protein and dietary fibre, especially the viscous fibre type as well as more solid food structure, would promote satiety and related postprandial gastrointestinal responses.

4 Subjects and Methods

4.1 STUDY POPULATION AND DESIGN

Healthy normal-weight individuals were recruited to participate in the studies (Table 4). The studies were performed at the Department of Clinical Nutrition at the Kuopio campus of the University of Eastern Finland (*Studies I–III* and *V*) or at the Department of Physiology at the University of Oulu (*Study IV*).

A screening phase preceded all the studies. Volunteers were interviewed about their medical history, dietary habits and physical activity. Baseline anthropometric and biochemical assessments were performed to ensure normal clinical status and blood measures. Exclusion criteria included any food intolerance or allergy, breakfast skipping, modification of diet or exercise patterns during the past year to lose weight, any medication (except oral contraceptives) or smoking. The Three-Factor Eating Questionnaire (TFEQ) (Stunkard and Messick, 1985) and Bulimic Investigatory Test Edinburgh (BITE) (Henderson and Freeman, 1987) were used to describe the eating behavior of the volunteers and exclude individuals with potentially abnormal eating behavior. Participants were individually familiarized with the study protocol and measurements prior to the actual test visits.

The Research Ethics Committee of Hospital District of Northern Savo and Northern Ostrobothnia Hospital District approved all the study protocols. The studies were performed in accordance with the principles of the Declaration of Helsinki. All participants signed an informed consent before the initiation of the study.

Table 4. Clinical characteristics of the study populations.

	Study I	***Study II***	***Study III***	***Study IV***	***Study V***
Gender (female/male)	13/3	15/5	16/4	0/8	11/2
Age (y)	26.1±1.0	23.3±0.9	22.6±0.7	24.0±0.8	23.3±1.1
Weight (kg)	67.2±3.0	62.2±1.9	62.0±1.8	76.8±2.4	62.8±2.3
Height (cm)	168.8±2.3	168.9±2.1	169.0±2.0	181.4±1.9	169.9±2.0
BMI (kg/m^2)	23.5±0.8	21.7±0.3	21.6±0.3	23.3±0.5	21.7±0.4
TFEQ					
Restraint (Factor 1)	10.4±0.9	8.6±0.9	10.5±1.1	-	8.9±1.2
Disinhibition (Factor 2)	4.2±0.5	4.1±0.6	4.0±0.6	-	4.8±0.6
Hunger (Factor 3)	3.4±0.3	4.0±0.5	3.1±0.5	-	4.1±0.6
BITE					
Symptoms	3.3±0.6	3.9±0.9	2.6±0.7	-	3.8±0.7
Severity	-	1.2±0.3	0.7±0.2	-	0.9±0.3

Data are mean ± standard error of the mean; BMI, body mass index; BITE, Bulimic Investigatory Test Edinburgh; TFEQ, Three-Factor Eating Questionnaire.

Each study had a single-blind (participants unaware of the nature of the treatment), randomized, crossover design where all participants tested each test product with a minimum of 2 days between the test days. The participants were instructed to maintain their habitual diet and exercise routines as stable as possible during the whole study period. On the day preceding each test day participants were advised to refrain from heavy exercise, avoid alcohol consumption for 2 days before the test day throughout the study. Subjects were requested to arrive to the laboratory unit each time by the same way (e.g. walking, cycling, car or bus) and to avoid extra physical stress before the beginning of the test session. Prior each test period participants were weighed and their overall exercise and alcohol consumption during the previous day were checked by an interview.

All the test visits began in the morning between 07.30 am–08.00 am after a 10–12 hour fast. In *Studies I–III,* during the first visit an oral glucose tolerance test (OGTT, 75 g glucose dissolved in 300 ml water) was performed to ascertain normal glucose tolerance. The OGTT procedure had otherwise exactly the same study protocol as the following test sessions to familiarize the subjects with the study protocol and measures. During the actual visits in each study, subjects consumed one of the test products in a randomized order in a fixed time.

In each study blood samples were taken to determinate the pre- and postprandial metabolic, hormonal and physiological responses (Table 5). Samples were taken via an indwelling cannula inserted into the antecubital vein 10 min prior the first blood sampling. Blood samples were taken in fasted condition at baseline and in fixed time points after the ingestion of the test product. Subjects rated their appetite sensations at the concomitant time points immediately after blood sampling. Subjects were requested to avoid any extra physical activity and stay in sitting position during the test period to minimize the effects of body posture on postprandial responses.

Table 5. Characteristics of the *Studies I–V.*

	Study I	***Study II***	***Study III***	***Study IV***	***Study V***
Test products	Vegetable patty	Porridge	Beverage	Model foods	Beverage
Main ingredients	Psyllium, soy	Oat and wheat bran	Oat bran	Caseinate, whey protein	Caseinate, whey protein
Physical state at the time of consumption	Solid	Semisolid	Liquid	Liquid / solid	Liquid
Study period (h)	2	3	3	4	4
Structure modification	–	–	beta-glucanase treatment	TG-crosslinking	TG-crosslinking
Biochemical measurements	Glucose, insulin, ghrelin, GLP-1, PYY	Glucose, insulin, ghrelin, PYY	Glucose, insulin, ghrelin, CCK, GLP-1, PYY, GE	Glucose, insulin, CCK, GLP-1, PYY	Glucose, insulin, amino acids, GE
Appetite sensations	Hunger, satiety, desire to eat, fullness, desire to eat the test food	Hunger, satiety, desire to eat, fullness, thirst	Hunger, satiety, desire to eat, fullness	Hunger, satiety, desire to eat, fullness, thirst	Hunger, satiety, desire to eat, fullness, thirst
Food intake	*ad libitum* - meal, 2-day food diary (0, I)	*ad libitum* - meal, 2-day food diary (0, I)	*ad libitum* - meal, 2-day food diary (0, I)	–	4-day food diary (00, 0, I, II)

CCK, cholecystokinin; GE, gastric emptying; GLP-1, glucagon-like peptide 1; PYY, peptide YY; TG, transglutaminase; food diaries: 00, two days before the test day; 0, the previous day; I, remaining of the test day; II, next day; –, not applied/not measured.

4.2 TEST PRODUCTS IN *STUDIES I–V*

The test products used in these studies included either DF (*Studies II* and *III*), proteins (*Studies IV* and *V*) or both (*Study I*) as ingredients of interest (Table 5). All the test products were prepared with commercially available ingredients which were provided by VTT Technical Research Centre of Finland.

Four isoenergetic and equal-weight solid vegetable patties were used as test products in *Study I* (Table 6). The baked patties were prepared using potato/union mix, potato flour, vegetable oil and water together with psyllium fibre and/or soy protein isolate. Psyllium is soluble and highly viscous partly fermentable dietary fibre. Soy protein is high quality vegetable protein composed mainly of soluble protein fraction. Patties were seasoned with salt, parsley and black pepper. Isoenergetic white wheat bread without added fibre or protein was the internal reference sample. An *ad libitum* meal (including oat and rye bread, margarine, cheese, ham, tomato and cucumber slices, non-caloric orange juice, tap water, coffee, tea, milk and sugar) was provided 2 h after the test meal consumption.

Table 6. Energy and macronutrient composition of the test products in *Study I*[1].

	WWB	**LFLP**	**HFLP**	**LFHP**	**HFHP**
Portion size (g)	121	230	230	230	230
Energy (kJ/kcal)	1250/300	1250/300	1250/300	1250/300	1250/300
Energy density (kJ/g)	10.3	5.4	5.4	5.4	5.4
Carbohydrates, (g/E%)	52/71	33/49	32/47	23/32	21/28
Total fibre (g)	3.4	7.6	27.3	6.2	25.8
- psyllium[2] (g)	-	-	23.0[3]	-	23.0[3]
Protein[3] (g/E%)	9.2/12	2.8/4	2.6/4	19.7/28	18.4/25
Fat (g/E%)	5.7/17	14.4/47	15.7/51	12.8/40	13.6/41

[1]Ingested with 400 ml of tap water; [2]psyllium powder (dietary fibre (DF) content 85%), FiberHUSK, W. Ratje Froeskaller ApS, Denmark; [3]soy protein isolate, SUPRO EX 33 IP Non-GM, Solae LLC; E%, percentage of total energy; WWB, white wheat bread; LFLP, low-fibre low-protein; HFLP, high-fibre low protein; LFHP, low-fibre high-protein; HFHP, high-fibre high-protein.

In Study II, four isoenergetic and equal-weight semisolid porridges were provided as test meals (Table 7). In brief, the porridges were prepared using whipped porridge base, made of semolina, black currant juice concentrate, wild berry flavoured juice, maltodextrin, rapeseed oil and water, in which the brans were added just before serving the meals. Three of the meals were enriched either with oat bran, wheat bran, or combination of these, and the fourth one was low-fibre porridge. Oat bran contains both soluble and insoluble fibre fractions, including beta-glucan which is soluble, viscous and fermentable DF type. Wheat bran is insoluble DF with non-viscous and non-fermentable attributes. An *ad libitum* meal, which consisted of vegetable soup, oat and rye breads, margarine, soft cheese, sliced cucumber, non-caloric orange juice and tap water, was offered 3 h after the test meal consumption.

Table 7. Energy and macronutrient composition of the test products in *Study II*[1].

	No added fibre[2]	**Wheat bran**[3]	**Oat bran**[4]	**Combination**[5]
Portion size (g)	300	300	300	300
Energy (kJ/kcal)	1250/300	1250/300	1250/300	1250/300
Energy density (kJ/g)	4.2	4.2	4.2	4.2
Carbohydrates (g/E%)	56.8/83	54.5/80	52.9/77	56.7/89
Total DF (g)	1.5	10.3	10.6	10.1
- insoluble DF (g)	1.5	10.3	5.5	7.6
- soluble DF (beta-glucan, g)	-	-	5.1	2.5
Protein (g/E%)	4.4/6	6.3/9	8.4/12	7.3/10
Fat (g/E%)	3.7/11	3.7/11	3.7/11	3.7/11

[1]Ingested with 400 ml of tap water; [2]Test meal with no added dietary fibre (DF); [3]test meal with DF from finely ground wheat bran (Sydänystävä wheat bran, Raisio plc, Finland); [4]test meal with DF from oat bran concentrate (GI Trim Naturel, Suomen Viljava Oy, Finland); [5]test meal with DF from wheat and oat brans; E%, percentage of total energy.

Two isoenergetic and isovolumic oat-bran concentrate (GI Trim Naturel, Valioravinto Oy, Finland)-enriched, high-fibre beverages which differed only in viscosity level were used as test products in *Study III* (Table 8). The flavored test beverages were prepared by mixing wild berry-flavored juice, blackcurrant juice concentrate and sucrose in tap water. In case of the high-viscous beverage the oat bran concentrate was added in the beverage just before serving. In case of the low-viscous beverage, viscosity was reduced by enzymatic (beta-glucanase; endo-(1,4)-beta-glucanase) treatment. A total of 0.2 g of beta-glucanase was used to treat the beverage with 30 g of oat bran concentrate (Table 8). The treatment resulted in a marked degradation of the beta-glucan molecules and distinctive distribution of molecular weight fractions compared with the high-viscous test beverage (Table 9). Paracetamol (1500 mg) was used in the test beverages to assess GE. Three hours after the test product consumption, an *ad libitum* meal (vegetable soup, oat and rye breads, margarine, cheese, tomato and cucumber slices, noncaloric juice, and tap water) was provided.

Table 8. Energy and macronutrient composition of the test products in *Study III*[1].

	Low-viscous beverage	**High-viscous beverage**
Portion size (ml)	300	300
Energy (kJ/kcal)	1250/300	1250/300
Energy density (kJ/g)	4.2	4.2
Protein (g/E%)	7.8/10.7	7.8/10.7
Fat (g/E%)	3.3/9.8	3.3/9.8
Carbohydrates (g/E%)	57.9/79.5	57.9/79.5
- total DF (g)	10.2	10.2
- insoluble DF (g)	5.1	5.1
- soluble DF (g)	5.1	5.1
Oat bran concentrate[2] (g)	30.0[3]	30.0

[1]Ingested with 200 ml of tap water; [2]GI Trim Naturel, Suomen Viljava Oy, Finland; [3]viscosity eliminated in low-viscous oat bran beverage using beta-glucanase (endo-(1,4)-beta-glucanase, Veron HF, Röhm, AB Enzymes) treatment; DF, dietary fibre; E%, percentage of total energy.

Table 9. Molecular weight distribution and viscosity of the oat bran beverages.

	Low-viscous beverage	**High-viscous beverage**
Molecular weight, MW		
> 1 000 000 (%)	5	50
1 000 000 - 100 000 (%)	10	35
< 100 000 (%)	85	15
Viscosity at 20 min (mPa·s)	< 250	> 3000

In *Study IV,* three equal-weight dairy protein (sodium caseinate, whey protein isolate with very low caseinomacropeptide content) based model foods were served as test products (Table 10). All the test products were prepared by mixing the protein powder with water until a smooth solution was formed after which aroma and sweetener were added. For the transglutaminase (TG, gamma-glutamyl-peptide, amine-gamma-glutamyl transferase)-crosslinked caseinate test product (Cas-TG), TG was added in the mixture to induce crosslinking. For the non-crosslinked caseinate (Cas) and whey protein (Wh) TG was inactivated. The texture analysis of the products showed that Wh was a low viscosity fluid (comparable to e.g. water or skim milk), Cas was a high-viscous fluid with some elasticity and Cas-TG a very strong elastic gel (comparable to e.g. thick marmalade) at protein concentration of 13%. The puncture test indicated that the firmness of the Cas-TG product was much higher than that of Cas or Wh. The analysis of the viscosity of Wh and Cas showed that the viscosity of the syrup resembling Cas was much higher than the viscosity of Wh, which was almost like water.

Table 10. Energy and macronutrient composition of the test products in *Study IV*[1].

	Cas	**Cas-TG**	**Wh**
Portion size (g)	400	400	400
Energy (kJ/kcal)	976/230	976/230	950/223
Energy density (kJ/g)	2.4	2.4	2.4
Protein (wt%/E%)	13.2/91.7	13.2/91.7	12.9/92.2
Carbohydrates (wt%/E%)	0.9/6.5	0.9/6.5	1.0/6.9
Fat (wt%/E%)	0.12/1.8	0.12/1.8	0.05/0.8

[1]Ingested with 400 ml of water; Cas, caseinate (Sodium caseinate (mainly casein, proportion of individual caseins similar as in milk), EM 7, DMV International, The Netherlands); Cas-TG, transglutaminase (Activa MP, Ajinomoto Foods Europe SAS, France) treated caseinate; Wh, whey protein (Whey protein isolate (mainly beta-lactoglobulin), *Bi*PRO®, Davisco Foods International, Inc., USA); E%, percentage of total energy.

Three equal-weight dairy protein (sodium caseinate, whey protein isolate with very low caseinomacropeptide content) based beverages were used as test products in *Study V* (Table 11).

For the TG-crosslinked caseinate test product (Cas-TG), a batch of TG-crosslinked sodium caseinate powder was prepared at VTT. In brief, powder was produced by mixing sodium caseinate with water in a mixer until a homogeneous solution was obtained. In a fermenter TG suspension and the sodium caseinate solution were incubated for the transglutaminase reaction. The enzyme reaction was inactivated by heat treatment. The final product was frozen and freeze-dried. The non-enzyme-treated reference powder was prepared according to the same protocol, but the TG in the suspension was inactivated prior to adding it into the sodium caseinate solution.

The extent of crosslinking of the TG-treated caseinate was very high as indicated by the SDS-PAGE results. Almost all caseins were disappeared after TG-treatment due to the formation of covalent crosslinks between caseins. The TG dosage was about 200 nkat/g protein. The high TG dosage was chosen to maximize the structural differences between the caseinate containing test products in order to show the possible postprandial effects.

The test beverages were prepared by mixing glucose and protein powder in water until completely dissolved. Aroma was used to improve the taste of the beverages. Glucose (40 g per test product) was included in the beverages to stimulate glucose-dependent postprandial responses and to mimic the nutritional composition of a mixed diet. ^{13}C acetic acid was used in the beverages as a marker for GE. The test beverage with TG-treated caseinate showed a higher viscosity than the beverages with non-crosslinked caseinate or whey protein, yet the products remained pourable at protein concentration 6%.

Table 11. Energy and macronutrient composition of the test products in *Study V*[1].

	Cas	Cas-TG	Wh
Portion size (g)	500	500	500
Energy (kJ/kcal)	1194/281	1172/276	1163/274
Energy density (kJ/g)	2.39	2.34	2.33
Protein (g/E%)	28.6/41	28.6/41	30.0/44
Carbohydrates (g/E%)	41.0/58	39.7/58	38.2/56
Fat (g/E%)	0.3/1	0.3/1	0.1/0

[1]Ingested with 100 ml of tap water; Cas, caseinate (Sodium caseinate (mainly casein, proportion of individual caseins similar as in milk), EM 7, DMV International, The Netherlands); Cas-TG, transglutaminase treated caseinate; Wh, whey protein (Whey protein isolate (mainly beta-lactoglobulin), *Bi*PRO®, Davisco Foods International, Inc., USA); E%, percentage of total energy.

4.3 METHODS

4.3.1 Anthropometric measurements

Body height (KaWe REF 44 444, Person-Check, Medizintechnik KaWe, Kirchner & Wilhelm, Germany) and weight (Seca 880, Seca Vogel & Halke, Hamburg, Germany) were measured in fasted state in light indoor clothes using regularly calibrated devices. Body mass index (BMI) was calculated dividing the body weight by the squared body height (kg/m^2). Weight was measured twice and the mean value was used in calculations. Measured height was rounded to the nearest 0.5 cm.

4.3.2 Appetite measurements and food records

Visual Analogue Scales (VAS) were used in *Studies I–V* to obtain the individual appetite (hunger, satiety, desire to eat, fullness, thirstiness) and pleasantness ratings induced by the test meals (Blundell et al., 2010). Each self-assessed VAS consisted of 100 mm horizontal unstructured line anchored with unipolar verbal descriptions (in Finnish) at either end expressing the weakest or strongest statement on sensation in question (i.e. 'I am not hungry at all' or 'I have never been more hungry'). The participants were advised to draw a vertical line on the horizontal axis corresponding to their sensations at the time of assessment. VAS ratings were measured in millimeters, resulting in scores between 0 and 100 for statistical analyses.

Detailed 24 h food records were used *Studies I–III* and *V* to monitor individual food intake (Table 5). Study participants were advised to fill in food record so that all food items and beverages were listed as they were consumed. The average individual daily energy and macronutrient intake from the food records were analyzed by using the MICRO-NUTRICA database (version 2.5; Finnish Social Insurance Institution, Turku, Finland).

4.3.3 Gastric emptying

In *Study III*, GE was assessed using an indirect method, the acetaminophen (paracetamol) absorption test where 1500 mg of the marker was dissolved in the test products (Para-Tabs, Orian Pharma, Orion Corporation, Espoo, Finland). Fluorescence polarization

immunoassay (Abbott TDX, Abbott Laboratories, Diagnostics Division) was employed to quantify serum paracetamol concentrations.

In *Study V*, GE was determined by a standardized 13C-Acetate Breath Test method in combination with the quantitative isotope gas mixture analyser, IRIS -13C-Breath Test System (IRIS, non-dispersive infrared spectroscopy; Wagner Analysen Technik GmbH, Bremen, Germany). The estimation of the GE rate is based on monitoring the appearance of $13CO_2$ in breath test samples following the consumption and metabolism of 13C-acetate labelled test product adjusted by body weight and height of individual participants. Analysis of the $13CO_2$ appearance in the breath samples provides estimates of individual GE parameters, as described by the time with maximum speed of GE after ingestion of the test meal (t_{lag}), the time when first half of the 13C-labelled substrate dose of the test meal has been metabolised ($t_{1/2}$) and the GE coefficient (GEC), which is a measure of initial gradient of GE.

4.3.4 Analytical methods

Blood samples

Fluoride citrate-containing tubes were used for plasma glucose samples in all studies. In S*tudies I–III* and *V*, plasma samples were collected in prechilled EDTA-containing tubes for the determination of insulin, amino acids, ghrelin, CCK, GLP-1, and PYY concentrations. Amino acids, insulin, ghrelin, CCK, GLP-1 and PYY samples were centrifuged within 15 min for 15 min at 1700 x g at 4°C. Glucose samples were centrifuged at 2400 x g for 10 min at 4°C. All samples were immediately stored at -70°C until analyzed. In *Study I,* insulin was measured using serum samples. The samples were collected in prechilled tubes, allowed to clot in ice for 30 min and then centrifuged at 2400 x g for 10 min at 4°C.

Plasma glucose was analyzed using an enzymatic photometric assay (Konelab 20XTi Clinical Chemistry Analyzer, Thermo Electron Corporation, Vantaa, Finland) in all studies. The intra-assay CV for the plasma glucose was 2.7% at 10.2 mmol/l and the inter-assay CV was 4.1% at 2.05 mmol/l and 1.8% at 8.2 mmol/l. Plasma insulin was measured using a luminometric immunoassay (ADVIA Centaur Immunoassay System, Siemens Medical Solutions Diagnostics, Tarrytown, NY, USA) in all other studies. For plasma insulin, the intra-assay CV was 2.7% at 667 pmol/l and the inter-assay CV was 6.6% at 41 pmol/l and 5.1% at 444 pmol/l. In *Study I* insulin concentrations were determined using a luminometric immunoassay (ACS:180 PLUS, Bayer/Chiron, USA). The intra-assay CV for the serum insulin was 7.7% for the whole measuring range and the inter-assay CV was 9% at 109.7 pmol/l and 7.9% at 847.3 pmol/l.

Radioimmunoassay (RIA) technique was employed for the analyses of plasma total ghrelin, i.e. active octonyl (acylated) ghrelin and inactive des-octonyl (non-acylated) ghrelin and plasma total PYY, recognizing both $PYY_{1–36}$ and $PYY_{3–36}$ (Linco Research Inc., St. Charles, MO, USA). The inter-assay CV for the total ghrelin RIA kit was 8.1% at 191 pmol/l and 13.5% at 469 pmol/l and the intra-assay CV was 9.5% at 150 pmol/l and 8.2% at 362 pmol/l. The inter-assay CV of the total PYY RIA kit was 11.3% at 14 pmol/l and 8.8% at 50 pmol/l and the intra-assay CV was 11.0% at 15 pmol/l and 8.0% at 51 pmol/l. A fluorometric enzyme immunoassay (ELISA, Linco Research Inc., St. Charles, MO, USA) was used to analyze plasma GLP-1 concentrations. The assay measures active GLP-1, i.e. $GLP\text{-}1_{7–36amide}$ and $GLP\text{-}1_{7–37}$. The inter-assay CV of the total GLP-1 ELISA kit was 20.5% at 6.8 pmol/l and 10.1% at 42.5 pmol/l and the intra-assay CV was 20.6% at 8.1 pmol/l and 14.2% at 42.0 pmol/l.

Plasma CCK was analyzed with Euria-CCK RIA (Euro-Diagnostica). The kit recognizes CCK 26–33 sulfate (100%) and CCK-33 sulfate (134%) but does not significantly cross-react with nonsulfated CCK 26–33 (<0.01%), CCK 30–33 (<0.01%), and gastrin-17 sulfate (0.5%), or with nonsulfated gastrin-17 (<0.01%). The intra-assay CV was 5.5% at 4.4 pmol/l and 2% at 20.6 pmol/l and the inter-assay CV for CCK was 13.7% at 4.2 pmol/l and 4.1% at 20.6 pmol/l.

In *Study IV*, prechilled EDTA and trasylol (250 KIU/5 ml) containing tubes were used for plasma insulin, CCK, GLP-1 and PYY. Immediately after blood sampling 50 µl of protease dipeptidyl peptidase IV (DPP IV) inhibitor (DPP IV Inhibitor, Millipore) was injected to the plasma sample tubes to prevent the degradation of the native GLP-1 molecule. Glucose, insulin, CCK, GLP-1, and PYY samples were centrifuged for 10 min at 1700 x g at 4°C. All samples were immediately frozen and stored at -70°C until analysed. Total plasma PYY, i.e. both $PYY_{1–36}$ and $PYY_{3–36}$, and active plasma GLP-1, i.e. $GLP\text{-}1_{7–36amide}$ and $GLP\text{-}1_{7–37}$, concentrations were quantified in a direct assay with the use of a Human Gut Hormone Panel Milliplex kit (Millipore, St Charles, MO, USA) utilizing a Bio-Plex instrument based on Luminex xMAP technology (Bio-Rad Laboratories Inc., CA, USA). The intra-assay CV for the total GLP-1 was 10.8% at 40.1 pg/ml and 10.6% at 84.9 pg/ml and the inter-assay CV was 28.9% at 26 pg/ml and 15.8% at 202 pg/ml. For the total PYY, the intra-assay CV was 4.1% at 78 pg/ml and 2.3% at 141.3 pg/ml and the inter-assay CV was 13.1% at 74.5 pg/ml and 12.2% at 164.1 pg/ml.

Plasma CCK concentrations were analyzed after extraction using a radioimmunoassay kit (Euria-CCK RIA, Euro-Diagnostica AB, Malmö, Sweden). The kit recognizes CCK 26–33 sulfate (100%) and CCK-33 sulfate (134%) but does not significantly cross-react with nonsulfated CCK 26–33 (<0.01%), CCK 30–33 (<0.01%), and gastrin-17 sulfate (0.5%), or with nonsulfated gastrin-17 (<0.01%). The intra-assay CV for CCK was 5.5% at 4.4 pmol/l and 2.0% at 20.6 pmol/l and the inter-assay CV was 13.7% at 4.2 pmol/l and 4.1% at 20.6 pmol/l.

Plasma amino acid concentrations were analysed with a Mass TRAK™ Amino Acid Analysis Application Solution (Waters, MA, USA). AccQ•Fluor reagent kit, Mass TRAK™ Amino Acid Analysis concentrate A and eluent B were obtained from Waters (Milford, MA, USA). Amino Acid Standard Solution, Amino Acid Standards Physiological, Basics, L-isoleusine and glutamine were obtained from Sigma-Aldrich (St. Luis, MO, USA). After dilution with water and adding acetonitrile and norvaline (0.025 mM) as an internal standard, the samples were filtrated through a Waters Sirocco plate, freeze-dried and reconstituted with 50 µl of water. Derivatization was done with an AccQ•Fluor reagent kit. Samples were kept at 5°C before and during analysis. Analysis was performed on an Acquity UPLC system (Waters, USA) with a diode array detector. Chromatography was performed using an Acquity Mass Trak™ column (Waters Corporation, USA) and gradient elution at 43°C. Signal was detected at 260 nm.

Quality assurance of laboratory processes

The quality assurance system of the laboratory included the pre-analytical, analytical and post- analytical phases of the laboratory work. The analytical methods as well as the pre-analytical and post-analytical procedures are validated and documented in the quality manual and work instructions of the laboratory and the instructions of the kit manufacturer. The internal quality control procedures were applied to all biochemical analytes on the automatic analyzers and the manual methods. Several control samples (normal, low and high levels) were assayed in each run. Manual analyses were performed in duplicate.

The experienced laboratory technologists performed result verification for each analytical run to decide on the acceptance or rerun. The verification process included instrument error messages, sample based interferences, and reaction details. The samples were visually evaluated especially for haemolysis and lipaemia. The overall rate of haemolytic samples was less than 5%. In case the haemolysis was considered moderate or severe, spare sample was used in the analysis.

Food samples

The aim of the substudies *III–V* of this thesis was to investigate the effect of enzymatic viscosity reduction (*Study III*) and enzymatically induced structure modification of sodium caseinate (*Studies IV* and *V*) on the postprandial physiological and appetite responses. Thus, to verify the changes in rheological properties of the test products the following characterization was performed in each substudy.

The viscosity of the low- and high-viscous test beverages in *Study III* was measured at a shear rate of $50 \cdot s^{-1}$ at 20°C using a standardized rheometer (StressTech CC 25 CCE, ReoLogica Instruments). A size-exclusion HPLC-analyzing technique was used to determine the molecular weight distribution of beta-glucan in these beverages (Suortti, 1993).

In *Study IV* the texture of all the milk protein based test products was measured using a Texture Analyser device (TA-HDi, Stable Micro Systems, UK). The viscosity of the liquid-like test products, non-crosslinked caseinate and whey protein, was measured at 29°C with a stress controlled rotational rheometer (AR-G2, TA Instruments, UK) equipped with a four-bladed vane geometry. The steady-state viscosity was measured with a gradually increasing shear stress with values resulting in shear rates in the range 0.1-150 s^{-1}.

The level of protein crosslinking of the sodium caseinate in *Study V* was analysed by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) (Ercili Cura et al., 2010). The viscosity of the test products was measured at 20°C with a stress controlled rotational rheometer (AR-G2, TA Instruments, UK) equipped with a concentric cylinder geometry. The steady-state viscosity of the samples was measured in duplicate with a gradually increasing shear stress with values resulting in shear rates in the range 0.1-500 s^{-1}.

4.3.5 Statistical analysis

The data analyses were performed with SPSS for Windows software (SPSS for WINDOWS, versions 11.5, 14.0 and 17.0, USA). The results are expressed as mean and standard error of the mean (SEM) with a value $P \leq 0.05$ (2-sided) as a criterion for the statistical significance, if not otherwise stated.

In *Studies I–III*, the results were analyzed and expressed as the absolute changes from the fasting level (baseline subtracted) to diminish the possible effect of differences in fasting levels within the participants and between meals. ANOVA was used for repeated measures with treatment and time as within-participant factors and Huynh-Feldt as a correction factor to compare the responses after different test beverages. The analysis provides p-values for the differences between the treatments, differences over time course, and for the interaction of treatment with time. Where a significant main effect of product or product x time interaction was observed ($p<0.05$), post-hoc analyses were performed using the Sidak correction for multiple comparisons. The incremental areas under the curve (AUC) were calculated so that the AUC below the baseline, when detected, was subtracted from the area above the baseline. ANOVA was used for repeated measures to compare the AUC after the

test products with Huynh-Feldt as a correction factor and Sidak correction for the post-hoc analyses.

In Studies IV and V, linear mixed-effects modelling was used to compare the effects of the test products on the postprandial responses. In the analysis, the baseline value of each parameter was used as a covariate to take into account the possible effect of baseline differences on the analysis. The method takes into account the sources of variation where product, time and product*time interaction were used as fixed factors and subject as a random factor. Where a significant main effect of a product, time or product x time interaction was observed ($p<0.05$), post-hoc analyses were performed using the Bonferroni correction for multiple comparisons.

5 Results

This thesis consists of series of postprandial studies in which the effects of DF and protein and their enzymatic structure modifications were investigated in healthy normal-weight subjects. The postprandial effects of the tested ingredients and structures are presented as changes in the target variables, i.e. in physiological responses such as GI hormone release and GE and reflections in appetite ratings and energy intake.

5.1 EFFECTS OF DIETARY FIBRE AND PROTEIN ON PHYSIOLOGICAL RESPONSES

The effects of DF and protein were studied in solid (vegetable patties, gel), semisolid (porridge) and liquid (beverage) model foods. Depending on the study, psyllium, oat and wheat brans and enzymatically depolymerized oat bran were used as DF source, and soy protein, caseinate, enzymatically crosslinked caseinate and whey protein as protein sources.

5.1.1 Effects of dietary fibre and its structure modification (*Studies I–III*)

Gastrointestinal hormone responses

Fibre enrichment and fibre type. Dietary fibre enrichment (10.0% DF, psyllium) of vegetable patties strongly modified postprandial hormonal responses. Psyllium enrichment of solid vegetable patties attenuated the typical decline of postprandial ghrelin concentrations and lowered the total ghrelin response (AUC) compared with the low-fibre low-protein product ($p<0.05$, *Study I*) (Figure 7 C). Psyllium enrichment modified also the postprandial GLP-1 response (*Study I*) (Figure 7 D). The psyllium-rich high-protein product suppressed the GLP-1 response for the entire experimental period, and the response was significantly lower compared with the low-fibre products ($p<0.05$) (Figure 7 D). Psyllium enrichment did not induce significantly different postprandial PYY response between the high- and low-fibre test products.

The enrichment of semisolid porridges with oat bran (3.5% DF), wheat bran (3.4% DF) or their combination (3.4% DF) did not significantly modify the postprandial ghrelin or PYY responses among the test products (*Study II*). Neither were there any significant differences in these responses between the DF levels, i.e. fibre-enriched vs. low-fibre porridges.

Viscosity. The decline in viscosity caused by depolymerization of beta-glucan in oat bran-enriched (3.4% DF) beverages affected the GI hormone responses (*Study III*). A beverage with enzymatically decreased viscosity induced greater postprandial decline in plasma ghrelin concentration than the one with higher viscosity ($p=0.02$). The test beverage with reduced viscosity induced also greater postprandial increase in the satiety-stimulating peptide, CCK, GLP-1 and PYY, concentrations and increased the total CCK, GLP-1 and PYY release (AUC) as compared with the beverage with higher viscosity ($p\leq0.05$) (Figure 8).

Glucose and insulin responses

Fibre enrichment and fibre type. Postprandial glucose and insulin responses were affected by the use of soluble viscous DF in solid and semisolid food matrix. Both psyllium (10.0% DF) in solid vegetable patties (*Study I*) and oat bran (3.5% DF) in semisolid porridge (*Study II*)

lowered postprandial glucose and insulin concentrations but with different intensity. Psyllium enrichment suppressed glucose and insulin responses during the entire study period compared with the low-fibre products ($p<0.05$, (Figure 7 A, B). Also oat bran in the porridge produced the lowest overall plasma glucose response, especially at the end of the follow-up period (3 h), when compared with the porridges enriched with wheat bran or combination of oat and wheat bran or the one with no DF enrichment (*Study II*). Postprandial insulin response was lower after oat bran enrichment already during the first hour of the follow-up period compared with the combination or wheat bran porridge ($p<0.05$) as well as at the end of the follow-up period (3h) compared with the wheat bran porridge. The enrichment of porridge with both oat and wheat bran elicited significantly increased postprandial insulin response at 45 ($p=0.001$) and 60 min ($p=0.03$) as compared with the meal with no DF enrichment.

Viscosity. Viscosity of the oat bran-enriched beverages in *Study III* modified also postprandial glucose and insulin responses (Figure 8 A, B). Low-viscous beverage increased postprandial glucose ($p<0.05$) and insulin responses ($p<0.05$) compared with the high-viscous beverage. The total postprandial insulin response (AUC) ($p=0.007$), but not the total glucose response, was higher after the beverages with lower viscosity.

Gastric function

Viscosity of the oat bran-enriched test products affected gastric emptying rate (*Study III*). GE, as measured with the paracetamol absorption test, was enhanced after the low-viscous oat bran beverage compared with the high-viscous oat bran beverage. This was indicated as higher peak paracetamol concentration (at 90 min, $p=0.020$) and a tendency for a greater total paracetamol response (AUC) for the low-viscous beverage ($p=0.051$) (Figure 8 G).

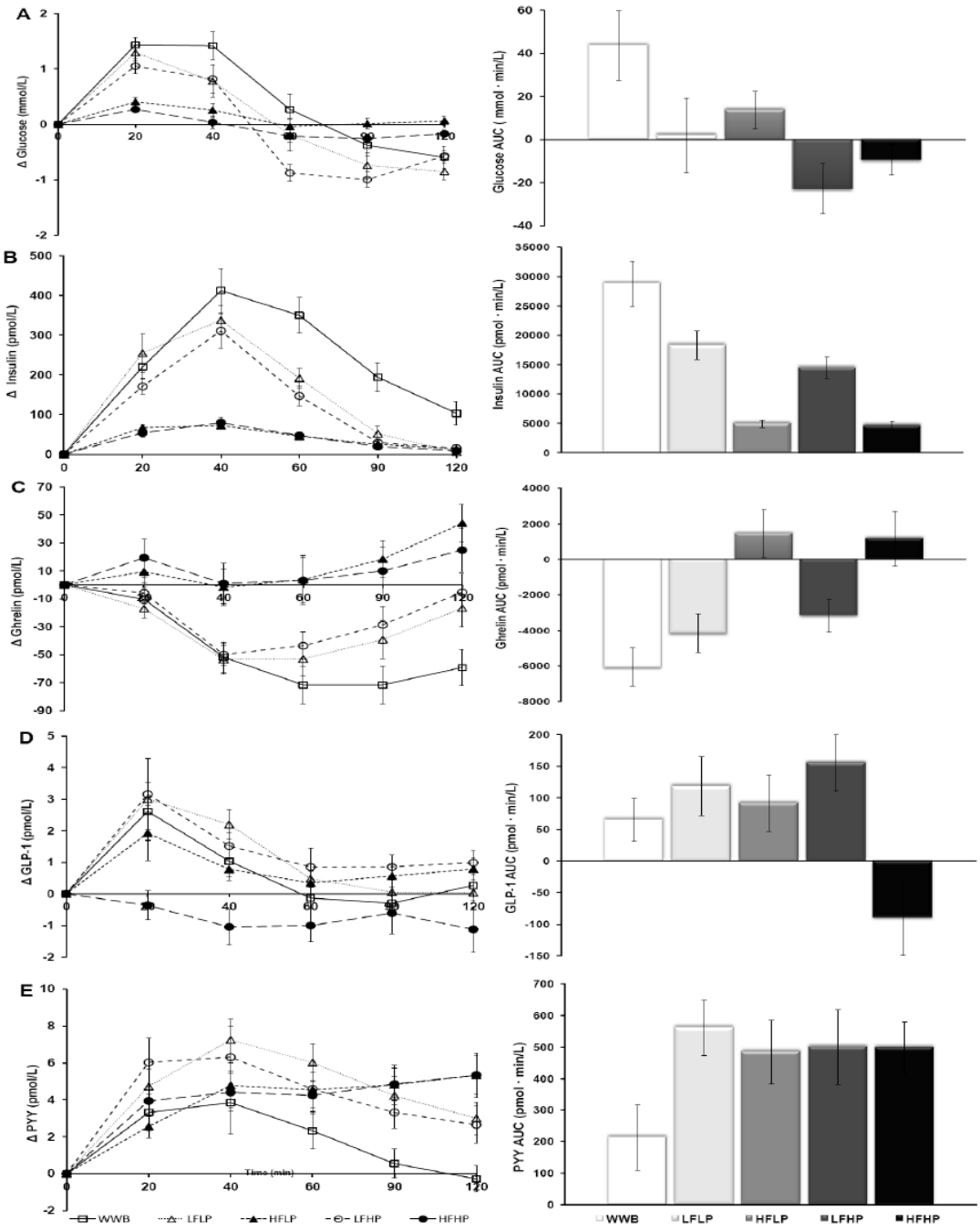

Figure 7. Changes in the concentrations of A) plasma glucose, B) serum insulin, C) plasma ghrelin, D) plasma glucagon-like peptide 1 (GLP-1) and E) plasma peptide YY (PYY) during the 120 min postprandial period after the vegetable patties low or high in dietary fibre and/or protein in *Study I*. Corresponding areas under the curve (AUC) are presented as function of time. Values are means±SEM, *n*=16. WWB, white wheat bread; LFLP, low-fibre low-protein; HFLP, high-fibre low protein; LFHP, low-fibre high-protein; HFHP, high-fibre high-protein.

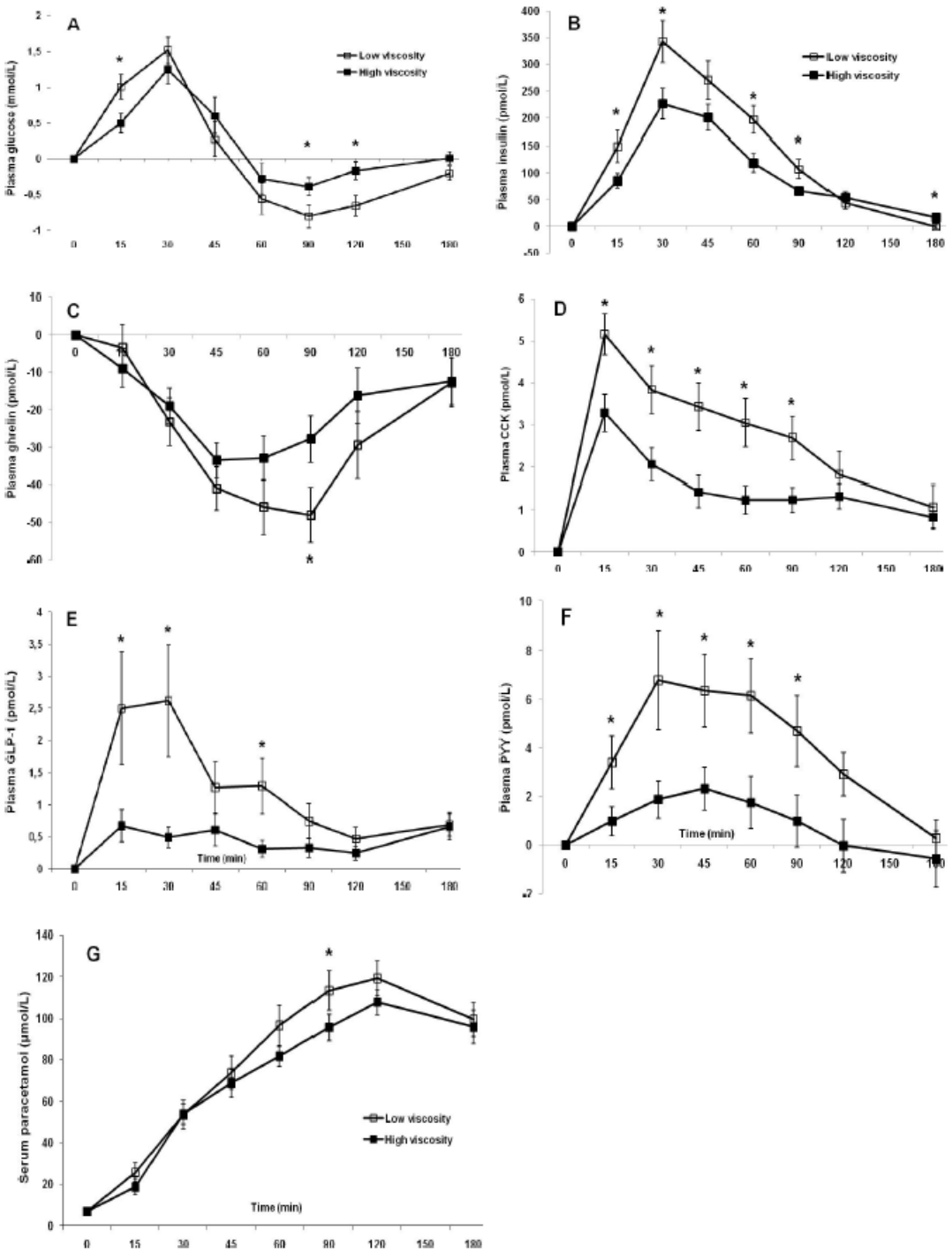

Figure 8. Changes in the concentrations of the plasma A) glucose, B) insulin, C) ghrelin, D) cholecystokinin (CCK), E) plasma glucagon-like peptide 1 (GLP-1), F) peptide YY (PYY) and G) serum paracetamol during the 180 min study period after the low- and high-viscous oat bran beverages in *Study III*. Values are means±SEM, n=20, except for CCK, n=17 and for paracetamol, n=10. For each time point, significant differences in means are indicated by asterisk (*); $p<0.05$, General Linear Model with Sidak adjustment.

5.1.2 Effects of dietary protein and its structure modification (*Studies I, IV* and *V*)

Gastrointestinal hormone responses

Protein enrichment, protein type and protein structure modification. Protein enrichment, protein type (caseinate vs. whey protein) and crosslinking of caseinate in such a way that also the physical state of the test product changed from high-viscous to strong elastic gel (solid), affected the postprandial GI hormone release.

Soy protein enrichment together with psyllium fibre in vegetable patties (*Study I*) suppressed GLP-1 response for the entire experimental period, and the response was significantly lower compared with the low-fibre low-protein product ($p<0.05$) (Figure 7 D).

The crosslinked solid caseinate suppressed postprandial CCK response already in the beginning of the follow-up period (15 min) as compared with the test product including non-crosslinked caseinate ($p<0.001$). Crosslinked solid caseinate tended to suppress also the postprandial GLP-1 response compared with the non-crosslinked caseinate and liquid whey protein. On the other hand, the non-crosslinked caseinate stimulated CCK release more than the crosslinked solid caseinate or liquid whey protein ($p<0.05$). Neither the protein type nor the protein structure modification affected PYY response.

Glucose and insulin responses

Protein type and protein structure modification. Postprandial glucose and insulin responses were affected by protein enrichment (*Study I*) and by the modification of physical state and structure of the protein-rich test products (*Study IV*).

Even though psyllium enrichment of the vegetable patties (*Study I*) dominated glucose and insulin responses, also soy protein enrichment had effects. The soy-enriched high-fibre product lowered postprandial glucose response more than the low-protein high-fibre product ($p<0.05$). This was seen also as a smaller total glucose response (AUC) after high-protein versus the low-protein psyllium-enriched product ($p<0.05$). The total insulin response (AUC) was not affected by the soy protein enrichment.

The structure modification of caseinate affected glucose and insulin responses when the physical state of the test product was also changed (*Studies IV*). Both glucose and insulin responses were attenuated after the crosslinked solid caseinate compared with the non-crosslinked caseinate ($p<0.05$) (*Study IV*). However, when the structure modification changed only the molecular structure of the caseinate leaving the physical state unaffected, no significant differences in postprandial glucose and insulin responses were observed between the crosslinked and non-crosslinked caseinate beverages (*Study V*).

Postprandial glucose and insulin responses were not affected by the milk protein type (caseinate vs. whey protein) either when the physical state of the protein-rich test products clearly differed (*Study IV*) or when the physical state of the products was comparable (liquid) (*Study V*).

Gastric function

Protein type and protein structure modification. Gastric function, as assessed by GE rate, was not affected by crosslinking of caseinate, at least in the situation when the physical state of the products was comparable (*Study V*). Instead, the protein type seemed to influence GE; GE (tlag) tended to be slower after the non-crosslinked caseinate than after the whey protein ($p=0.061$).

Amino acid responses

Protein type and protein structure modification. As expected, whey protein- and caseinate-specific amino acid profile was reflected in individual postprandial amino acid concentrations (*Study V*). The concentrations of glutamic acid, lysine / tyrosine, isoleucine, leucine and tryptophan were increased more after whey protein than after non-crosslinked or crosslinked caseinate. On the other hand, postprandial concentrations of valine, histidine, phenylalanine and proline were lower after whey protein than after non-crosslinked or crosslinked caseinate. The milk protein-specific amino acid profile was also reflected in branched-chain amino acid and essential amino acid concentrations in which the levels were significantly higher after the whey protein than after the crosslinked and non-crosslinked caseinate ($p<0.05$). The postprandial total amino acid concentration was not significantly affected by the milk protein types.

Structure modification of caseinate, when the physical state was unaffected, did not significantly modify any of the individual amino acid responses when compared with the beverage with non-crosslinked caseinate (*Study V*). The postprandial branched-chain amino acid, essential amino acid and total amino acid responses were also comparable between the crosslinked and non-crosslinked caseinate (*Study V*).

5.2 EFFECTS OF DIETARY FIBRE AND PROTEIN ON APPETITE AND FOOD INTAKE

5.2.1 Dietary fibre (*Studies I–III*)

Fibre enrichment, fibre type and appetite and food intake. Enrichment of the solid test products (vegetable patties) with psyllium fibre (10.0% DF) reduced the postprandial desire to eat the test food more than did the consumption of the low-fibre products ($p<0.05$) (*Study I*). Instead, the other appetite ratings, hunger, satiety, fullness and desire to eat, were not significantly affected by the fibre enrichment. The postprandial appetite ratings were neither differently affected by enrichment of semisolid test foods (porridge) with oat or wheat bran as compared with the low-fibre test product nor by DF type as compared among oat and wheat bran and combination of these (*Study II*). *Ad libitum* food intake was neither affected by the enrichment of test products with psyllium fibre (*Study I*) nor oat or wheat bran (*Study II*).

Structure modification and appetite and food intake. Lowering of viscosity induced by oat beta-glucan in the beverage model modified postprandial appetite ratings so that the product with reduced viscosity induced greater postprandial satiety compared with the product with higher viscosity ($p<0.05$) (*Study III*). On the contrary, total energy intake, when energy intake at *ad libitum* meal and during the rest of the test day were combined, was higher after the low-viscous beverage than after the high-viscous one ($p=0.03$) (*Study III*).

5.2.2 Dietary protein (*Studies I, IV* and *V*)

Protein enrichment, protein type and appetite and food intake. Soy protein enrichment of the vegetable patties (*Study I*) or the protein type (caseinate vs. whey protein, *Studies IV* and *V*) did not specifically affect any of the postprandial appetite ratings.

Structure modification and appetite. The enzymatic structure modification of the caseinate which also solidified the food matrix increased fullness ratings more than did the test product with non-crosslinked caseinate in a high-viscous form (*Study IV*). Instead, when

only the molecular structure, but not the physical state of the caseinate containing beverages was modified by crosslinking, no differences were observed in postprandial appetite ratings between the products (*Study V*). Neither were there any differences in subsequent *ad libitum* energy intake ($p<0.05$) which was measured only in *Study V*.

6 Discussion

6.1 METHODOLOGICAL ISSUES

6.1.1 Study populations

In all the studies, the study subjects were young healthy normal-weight individuals. This approach was chosen since it provides a basis for understanding of the potential difference in normal as compared with potentially altered physiological conditions, such as in obesity (Ranganath et al., 1996; English et al., 2002; Batterham et al., 2003; Blundell et al., 2005). Volunteers were systematically screened using standard biochemical and anthropometric assessments as well as interviewed about their medical history, dietary habits and physical activity to ensure their clinical status and to exclude individuals with abnormal dietary and physical habits which could likely affect the outcome variables. In addition, TFEQ and BITE questionnaires were used to characterize the eating behavior of the volunteers and exclude individuals with potentially abnormal eating behavior. Deviations in the normal eating behavior, e.g. restrictive or uncontrollable eating, have been shown to affect physiologic responses (Martins et al., 2008), such as metabolic (Keim and Horn, 2004; Martins et al., 2009) and GI peptide response (Burton-Freeman, 2005), appetite ratings (Martins et al., 2010) and food intake (Laessle et al., 1989). Therefore, by excluding individuals with atypical characteristics or behaviours, the effect of these confounding variables on the postprandial responses was minimized and the homogeneity of the study group was increased.

In *Study IV* only males were included in the experiment by which the possible influence of menstrual cycle on appetite regulation was eliminated and the variability of the study group was further diminished. In other studies it was not possible to have a reasonable number of male subjects and therefore both genders were included.

A limitation related to the study populations used was the relatively low number of subjects included in the studies. Therefore, it is possible that the power of the studies was insufficient to disclose all the true differences among test products in (Flint et al., 2000). However, in the field of postprandial appetite and/or food intake research, the number of the subjects included in the studies of this work sets well within the range of number of participants involved in the majority of other postprandial studies (Appendices 1 and 2).

6.1.2 Analytical methods

In the substudies of this thesis routine analytical methods were applied to determine the pre- and postprandial analyte concentrations in the samples. Plasma and serum samples were used in the analyses; both are frequently analysed body fluids in which diverse short- and long-term metabolic responses and changes, such as organ cross-talk, are reflected.

The analytical methods as well as the pre-analytical and post-analytical procedures are validated and documented in the quality manual and work instructions of the laboratory. This procedure ensures that the laboratory work is performed in a standardized way.

Glucose and insulin were measured using automated clinical chemistry methods which have acceptable imprecision for clinical diagnostic and research use. The GI peptides were analysed with methods commonly used for research purposes. These methods were also validated in the laboratory.

The internal quality control procedures were applied to all biochemical analytes on the automatic analyzers and to the manual methods. Several control samples (normal, low and high levels) were assayed in each run. In the manual procedure, the analyses were performed in duplicate. These practices were used to minimize the variation and errors originating from the reagents, manual procedures, calibration, equipment and methodology. The acceptance of the results for each analytical run was based on the instrument error messages, sample based interferences and reaction details.

6.1.3 Study design

Design

Different approaches can be used to study appetite regulation and eating behavior. Nevertheless, all these protocols suffer from several study-specific limitations which potentially interfere or modulate the responses.

A randomized single-blind crossover design was applied in all studies in this work. Although recommended (Blundell et al., 2010), double-blind conditions were not used since it was challenging or even impossible to mask especially the attributes of different DF types in the test products (e.g. *Study II* and *Study IV).* In the crossover procedure each subject consumes each test product in a random order. A major strength of the method is that the comparisons among test products are performed within the same subject. With this design several unidentified and/or uncontrolled individual-specific factors with regard to appetite ratings and food intake are controlled for. This increases the statistical power of the studies.

The duration of the observation period should be optimized to observe the potential effects of the tested foods or food components on the test variables (Blundell et al., 2010). Within the substudies of this thesis the study period varied from two to four hours. A period of three to four hours (*Studies II–V*) is likely to be sufficient for observing the short-term changes in GI hormone responses and appetite, but an extended study period in *Study I* might have been beneficial.

Setting

All studies in this thesis were performed in a controlled laboratory setting where either individual cabins or separate places were reserved for the consumption of the test products. This experimental setting, commonly used in postprandial studies, guarantees quantitatively accurate and reliable measurements of appetite sensations and food intake. It also ensures the sensitivity to the experimental manipulations without interference of multiple environmental factors. Previous studies have demonstrated that a variety of factors in the environment may distract or interfere with the eating occasion (Wansink, 2004; Wansink, 2010). Especially, the presence of other people clearly affects the eating behavior of individuals (Hermans et al., 2009; Salvy et al., 2009; Hermans et al., 2012).

Even though laboratory settings, in which several confounding factors can be controlled for, may be a proper procedure in many ways, it raises the question whether the results can be extrapolated into real life situations. At the same time, in appetite research the optimal experimental protocol likely remains elusive due to the complex nature of eating behavior (Blundell et al., 2010). As the purpose of this study was to investigate the effects of experimental test products on postprandial physiology and appetite, controlled laboratory condition free of distracting variables was an appropriate choice. If considered worth further examination, more realistic settings can be applied in future.

Visual analogue scales

Visual analogue scales (VAS) were used in all studies to assess self-reported appetite prior and after the consumption of the tested foods. VAS questionnaires as a tool for accessing and assessing subjective appetite sensations have been shown to be sensitive, reliable and valid when used within an appropriate study design and analysis (Flint et al., 2000; Stubbs et al., 2000; Blundell et al., 2010). They are also useful adjuncts to other measures, such as food intake and plasma measures (Stubbs et al., 2000).

Different appetite sensations, especially hunger, satiety, fullness, desire to eat and thirst, were measured. Although a general measure of appetite or a mean score of several of the feelings (e.g. combined hunger and desire to eat-measures) could have been used, the multiple scale method was preferred in order to measure different sensations and to differentiate among them, since they may reflect different somatic sensations and aspects of appetite. For example, hunger and thirst may be sometimes confused with each other, whereas fullness is not a synonym for satiety. Furthermore, different types of sensations deviate in their intensity or duration in addition to sensitivity and reliability (Porrini et al., 1995; Merrill et al., 2002). This also supports the use of multiple scales to describe the different aspect of appetite. Additionally, the use of a standard set of appetite-related questions including the ones assessed in this thesis, is recommended to increase the uniformity in the field of appetite research (Blundell et al., 2010).

During the screening phase of each study, the subjects were individually familiarized with the VAS scales to increase the reliability of the method. Furthermore, the randomization of the test products further diminished the possible systematic effect due to unfamiliarity with the use of VAS scales.

In the study design, appetite sensations were assessed immediately after blood drawing. Hence, it is possible that the experience of blood sampling affected the subjective evaluation of the appetite sensations. However, also in this case the randomization of the test products diminished this effect among the test products, albeit the absolute effect of the blood drawing on the evaluation of the appetite sensations remains unknown.

Ad libitum meal

In *Studies I–III*, an *ad libitum* meal was used as a complementary postmeal appetite indicator to measure the effects of the test meals on subsequent food intake. *Ad libitum* procedure is widely used in appetite research, and it has been shown to be a highly reproducible method (Arvaniti et al., 2000; Gregersen et al., 2008). *Ad libitum* method has, however, it's drawbacks; the palatability of the *ad libitum* meal may mask the subtle effects of the preload / test meal (Yeomans, 2000). It has also been speculated that if consumed repeatedly the amount may be affected by the frequent consumption of the same *ad libitum* meal (Bertenshaw et al., 2009). Even though appetite ratings are also related to energy intake, they are, however, not reliable predictors of energy intake used as such (Flint et al., 2000; Stubbs et al., 2000; Parker et al., 2004). Therefore, combined use of these methods is often recommended (Stubbs et al., 2000; Gregersen et al., 2008; Blundell et al., 2010).

A buffet-like setting was prepared for *ad libitum* test meals. The meal included surplus of everyday savoury food items consumed typically during lunch time. This method allowed for measurement of the possible effects of the test meals (at breakfast) on subsequent energy intake (at lunch), i.e. reflecting short-term energy compensation. Furthermore, when the foods are offered in excess, it reduces the tendency to clean one's plate and diminish the effect of offered serving size on food consumption. On the other hand, availability of a great variety of foods may, by itself, increase food intake (Rolls et al., 1981; Norton et al., 2006)

and delay satiation (Hetherington et al., 2006). However, in the present studies, to diminish this effect, the assortment of offered foods was rather limited and always the same, consisting only of a few savoury food items and beverages. Furthermore, even though the variety of presented foods would have affected the total energy intake, it is important to note that the focus of the measurements was on the possible difference in energy intake among the test products or different conditions, not on the intake itself.

6.1.4 Test products

Standardization of the test products or conditions, i.e. unifying all the characteristics of the test products except the tested variable, is one of the crucial issues to obtain reliable results. In addition to DF, dietary protein and food structure / physical state, several other attributes of foods, such as energy content (Rolls, 2009), volume (Rolls et al., 1998; Rolls et al., 2000), portion size (Kral and Rolls, 2004; Ello-Martin et al., 2005) and sensory properties, including palatability (Yeomans, 1998; Sorensen et al., 2003), have been demonstrated to affect postprandial appetite and food intake. Therefore, it is possible that inadequate standardization of these attributes could have contributed to the observed inconsistencies in the outcome measures among previous studies, also in the studies investigating the effects of DF, protein and food structure / physical state on appetite and food intake.

In the present studies, the portion size, energy content (energy density) and macronutrient composition was nearly identical within one experiment, which is one of the strengths of these studies. When the potential sources of variation are controlled for, i.e. the characteristics of the test products are matched as far as possible, the initial condition or target variable in the test products can be investigated and the true effects elicited. This approach was available especially in *Study III* in which the two oat bran-enriched beverages differed only in viscosity level and in *Study V* in which the two caseinate-enriched beverages differed only in relation to crosslinking of the protein. However, when considering the comparability among all the substudies, it would have been beneficial to have a common control meal across all studies to facilitate the interpretation of the data.

Even with the assistance of modern food technology it is not always possible to construct products with totally comparable attributes. This is especially challenging when macronutrient composition or palatability is considered, since any changes in the composition or nature of the used ingredients will affect these factors. Moreover, the specific attributes of the target ingredients increase the challenge; DF types as well as the major milk proteins, casein and whey protein, differ greatly in many aspects, and these differences may be hard to disguise, as indicated in *Studies I, II* and *IV*. Obviously the food type / matrix used (e.g. liquid, semisolid, solid) plays a key role when different ingredients and/or conditions are tested, albeit the matrix *per se* likely has modulating effects on the subsequent responses as was demonstrated in the *Study IV*. Additionally, model foods, which are not comparable to real foods, are often used because the variety of the appropriate test products is usually limited. However, the main purpose of this kind of studies is to disclose the true effects of the target variables, and based on the findings formulate a concept of the putative mechanism behind the effects.

The type of offered food should also be suitable for the time of the eating occasion. Among the present studies, the porridge (*Study II*) and the beverages (*Studies III* and *V*) represented the most typical foods to be consumed for breakfast, whereas the vegetable patties (*Study I*) and the model foods (*Study IV*) may have been less representative breakfast products.

6.1.5 Postprandial indicators of gastrointestinal physiology

Gastrointestinal physiology is the determinant factor underlying appetite and food intake control. Therefore, one of the initial objectives of the study was to investigate the effects of the tested variables on physiological responses, i.e. GE, postprandial metabolism and GI hormone response.

The key functions of the stomach, i.e. storage, mixing and initial digestion are preparatory processes for the actual digestion in the small intestine. GE is the main regulatory action between these processes. Besides digestion, GE rate regulates several postprandial responses including appetite sensations and metabolic and GI hormone responses. Intestinal GI hormones have been shown to modulate GE rate by adjusting gastric functions to the digestion capacity of the upper small intestine (Liddle et al., 1986; Naslund et al., 1999; Levin et al., 2006; Witte et al., 2009). In *Study III,* GE was measured using paracetamol and in *Study V* standardized 13C-acetate breath test method. Although indirect measures, both paracetamol (Naslund et al., 2000; Willems et al., 2001; Glerup et al., 2007) and breath test method (Braden et al., 2007; Sanaka and Nakada, 2010) have been shown to be feasible and reliable techniques to assess GE. Furthermore, both of these methods were simple, safe, rather inexpensive and non-invasive ways to measure GE. At the time of the individual substudies the measurement of the GE rate was limited to the available methods and therefore two different techniques were used.

Depending on the study (Table 5), a small group of different GI hormones were measured. In general, the hormones were selected due to convincing evidence of their fundamental role in appetite and food intake regulation (e.g. de Graaf et al., 2004; Wynne et al., 2005; Wren and Bloom, 2007; Delzenne et al., 2010; Mars et al., 2012). One of the original ideas linked to the appetite-related GI peptides has been to use them as indicators of satiety (e.g. de Graaf et al., 2004; Delzenne et al., 2010). Despite significant progress in this area, it has been rather challenging to delineate the entire complexity of appetite regulation under assessment of few measurable biomarkers (Delzenne et al., 2010), nutrients and short- and long-term regulators.

Metabolic indicators, such as glucose and insulin, are essential markers of postprandial physiology. Accordingly, these factors, measured also in all substudies of this thesis, are frequently assessed to interpret the effects of test variables on glucose and insulin metabolism. Both of these factors contribute also to appetite regulation; glucose dynamics (Campfield and Smith, 2003) and insulin concentration (Verdich et al., 2001; Flint et al., 2007) have been shown to be related to postprandial appetite and food intake control. Additionally, oral glucose stimulates the release of incretins (i.e. GLP-1 and GIP), which also affect appetite control.

6.2 CONSIDERATION OF THE MAJOR RESULTS

6.2.1 Effects of dietary fibre on physiological responses, appetite and food intake

In *Study I,* soluble and highly viscous psyllium fibre in solid vegetable patties clearly attenuated postprandial glucose, insulin, ghrelin and GLP-1 responses while postprandial PYY secretion was not significantly affected by psyllium enrichment. In *Study II,* the greatest amount of soluble, viscous beta-glucan in oat bran-enriched porridge attenuated postprandial glucose and insulin responses, albeit GI peptide responses, ghrelin and PYY were not significantly different among the test porridges.

The physicochemical properties, especially viscous characteristics of psyllium and beta-glucan in oat bran (Marlett and Fischer, 2003; Slavin et al., 2009) most likely underlie the

distinct postprandial physiological responses observed after the consumption of these fibres. Psyllium is unique among viscous fibres since it survives transit throughout the gut, while other viscous fibres, such as beta-glucan and pectin are rapidly and completely fermented in the large intestine (Fischer et al., 2004). A number of previous studies have demonstrated the effect of increased viscosity on decreased postprandial glucose and insulin responses (Jenkins et al., 1978; Braaten et al., 1991; Wood et al., 1994; Wolf et al., 2003; Panahi et al., 2007), whereas the effects of viscous or other DF types on GI hormone responses are less clear (Karhunen et al., 2008; Zijlstra et al., 2009b). In *Study I*, the amount of viscous psyllium fibre (23 g) included in the high-fibre test products was nearly five times larger than the amount of beta-glucan (~ 5 g) in the oat bran-enriched test product in *Study II*. This might partly explain the more pronounced postprandial responses after psyllium fibre than beta-glucan consumption. Although it is probable that the level of viscosity affected also the GE rate differently between these studies, the postgastric effects likely played even more pronounced role in attenuating and delaying the postprandial GI responses than the GE *per se* (Marciani et al., 2001).

In *Study II*, beta-glucan in oat bran was consumed incorporated into *semisolid* porridges, whereas in *Study I* psyllium was ingested as a part of *solid* vegetable patties. Due to the solid food matrix and the amount of psyllium used in the test products, the hydration of psyllium likely continued also during the intestinal phase, increasing the level of viscosity of the chyme more than the beta-glucan in oat bran (Dikeman et al., 2006). This in turn likely attenuated but prolonged the digestion and absorption processes of nutrients extending the time available to affect postgastric mechanisms, and thus resulted in clear differences in both metabolic and GI peptide responses in *Study I*. On the other hand, in *Study II* the amount of beta-glucan and thus the level of viscosity were possibly too low or too similar to elicit differences in GI hormone responses between the test products like those observed in *Study I*.

In addition to the soluble viscous DF, insoluble low-viscous wheat bran was used in the test products in *Study II*. However, wheat bran as such had no clear postprandial effects unlike beta-glucan in oat bran, which signifies again the importance of solubility and/or viscosity on the postprandial responses during the small intestinal phase. Hence, this implies that the dominating attributes of different DF types are indicated in different part of the GI tract and during different time frame. When the postprandial effects of insoluble low-viscous DF are considered, their role is less evident in short-term study designs investigating acute metabolic effects. The most pronounced effects of this DF type may appear later and more indirectly, i.e. from the effects during the colonic phase (Wong et al., 2006; Papathanasopoulos and Camilleri, 2010). The effects of soluble viscous DF instead are likely to appear already shortly after the consumption of the test products during the small intestine phase, although the effects then continue also in the large intestine often through more rapid fermentation that in the case of insoluble fibre (Slavin et al., 2009).

Besides factors related to DF, the fat content of the test products in the studies differed: in *Study I* the amount of fat was about three times higher than in *Study II*. It has been well demonstrated that postprandial PYY secretion is stimulated by dietary fats (Adrian et al., 1985a; MacIntosh et al., 1999; Essah et al., 2007). Therefore, a greater amount of dietary fat together with increased and prolonged effects of psyllium-induced viscosity explain the augmented postprandial PYY release especially at the end of the study period in *Study I*. Furthermore, the experimental period in *Study I* was limited to two hours, and it would have been interesting to follow especially the PYY response longer, i.e. whether the increased PYY concentration after the high-fibre products would have continued, as shown

in other studies with beta-glucan (Beck et al., 2009a; Vitaglione et al., 2009), and resulted in significant difference also between the high- and low-fibre products.

Despite the clear postprandial effects of viscous DF on metabolic and GI peptide responses, especially in *Study I*, neither satiety/fullness/hunger ratings nor *ad libitum* energy intake was significantly different among the test products in these studies. Numerous previous short-term studies clearly indicate that viscous DF types, such as guar gum, psyllium, pectin and beta-glucan are effective in increasing satiety and/or fullness or reducing hunger compared with low or no fibre condition even at relatively low doses (Slavin and Green, 2007), although these effects are not always demonstrated (Frost et al., 2003). Also insoluble and/or non-viscous DF types may stimulate postprandial satiety/fullness or reduce hunger (Delargy et al., 1995; Delargy et al., 1997; Samra and Anderson, 2007), but these effects are not always detected (Weickert et al., 2006; Freeland et al., 2009). Studies investigating the effects of different DF types on *ad libitum* energy / food intake have shown conflicting results, either with (Delargy et al., 1997; Samra and Anderson, 2007; Freeland et al., 2009) or without effects (Burley et al., 1987; Hamedani et al., 2009), which are likely due to the different study designs, populations, DF types and dosages used.

Several explanations for the non-significant findings in the subjective appetite and energy intake measures may be proposed. Although the test products were enriched with a considerable amount of DF (i.e. 26–27 g in *Study I* (100% of recommended (25–35 g) daily DF intake); ~ 10 g in Study II (40% of recommended (25–35 g) daily DF intake)), the food matrix (solid in *Study I*, semisolid in *Study II*) may have partly masked the subtle postprandial effects of the used DF types. It could be possible that the satiety-stimulating and/or hunger-reducing effects of DF are better demonstrated when liquid matrices are used (Lyly et al., 2009; Perrigue et al., 2009; Vuksan et al., 2009; Lyly et al., 2010; Perrigue et al., 2010; Georg Jensen et al., 2011; Monsivais et al., 2011), a notion supported by the recent review (Wanders et al., 2011). Indeed, in *Study III* in which oat bran-enriched beverages were used as test products, both satiety ratings and *ad libitum* food intake were significantly affected. It is also possible that other characteristics of the test products, such as volume and energy content are more powerful determinants of subsequent appetite sensations and energy intake than DF content *per se* when more solid food forms are used. Thus, the fact that the test products in *Studies I* and *II* were isoenergetic and isovolumic may partly explain the comparable results. It is also possible that "learned satiety", a concept suggesting learned associations between the sensory attributes of food and the postprandial experience of satiety leading to subsequent adjustment in meal size (Booth, 1985), might have affected food consumption at *ad libitum* meals and masked the possible effects of DF. Furthermore, all participants consumed the same test meals with the same energy content which may have resulted in too low or high energy intakes in proportion to their total individual daily energy requirements, and thus may have affected the results. In addition, the amount and type of DF might not affect subjective sensations or short-term energy intake acutely, but might need a longer period to affect those (Greenway et al., 2007). From the physiological point of view it means that the whole length of intestine, including the role of DF in the large bowel, is needed to demonstrate the favourable effects of DF on appetite and energy intake.

The observation that different GI hormone responses were not reflected in concomitant appetite sensations or subsequent food intake are in line with the results of several previous studies which have also been unable to demonstrate the direct relationship between the postprandial GI hormone responses and appetite sensations (Diepvens et al., 2008; Smeets

et al., 2008; Veldhorst et al., 2009d; Maffeis et al., 2010) and/or subsequent energy intake (Veldhorst et al., 2009d). These findings emphasize two important aspects: first, it is likely that appetite-related GI hormone release is mainly a nutrient-related physiological reaction in which also other physicochemical factors in the luminal environment after food consumption play a marked role. Indeed, it has been suggested that GI peptides, especially GLP-1 and PYY, do not likely contribute individually to a difference in satiating capacity of foods, and thus cannot be interpreted in isolation (Mars et al., 2012). Secondly, food intake is controlled also by several external (environmental) non-metabolic factors that may override the subtle and transient internal metabolic and GI hormone effects. It is also likely that individual sensitivity to dietary influences varies considerably and may be even diminished due to modern eating style and dietary characteristics. Therefore the effects of "short-term" dietary treatments on appetite / food intake may not be easily demonstrated.

In conclusion, soluble and viscous dietary fibres modify postprandial physiology, affecting metabolic responses and satiety-related peptide secretion from the GI tract. The impact and magnitude of DF on these measures is attributable to the amount and type of DF used in the test products. The effect of DF type and amount on appetite sensations and short-term food intake is less clear and warrants further clarification.

6.2.2 Effects of dietary protein on physiological responses, appetite and food intake

The effects of protein enrichment and protein type on postprandial responses were investigated in *Studies I*, *IV* and *V*. In *Study I*, soy protein together with psyllium fibre in solid vegetable patties attenuated postprandial GLP-1 response during the entire experimental period. In *Study IV*, the non-crosslinked caseinate stimulated postprandial CCK secretion more than whey protein. In *Study V*, caseinate and whey protein-specific profiles were observed in postprandial amino acid responses.

Some earlier studies, but clearly not all, suggest that dietary proteins have protein-specific effects on postprandial metabolic, GI peptide and appetitive responses, which are suggested to relate to differences in postprandial behaviour of different protein types and amounts consumed. The postprandial effects of protein and DF interactions are less studied, and the combined effects of soy protein and large quantity of psyllium fibre have not been previously investigated. Overall, soy protein enrichment of the test products in *Study I* did not markedly modify the postprandial metabolic or GI hormone responses except for GLP-1 which was practically abolished after the soy-psyllium combination. Although the reason for this response remains unknown, these results indicate that the combination inhibited all the indirect and direct, i.e. early phase neural and second phase enteroendocrine mediators contributing to stimulated GLP-1 response, an effect which was not observed after separate consumption of soy- or psyllium-rich test products. Interestingly, PYY response did not show a similar pattern after the soy-psyllium combination, although both of these peptides are secreted from the intestinal L-cells. The virtually identical PYY responses after the soy-psyllium and the solely psyllium-enriched test product and the PYY response after the products with only soy protein demonstrate that attributes related to psyllium fibre rather than soy protein were primarily responsible for the stimulated PYY response. However, it should be noted that the amount of protein in the soy protein-enriched test meals in *Study I* was modest (25–28 E%) compared with some earlier studies (Erdmann et al., 2003 (99 E%); Batterham et al., 2006 (65 E%); Bowen et al., 2006a (71 E%)), and therefore it cannot be ruled out that the responses might have been different if a larger quantity of protein would have been ingested. On the other hand, the amount of protein in the test products in this study was realistic (~ 20 g), and for the most

part, if the protein content of the vegetable patties would have been increased more, the palatability of the test product, which was already low especially with the high-fibre products, would have likely decreased too much to be acceptable anymore.

As was shown in the Review of Literature, dietary protein modulates postprandial CCK, GLP-1 and PYY responses, albeit in different temporal manner. In *Study IV*, protein type affected CCK response, but neither GLP-1 nor PYY release was significantly different between the non-crosslinked caseinate and whey protein. In contrast to the steady decline after the initial peak in CCK response after the non-crosslinked caseinate, a biphasic CCK response following the whey protein was observed. A similar CCK response has been observed also previously after ingestion of whey protein alone (Bowen et al., 2006a) and in combination with casein (Bowen et al., 2006b). It is likely that this difference is due to the postprandial protein-specific effects on GE rate and digestion kinetics. It is well known that casein precipitates in the acidic stomach conditions, and after initial pepsin-induced hydrolysis it enters the small intestine slowly in the form of degraded peptides. On the other hand, whey protein leaves stomach rapidly as intact protein (Boirie et al., 1997). It has been suggested that the caseinomacropeptide (a peptide fragment of kappa-casein) is the first digested peptide of casein released from the stomach (Yvon et al., 1994; Ledoux et al., 1999), and in rats it was shown that caseinomacropeptide stimulated pancreatic secretion through CCK release more potently than whey protein (Pedersen et al., 2000). Furthermore, the caseinomacropeptide-poor whey protein used in this study and the difference in the physical form of the test products, i.e. the difference between high-viscous caseinate and low-viscous whey protein, may have also affected the difference in CCK response.

On the contrary, GLP-1 and PYY responses did not differ significantly between the non-crosslinked caseinate and whey proteins in *Study IV*, but a typical increase in GLP-1 concentration was observed after both of these proteins. However, it is possible that the number of participants in the study was too low to show significant difference in GLP-1 among the tested proteins due to the large interindividual variation in GLP-1 responses. Furthermore, it remains speculative if the presence of glucose or comparable carbohydrate source or fat could have affected the GLP-1 results, since they are also known to affect GLP-1 response. On the other hand, the typical increase in postprandial PYY response was not observed after any of the protein-based test products nor were there significant differences in PYY responses among the products. There is some evidence that different dietary proteins stimulate postprandial PYY release differently (Diepvens et al., 2008; Charlton et al., 2011) but there are only few studies, especially those utilising test products based exclusively on protein. Previously, it has been demonstrated that PYY is released in proportion to the energy content and macronutrient composition of the test meals (Adrian et al., 1985a; Degen et al., 2005), indicating that the larger the energy and dietary fat content of the meal is, the more PYY is released. Thus the fact that the test products contained only protein together with low and equal energy content (950 / 976 kJ), may partly explain the comparable PYY results observed in this study.

These temporal and quantitative differences observed in GI hormone release support again the previous notion that the secretion of these peptides is stimulated by different postprandial nutritional and physicochemical factors of the GI tract. Furthermore, a combination of certain ingredients in the test products may have combined and even unexpected effects on individual GI peptides as was shown in *Study I*, which demonstrates the complexity of the mechanisms involved in the regulation of the individual GI peptide responses. Moreover, the results show that one attribute of an ingredient mixture, e.g. viscosity induced by psyllium in *Study I*, can practically dominate the postprandial

metabolic and hormonal responses masking the possible but more subtle effects of the other ingredients.

Although earlier studies have demonstrated that protein content (Smeets et al., 2008; Hochstenbach-Waelen et al., 2009a; Veldhorst et al., 2009c; Veldhorst et al., 2009e) and in some cases protein type are potent determinants of short-term satiety (fullness/ reduced hunger) (Uhe et al., 1992; Hall et al., 2003; Veldhorst et al., 2009a; Pal and Ellis, 2010) and/or reduced energy intake (Hall et al., 2003; Anderson et al., 2004; Borzoei et al., 2006; Diepvens et al., 2008; Bertenshaw et al., 2009; Pal and Ellis, 2010), neither protein enrichment (*Study I*) nor protein type (*Study IV* and *V*) affected appetite ratings or *ad libitum* energy intake differently among the test products in the current studies. However, findings of the previous studies are still inconsistent, especially when subsequent energy intake is considered (Lang et al., 1998; Lang et al., 1999; Bowen et al., 2006b; Diepvens et al., 2008; Veldhorst et al., 2009c; Veldhorst et al., 2009e; Charlton et al., 2011). In *Study I*, the soy protein content may have been too low to exert marked responses in this study setting. Indeed, it may be that a considerable amount of protein (~ 40–50 g/single portion) is needed to elicit effects in appetite responses and/or energy intake (Uhe et al., 1992; Hall et al., 2003; Anderson and Moore, 2004; Bellissimo et al., 2008; Boelsma et al., 2010; Leidy and Racki, 2010; Pal and Ellis, 2010), but the feasibility of such doses in single foods remains limited.

Although in some earlier studies whey protein has been found to be more satiating than casein (Hall et al., 2003; Veldhorst et al., 2009a), others have found no difference (Bowen et al., 2006b; Lorenzen et al., 2012) or the results even were the opposite (Alfenas Rde et al., 2010; Abou-Samra et al., 2011; Acheson et al., 2011). The comparable satiety responses observed in *Studies IV* and *V* do not support that whey protein would be more satiating than casein. However, it has been suggested that the protein content of the test meal is the critical factor and that there is a bandwidth in protein quantity and concentrations where relatively more protein is more satiating and favours lower energy intake (Veldhorst et al., 2009a; Westerterp-Plantenga et al., 2009). Therefore, it is possible that the protein content in these studies was beyond the optimal bandwidth to show effects on satiety. Nevertheless, it is likely that these inconsistencies in the results on casein and whey proteins in the short-term studies are also affected by other variables, such as study design, study subjects, presence or absence and source of other nutrients and especially different physical properties of the used proteins. It should be noted that even within the same protein source several attributes can differ, such as hydrolysis or aggregation of the peptides (micelles) and purity of the isolates used in the test products which may also affect the results.

Taken together, dietary proteins, i.e. the amount and type of protein, have less pronounced effects on metabolic and GI peptide responses than DF even when high doses are used. It thus seems that DF, especially with distinctive characteristic like viscosity, affects postprandial physiology at relative low doses whereas dietary protein concentration can be increased considerably without marked postprandial effects. The effects of different protein types and/or amounts and concentrations on appetite sensations and short-term food intake are not obvious. However, in general the various methodological differences among different studies make it challenging to draw firm conclusions of the effects of different protein types and doses on appetite and energy intake.

6.2.3 Effects of structure modification on physiological responses, appetite and food intake

In Studies *III, IV* and *V* the effects of structural modifications of dietary fibre, protein and consequent food matrix on postprandial responses were investigated. Reduced viscosity in

Study III and protein structure modification which changed also the physical state of the test product (*Study IV*) affected postprandial metabolic and GI peptide responses. Specifically, a systematic increase in the hormonal responses was seen when test product viscosity was low (*Study III*) or when the solid protein-rich test product was changed into dispersion (*Study IV*). On the other hand, when only the primary protein structure but not the physical state of the test product was changed, no changes in the postprandial effects were detected (*Study V*).

In *Study III* the low-viscous beverage in which viscosity was reduced by depolymerization of beta-glucan, augmented practically all postprandial physiological responses including ghrelin, CCK, GLP-1 and PYY in comparison with the high-viscous beverage. Studies investigating the effect of viscosity *per se* on GI hormone release are still very limited which complicates the possibility to draw conclusions on the relationship between viscosity and GI peptide response. Even so, the augmented total ghrelin decline in *Study III* is in line with the results demonstrated by (Zijlstra et al., 2009b). They also observed a more pronounced decline in overall desacyl ghrelin response after a liquid milk-based product compared with a semi-solid product. In contrast, CCK, active ghrelin and GLP-1 responses were unaffected. These partly inconsistent results on GI peptides between these studies are probably due to the difference in the level of viscosity between the test products. Viscosity induced by beta-glucan in oat bran in *Study III* was higher as compared with the viscosity induced by the (different types of) starch in the study by (Zijlstra et al., 2009b). This difference could have affected the GE rate as well as digestion and absorption of nutrients in the small intestine differently. Therefore, as demonstrated in *Study III*, viscosity that was presumably high enough in the gastric and small intestine conditions was able to delay GE and subsequently attenuate GI peptide responses. Although the effect of viscosity on GE rate has been shown in earlier studies (Marciani et al., 2000; Marciani et al., 2001), in *Study III* both postprandial GE and GI peptide responses were measured, and the results suggests that GE is one of the possible mechanisms controlling the postprandial GI peptide release. However, it is equally possible that also the level of viscosity in the chyme during the intestinal phase (Dikeman et al., 2006) affected the GI peptide release by modulating the digestion rate and the contact of the nutrients with the enteroendocrine cells.

In *Studies IV* and *V*, the molecular structure of caseinate was changed by enzymatic crosslinking. However, due to the difference in protein concentration of the test products, liquid form of the test products was maintained in *Study V* whereas the higher caseinate concentration in *Study IV* resulted in solid gel test products. The difference in the physical form of the test products was reflected in the postprandial responses. Moreover, in *Study IV*, the solid crosslinked caseinate attenuated the postprandial glucose, insulin and CCK responses more than the high-viscous non-crosslinked caseinate at the beginning of the experimental period. The suppressed responses after the crosslinked caseinate are likely due to slower and reduced protein digestion and subsequent stimulation of CCK producing I-cells due to the more solid food form when compared with the non-crosslinked caseinate. It is also likely that the solid form of the crosslinked caseinate delayed GE rate more than non-crosslinked caseinate which contributed significantly to all the attenuated responses. Although the GLP-1 response was not significantly different among the caseinates, the responses were in the same direction as was observed with CCK, suggesting a possible effect of the physical state of the test products also on GLP-1 release. One previous study investigated the postprandial effects of dietary protein on GI peptide responses using solid and soup-like matrices (Martens et al., 2011), but no significant differences were detected in measured postprandial physiological responses including glucose, insulin and active

ghrelin response. Other food form-related studies, where mixed macronutrient meals were included, have shown inconsistent results on GI peptide responses. Solid food has been shown to stimulate CCK (Apolzan et al., 2011) and attenuate ghrelin response (Tieken et al., 2007) or no effects on GI peptide release has been observed, including CCK (Santangelo et al., 1998; Tieken et al., 2007; Leidy et al., 2010a), ghrelin and GLP-1 (Leidy et al., 2010a; Apolzan et al., 2011). These inconsistent results suggest that in addition to food form and the temporal nature of the food structure several other factors such as macronutrient and DF content as well as energy content and density are important determinants of GI peptide release.

Within the studies in this work the structure modification of DF (*Study III*) and protein (*Study IV*) was the factors that affected satiety/fullness ratings and subsequent energy intake significantly differently among the test products in each study. In *Study III* postprandial satiety and cumulative food intake (lunch + post lunch *ad libitum* food intake) increased after the low-viscous beverage when compared with the high-viscous beverage. A number of previous studies have investigated the effect of viscosity on appetite responses and energy intake. Increased viscosity induced by viscous fibres has been shown to enhance satiety/ fullness or decrease hunger and/or reduce acute energy intake in various studies (Wanders et al., 2011). The fact that satiety was more increased after the low-viscous than after the high-viscous beverage in the current study is in contrast with the majority of the previous findings. Although the reason for this finding remains unknown, it is possible that the lower viscosity which allowed rapid digestion and absorption of nutrients together with the depolymerized beta-glucan fractions and the insoluble part of DF in oat bran collectively resulted in increased satiety. Furthermore, in the case of the high-viscous beverage, the oat bran concentrate was added to the beverage bases just before consumption, and therefore the hydration of the beta-glucan may have continued also during the intestinal phase affecting the GI peptide responses and appetite sensations. The finding in *Study III* that energy intake at *ad libitum* meal three hours after the test beverage was not affected by the viscosity may be due to the fact that by that time the differences in postprandial metabolic responses had already disappeared, especially when a liquid matrix was used. Interestingly, cumulative energy, i.e. lunch and post lunch *ad libitum* food intake was greater after the low-viscous than after the high-viscous beverage which may indicate delayed effects on satiety through the actions of the soluble and partly fermentable beta-glucan during the transit through the lower parts of the GI tract (Delargy et al., 1997).

The effects of protein structure modification on appetite sensations and energy intake were investigated in *Studies IV* and *V*. In *Study IV* fullness was more increased after the solid crosslinked caseinate compared with the high-viscous non-crosslinked caseinate, whereas in *Study V* postprandial appetite ratings and energy intake were not affected by the structure modification in comparable food matrix. Although studies using solely protein based test products to investigate the role of the physical state of food on appetite ratings and acute food intake are very limited, two previous studies investigated the postprandial effects of dietary protein using solid-soup-like (Martens et al., 2011) and solid-liquid matrices (Martens and Westerterp-Plantenga, 2012). The results indicated that hunger was more decreased and fullness increased after the solid protein when compared with the soup-like or liquid meals, which supports the results observed in *Study IV*. Other studies with mixed macronutrient meals have shown that solid/semisolid foods increase satiety/fullness or decrease hunger (Haber et al., 1977; Hulshof et al., 1993; Tieken et al., 2007; Stull et al., 2008; Flood-Obbagy and Rolls, 2009; Leidy et al., 2010a; Apolzan et al., 2011; Leidy et al., 2011) and/or reduce acute food intake (Stull et al., 2008; Flood-Obbagy

and Rolls, 2009; Akhavan et al., 2011; Leidy et al., 2011) or subsequent caloric intake throughout the day (Tournier and Louis-Sylvestre, 1991; Mourao et al., 2007) more than liquid foods. Also no (Almiron-Roig et al., 2004) or opposite effects (Kissileff, 1985; Rolls et al., 1990; Chapelot and Payen, 2010) between solids and liquids on satiety response have been reported. In general it seems that liquids are less satiating than solid food forms (Mattes, 2006; Wolf et al., 2008; Pan and Hu, 2011). Consequently, liquids, whose cephalic phase responses are much smaller compared with solids, enter the body as inadequately detected and lead to weak satiety response and energy intake compensation (de Graaf, 2011). This indicates that inadequate sensory signalling undermines body's capacity to regulate energy intake at healthy levels due to the impairment of the congruent association between sensory signals and metabolic consequences (Wolf et al., 2008; de Graaf and Kok, 2010; Smeets et al., 2010). The results in *Studies IV* and *V* support the previous findings that solid food matrix enhances postprandial fullness compared with more liquid matrices, and when liquids with comparable macronutrient content and proteins with similar digestibility are used no differences are observed.

The effects of the structure modification on the outcome variables observed in the *Study III* and *IV* are novel findings, since no earlier human studies on GI hormone responses and appetite are available in which the effects of depolymerization of beta-glucan or enzymatic crosslinking of protein-based test products are studied. These findings are in line with previous studies showing that test products with varying physical state affect the postprandial responses. However, the effects are not solely dependent on the physical state of the test product, but the food structure and overall digestibility, i.e. the resistance to the digestive actions in the upper part of the GI tract, play a major role (Fardet, 2010). This was clearly shown in *Studies I, III* and *IV* where both metabolic and most of the GI peptide responses were attenuated after high-viscous (*Studies I* and *III*) and crosslinked test product (*Study IV*). Consequently, it is likely that in *Study V* the difference in viscosity between the caseinates (Solah et al., 2010) and the structure modification of the caseinate protein were not effective enough to modulate the following postprandial digestive actions, reflected in the similar metabolic and amino acid response after the crosslinked and non-crosslinked proteins.

In conclusion, these results clearly indicate that food-related attributes such as viscosity and physical state of food potently modulate short-term physiological responses and to less extent appetite sensations and energy intake. The attenuated glucose and insulin responses especially after high-viscous DF and solid form protein consumption may be considered beneficial, however the GI responses were also attenuated which may not be considered equally favourable. Even so, it is important to note that current knowledge of the role and the controlling factors of these peptides are still relatively limited. It is likely that in addition to macronutrients several other mechanisms such as chemosensory, energy sensing or energy level and microbiota related mechanisms exist to modulate the secretion of the GI peptides. There is also increasing evidence that the structure and physical state of food contribute to the secretory response of these peptides. Therefore, further studies are warranted to obtain a broader and more detailed insight into the complex system between foods or food ingredients and the metabolic and GI peptide response in general. A measurement of larger combination of multiple (bio)markers would clearly benefit the studies in this research area.

6.3 FUTURE PERSPECTIVES

Over the last few decades, the understanding of the appetite control has advanced remarkably. The wealth of data generated by recent research has revealed several fundamental mechanisms within and between the gut and the central nervous system controlling appetite and food intake (Wynne et al., 2005; Berthoud, 2008; Lenard and Berthoud, 2008). At the same time, the fact that the excess body weight is a plain consequence of disturbed energy balance, has enlarged to suggestions that disruptions in the controlling mechanisms, including homeostatic and hedonic systems, may result in chronic positive energy balance and thus overweight and/or obesity (Duca and Covasa, 2012).

In the context of globally escalating prevalence of overweight and obesity, the rationale for investigating the role of food as one of the means to alleviate the obesity problem is apparent and justified. As demonstrated in previous studies, various food properties are capable of modifying postprandial physiology and appetite to support energy balance. These include dietary fibre and protein as well as the structure and physical form of food (Howarth et al., 2001; Westerterp-Plantenga et al., 2009; de Graaf, 2011). However, due to the highly complex nature of appetite control, many GI functions and interactions between food properties and GI tract with respect to appetite control are still incompletely understood.

In this study, the aim was to elucidate the effect of selected dietary fibres, proteins and their structure modification in different food models on postprandial gastrointestinal physiology in relation to appetite. While the results of this study support the previous findings in general, the substudies of this thesis, especially *Studies III* and *IV* provided completely new findings about the possible mechanisms by which structural dietary attributes may modulate postprandial physiology and appetite. The key finding of this study was that both dietary fibre and protein can be used to increase the viscosity of gastrointestinal contents and that in turn will have an impact on gastric emptying, gastrointestinal hormone release and rates on digestion and uptake of nutrients. This in turn may provide potential health benefits for consumers in the form of foods designed for slower gastric emptying and digestion.

Future studies will undoubtedly provide more detailed insight into the complex mechanisms regulating appetite both in physiological and environmental level. The progress within the gut physiology has only recently discovered an elegant "taste" receptor system, i.e. "gut nutrient sensing", in the intestinal epithelium which already has been shown to control the GI hormone secretion (Kokrashvili et al., 2009; Gerspach et al., 2011; Rasoamanana et al., 2012) and likely contributes as a peripheral chemosensory system in the regulation of appetite. Furthermore, the recent observations on the remarkable endogenous changes after bariatric surgery have revealed a fresh insight into the appetite control.

Another interesting research area within appetite control lies in the CNS, in the mechanisms controlling food reward (hedonic response). Although it is clear that both homeostatic and hedonic systems modulate appetite, powerful hedonic signals can overcome physiological satiety signalling and result in excess energy intake (Berthoud et al., 2011a; Kenny, 2011). In this context, the recently introduced concept "reward homeostasis" suggests that also food-derived pleasure (hedonic reward) should be satisfied in order to facilitate body weight control (Bellisle et al., 2012).

Findings such as those indicated above will facilitate researchers to develop food-based strategies that utilize the capacity of homeostatic and hedonic systems to promote satiety, energy balance and overall health. However, the future challenge is to disclose the individual dietary components and/or synergistic combinations incorporated into the overall diet that support appetite control and optimal health in the long-term. To achieve this, a clearly improved understanding is needed on the relationship between the physicochemical and structural properties of food and the postprandial physiological processes (digestion, absorption) and responses (metabolism) in relation to appetite regulation. However, such advanced perspective requires a highly integrated approach involving various disciplines with *in vitro* and *in vivo* studies. Eventually, the information can be used to rationally engineer food components and matrices with designed functional behaviours in the body and ultimately combat the global health challenges, such as obesity, type 2 diabetes and cardiovascular diseases (McClements et al., 2009; Singh and Sarkar, 2011).

6.4 SUMMARY AND CONCLUDING REMARKS

The aim of this study was to investigate the role of selected dietary fibres and proteins and their structure modification on postprandial GI physiology and appetitive responses. Different food models varying in physical state were selected to examine specifically the effects of psyllium fibre and soy protein enrichment of vegetable patties (*Study I),* dietary fibre in oat and wheat bran included in porridge (*Study II*), the level of viscosity of oat bran-enriched beverages (*Study III*), sodium caseinate and whey protein (*Studies IV* and *V*) and enzymatically induced structure modification of sodium caseinate (*Studies IV* and *V*) on glucose, insulin and gastrointestinal peptide responses, gastric emptying, appetite sensations and short-term food intake in healthy normal-weight individuals.

In *Study I*, psyllium enrichment of solid test foods attenuated all the other metabolic and hormonal responses (i.e. glucose, insulin, ghrelin, GLP-1) except for PYY which in turn was increased after the fibre enrichment. At the same time, the effect of soy protein enrichment on these responses was less apparent, albeit when consumed together with psyllium fibre postprandial GLP-1 release was practically abolished. However, neither psyllium nor soy enrichment significantly affected postprandial hunger or satiety ratings or *ad libitum* food intake. In *Study II*, examining the postprandial effects of oat bran, wheat bran or combination of these in semisolid matrix, the oat bran rich in beta-glucan decreased postprandial plasma glucose and serum insulin responses, although GI peptide responses, appetite ratings or subsequent *ad libitum* food intake was not significantly different among the bran-enriched porridges. *Study III*, investigating the effects of viscosity, demonstrated that reduced natural viscosity of oat beta-glucan increased postprandial glycaemic and insulinaemic responses and accelerated GE. In addition, satiety and GI-originating ghrelin, CCK, GLP-1 and PYY responses were stimulated by the low-viscous beverage. On the other hand, cumulative energy intake was later increased after the low-viscous beverage compared with the high-viscous beverage. *Study IV* demonstrated that crosslinking of caseinate inducing the change of the food form from liquid to gel attenuated postprandial metabolic (i.e. glucose, insulin) and CCK responses, but did not significantly affect GLP-1 or PYY release. Furthermore, protein type affected CCK responses so that non-crosslinked caseinate stimulated CCK more than whey protein. Postprandial fullness was also more increased after crosslinked caseinate than after the non-crosslinked caseinate and low-viscous whey protein. *Study V*, investigating the effects of crosslinked caseinate in a

comparable physical food form, i.e. in beverage model, indicated that crosslinking without changing the food form had no significant effects on postprandial glucose or insulin responses, amino acid concentrations or on any of the appetite sensations when compared with the non-crosslinked caseinate.

The following conclusions can be made based on the results of the present study:
(1) Soluble dietary fibres modify postprandial physiology affecting metabolic and gastrointestinal peptide signals arising from the GI tract. The impact and magnitude of dietary fibre on these measures is likely to be attributable to the amount and type of fibre used in the test products, and the food matrix.
(2) Viscosity modulates postprandial metabolic and gastrointestinal peptide responses as well as satiety and *ad libitum* food intake implying the importance of structure of dietary fibre in the postprandial responses.
(3) In a meal context changes in dietary protein content seems to have less pronounced effects on metabolic and gastrointestinal peptide release than changes in dietary fibre content which depending on the fibre type might affect more prominently gastric emptying and GI peptide secretion.
(4) Crosslinking of caseinate modifies postprandial metabolic and gastrointestinal peptide responses when also the physical form of food is changed.
(5) The effects of dietary fibre, dietary protein and the physical form of food on appetite sensations and short-term food intake are complex and warrants further clarification both in terms of food composition and structure and their signaling in the gastrointestinal tract.

References

AACC, (2001). American Association of Cereal Chemists. The definition of dietary fiber. Report of the Dietary Fiber Definition Committee to the Board of Directors of the American Association of Cereal Chemists. *Cereal Foods World* 46, 112-126.

Abbott, C.R., Monteiro, M., Small, C.J., Sajedi, A., Smith, K.L., Parkinson, J.R., Ghatei, M.A. and Bloom, S.R. (2005). The inhibitory effects of peripheral administration of peptide YY(3-36) and glucagon-like peptide-1 on food intake are attenuated by ablation of the vagal-brainstem-hypothalamic pathway. *Brain Res* 1044, 127-131.

Abou-Samra, R., Keersmaekers, L., Brienza, D., Mukherjee, R. and Mace, K. (2011). Effect of different protein sources on satiation and short-term satiety when consumed as a starter. *Nutr J* 10, 139.

Acheson, K.J., Blondel-Lubrano, A., Oguey-Araymon, S., Beaumont, M., Emady-Azar, S., Ammon-Zufferey, C., Monnard, I., Pinaud, S., Nielsen-Moennoz, C. and Bovetto, L. (2011). Protein choices targeting thermogenesis and metabolism. *Am J Clin Nutr* 93, 525-534.

Adam, T.C. and Westerterp-Plantenga, M.S. (2005). Glucagon-like peptide-1 release and satiety after a nutrient challenge in normal-weight and obese subjects. *Br J Nutr* 93, 845-851.

Adrian, T.E., Ferri, G.L., Bacarese-Hamilton, A.J., Fuessl, H.S., Polak, J.M. and Bloom, S.R. (1985a). Human distribution and release of a putative new gut hormone, peptide YY. *Gastroenterology* 89, 1070-1077.

Adrian, T.E., Savage, A.P., Sagor, G.R., Allen, J.M., Bacarese-Hamilton, A.J., Tatemoto, K., Polak, J.M. and Bloom, S.R. (1985b). Effect of peptide YY on gastric, pancreatic, and biliary function in humans. *Gastroenterology* 89, 494-499.

Akhavan, T., Luhovyy, B.L. and Anderson, G.H. (2011). Effect of drinking compared with eating sugars or whey protein on short-term appetite and food intake. *Int J Obes (Lond)* 35, 562-569.

Akhavan, T., Luhovyy, B.L., Brown, P.H., Cho, C.E. and Anderson, G.H. (2010). Effect of premeal consumption of whey protein and its hydrolysate on food intake and postmeal glycemia and insulin responses in young adults. *Am J Clin Nutr* 91, 966-975.

Albertsson, P.A., Kohnke, R., Emek, S.C., Mei, J., Rehfeld, J.F., Akerlund, H.E. and Erlanson-Albertsson, C. (2007). Chloroplast membranes retard fat digestion and induce satiety: effect of biological membranes on pancreatic lipase/co-lipase. *Biochem J* 401, 727-733.

Alfenas Rde, C., Bressan, J. and Paiva, A.C. (2010). Effects of protein quality on appetite and energy metabolism in normal weight subjects. *Arq Bras Endocrinol Metabol* 54, 45-51.

Almiron-Roig, E., Flores, S.Y. and Drewnowski, A. (2004). No difference in satiety or in subsequent energy intakes between a beverage and a solid food. *Physiol Behav* 82, 671-677.

Altorf-van der Kuil, W., Engberink, M.F., Brink, E.J., van Baak, M.A., Bakker, S.J., Navis, G., van 't Veer, P. and Geleijnse, J.M. (2010). Dietary protein and blood pressure: a systematic review. *PLoS One* 5, e12102.

Anderson, G.H. and Moore, S.E. (2004). Dietary proteins in the regulation of food intake and body weight in humans. *J Nutr* 134, 974S-979S.

Anderson, G.H., Tecimer, S.N., Shah, D. and Zafar, T.A. (2004). Protein source, quantity, and time of consumption determine the effect of proteins on short-term food intake in young men. *J Nutr* 134, 3011-3015.

Anderson, G.H. and Woodend, D. (2003). Effect of glycemic carbohydrates on short-term satiety and food intake. *Nutr Rev* 61, S17-26.

Anderson, J.W., Baird, P., Davis, R.H.,Jr, Ferreri, S., Knudtson, M., Koraym, A., Waters, V. and Williams, C.L. (2009). Health benefits of dietary fiber. *Nutr Rev* 67, 188-205.

Apolzan, J.W., Leidy, H.J., Mattes, R.D. and Campbell, W.W. (2011). Effects of food form on food intake and postprandial appetite sensations, glucose and endocrine responses, and energy expenditure in resistance trained v. sedentary older adults. *Br J Nutr* 106, 1107-1116.

Arosio, M., Ronchi, C.L., Beck-Peccoz, P., Gebbia, C., Giavoli, C., Cappiello, V., Conte, D. and Peracchi, M. (2004). Effects of modified sham feeding on ghrelin levels in healthy human subjects. *J Clin Endocrinol Metab* 89, 5101-5104.

Arvaniti, K., Richard, D. and Tremblay, A. (2000). Reproducibility of energy and macronutrient intake and related substrate oxidation rates in a buffet-type meal. *Br J Nutr* 83, 489-495.

Astbury, N.M., Stevenson, E.J., Morris, P., Taylor, M.A. and Macdonald, I.A. (2010). Dose-response effect of a whey protein preload on within-day energy intake in lean subjects. *Br J Nutr* 104, 1858-1867.

Aston, L.M., Stokes, C.S. and Jebb, S.A. (2008). No effect of a diet with a reduced glycaemic index on satiety, energy intake and body weight in overweight and obese women. *Int J Obes (Lond)* 32, 160-165.

Badman, M.K. and Flier, J.S. (2005). The gut and energy balance: visceral allies in the obesity wars. *Science* 307, 1909-1914.

Baggio, L.L. and Drucker, D.J. (2007). Biology of incretins: GLP-1 and GIP. *Gastroenterology* 132, 2131-2157.

Baggio, L.L., Huang, Q., Brown, T.J. and Drucker, D.J. (2004). Oxyntomodulin and glucagon-like peptide-1 differentially regulate murine food intake and energy expenditure. *Gastroenterology* 127, 546-558.

Ballantyne, G.H. (2006). Peptide YY(1-36) and peptide YY(3-36): Part I. Distribution, release and actions. *Obes Surg* 16, 651-658.

Barone Lumaga, R., Azzali, D., Fogliano, V., Scalfi, L. and Vitaglione, P. (2012). Sugar and dietary fibre composition influence, by different hormonal response, the satiating capacity of a fruit-based and a β-glucan-enriched beverage. *Food Funct* 3, 67-75.

Batterham, R.L., Cohen, M.A., Ellis, S.M., Le Roux, C.W., Withers, D.J., Frost, G.S., Ghatei, M.A. and Bloom, S.R. (2003). Inhibition of food intake in obese subjects by peptide YY3-36. *N Engl J Med* 349, 941-948.

Batterham, R.L., Cowley, M.A., Small, C.J., Herzog, H., Cohen, M.A., Dakin, C.L., Wren, A.M., Brynes, A.E., Low, M.J., Ghatei, M.A., et al. (2002). Gut hormone PYY(3-36) physiologically inhibits food intake. *Nature* 418, 650-654.

Batterham, R.L., Heffron, H., Kapoor, S., Chivers, J.E., Chandarana, K., Herzog, H., Le Roux, C.W., Thomas, E.L., Bell, J.D. and Withers, D.J. (2006). Critical role for peptide YY in protein-mediated satiation and body-weight regulation. *Cell Metab* 4, 223-233.

Beck, E.J., Tapsell, L.C., Batterham, M.J., Tosh, S.M. and Huang, X.F. (2009a). Increases in peptide Y-Y levels following oat beta-glucan ingestion are dose-dependent in overweight adults. *Nutr Res* 29, 705-709.

Beck, E.J., Tosh, S.M., Batterham, M.J., Tapsell, L.C. and Huang, X.F. (2009b). Oat beta-glucan increases postprandial cholecystokinin levels, decreases insulin response and extends subjective satiety in overweight subjects. *Mol Nutr Food Res* 53, 1343-1351.

Beglinger, C., Degen, L., Matzinger, D., D'Amato, M. and Drewe, J. (2001). Loxiglumide, a CCK-A receptor antagonist, stimulates calorie intake and hunger feelings in humans. *Am J Physiol Regul Integr Comp Physiol* 280, R1149-1154.

Beglinger, S., Drewe, J., Schirra, J., Goke, B., D'Amato, M. and Beglinger, C. (2010). Role of fat hydrolysis in regulating glucagon-like Peptide-1 secretion. *J Clin Endocrinol Metab* 95, 879-886.

Bell, E.A., Roe, L.S. and Rolls, B.J. (2003). Sensory-specific satiety is affected more by volume than by energy content of a liquid food. *Physiol Behav* 78, 593-600.

Bell, E.A. and Rolls, B.J. (2001). Energy density of foods affects energy intake across multiple levels of fat content in lean and obese women. *Am J Clin Nutr* 73, 1010-1018.

Bellisle, F., Drewnowski, A., Anderson, G.H., Westerterp-Plantenga, M. and Martin, C.K. (2012). Sweetness, satiation, and satiety. *J Nutr* 142, 1149S-1154S.

Bellissimo, N., Desantadina, M.V., Pencharz, P.B., Berall, G.B., Thomas, S.G. and Anderson, G.H. (2008). A comparison of short-term appetite and energy intakes in normal weight and obese boys following glucose and whey-protein drinks. *Int J Obes (Lond)* 32, 362-371.

Benini, L., Castellani, G., Brighenti, F., Heaton, K.W., Brentegani, M.T., Casiraghi, M.C., Sembenini, C., Pellegrini, N., Fioretta, A. and Minniti, G. (1995). Gastric emptying of a solid meal is accelerated by the removal of dietary fibre naturally present in food. *Gut* 36, 825-830.

Berglund, M.M., Hipskind, P.A. and Gehlert, D.R. (2003). Recent developments in our understanding of the physiological role of PP-fold peptide receptor subtypes. *Exp Biol Med (Maywood)* 228, 217-244.

Bergmann, J.F., Chassany, O., Petit, A., Triki, R., Caulin, C. and Segrestaa, J.M. (1992). Correlation between echographic gastric emptying and appetite: influence of psyllium. *Gut* 33, 1042-1043.

Bertenshaw, E.J., Lluch, A. and Yeomans, M.R. (2008). Satiating effects of protein but not carbohydrate consumed in a between-meal beverage context. *Physiol Behav* 93, 427-436.

Bertenshaw, E.J., Lluch, A. and Yeomans, M.R. (2009). Dose-dependent effects of beverage protein content upon short-term intake. *Appetite* 52, 580-587.

Berthoud, H.R. (2004). Mind versus metabolism in the control of food intake and energy balance. *Physiol Behav* 81, 781-793.

Berthoud, H.R. (2008). Vagal and hormonal gut-brain communication: from satiation to satisfaction. *Neurogastroenterol Motil* 20 Suppl 1, 64-72.

Berthoud, H.R., Lenard, N.R. and Shin, A.C. (2011a). Food reward, hyperphagia, and obesity. *Am J Physiol Regul Integr Comp Physiol* 300, R1266-1277.

Berthoud, H.R., Shin, A.C. and Zheng, H. (2011b). Obesity surgery and gut-brain communication. *Physiol Behav* 105, 106-119.

Bi, S., Ladenheim, E.E., Schwartz, G.J. and Moran, T.H. (2001). A role for NPY overexpression in the dorsomedial hypothalamus in hyperphagia and obesity of OLETF rats. *Am J Physiol Regul Integr Comp Physiol* 281, R254-260.

Bjorck, I., Granfeldt, Y., Liljeberg, H., Tovar, J. and Asp, N.G. (1994). Food properties affecting the digestion and absorption of carbohydrates. *Am J Clin Nutr* 59, 699S-705S.

Blatt, A.D., Roe, L.S. and Rolls, B.J. (2011). Increasing the protein content of meals and its effect on daily energy intake. *J Am Diet Assoc* 111, 290-294.

Blom, W.A., Lluch, A., Stafleu, A., Vinoy, S., Holst, J.J., Schaafsma, G. and Hendriks, H.F. (2006a). Effect of a high-protein breakfast on the postprandial ghrelin response. *Am J Clin Nutr* 83, 211-220.

Blom, W.A., Lluch, A., Vinoy, S., Stafleu, A., van den Berg, R., Holst, J.J., Kok, F.J. and Hendriks, H.F. (2006b). Effects of gastric emptying on the postprandial ghrelin response. *Am J Physiol Endocrinol Metab* 290, E389-395.

Blom, W.A., Stafleu, A., de Graaf, C., Kok, F.J., Schaafsma, G. and Hendriks, H.F. (2005). Ghrelin response to carbohydrate-enriched breakfast is related to insulin. *Am J Clin Nutr* 81, 367-375.

Blundell, J., de Graaf, C., Hulshof, T., Jebb, S., Livingstone, B., Lluch, A., Mela, D., Salah, S., Schuring, E., van der Knaap, H., et al. (2010). Appetite control: methodological aspects of the evaluation of foods. *Obes Rev* 11, 251-270.

Blundell, J.E., Stubbs, R.J., Golding, C., Croden, F., Alam, R., Whybrow, S., Le Noury, J. and Lawton, C.L. (2005). Resistance and susceptibility to weight gain: individual variability in response to a high-fat diet. *Physiol Behav* 86, 614-622.

Boelsma, E., Brink, E.J., Stafleu, A. and Hendriks, H.F. (2010). Measures of postprandial wellness after single intake of two protein-carbohydrate meals. *Appetite* 54, 456-464.

Boirie, Y., Dangin, M., Gachon, P., Vasson, M.P., Maubois, J.L. and Beaufrere, B. (1997). Slow and fast dietary proteins differently modulate postprandial protein accretion. *Proc Natl Acad Sci U S A* 94, 14930-14935.

Bolton, R.P., Heaton, K.W. and Burroughs, L.F. (1981). The role of dietary fiber in satiety, glucose, and insulin: studies with fruit and fruit juice. *Am J Clin Nutr* 34, 211-217.

Bonjour, J.P. (2005). Dietary protein: an essential nutrient for bone health. *J Am Coll Nutr* 24, 526S-536S.

Booth, D.A. (1985). Food-conditioned eating preferences and aversions with interoceptive elements: conditioned appetites and satieties. *Ann N Y Acad Sci* 443, 22-41.

Bornet, F.R., Jardy-Gennetier, A.E., Jacquet, N. and Stowell, J. (2007). Glycaemic response to foods: impact on satiety and long-term weight regulation. *Appetite* 49, 535-553.

Borzoei, S., Neovius, M., Barkeling, B., Teixeira-Pinto, A. and Rossner, S. (2006). A comparison of effects of fish and beef protein on satiety in normal weight men. *Eur J Clin Nutr* 60, 897-902.

Bourdon, I., Olson, B., Backus, R., Richter, B.D., Davis, P.A. and Schneeman, B.O. (2001). Beans, as a source of dietary fiber, increase cholecystokinin and apolipoprotein b48 response to test meals in men. *J Nutr* 131, 1485-1490.

Bourdon, I., Yokoyama, W., Davis, P., Hudson, C., Backus, R., Richter, D., Knuckles, B. and Schneeman, B.O. (1999). Postprandial lipid, glucose, insulin, and cholecystokinin responses in men fed barley pasta enriched with beta-glucan. *Am J Clin Nutr* 69, 55-63.

Bowen, J., Noakes, M. and Clifton, P.M. (2006a). Appetite regulatory hormone responses to various dietary proteins differ by body mass index status despite similar reductions in ad libitum energy intake. *J Clin Endocrinol Metab* 91, 2913-2919.

Bowen, J., Noakes, M., Trenerry, C. and Clifton, P.M. (2006b). Energy intake, ghrelin, and cholecystokinin after different carbohydrate and protein preloads in overweight men. *J Clin Endocrinol Metab* 91, 1477-1483.

Braaten, J.T., Wood, P.J., Scott, F.W., Riedel, K.D., Poste, L.M. and Collins, M.W. (1991). Oat gum lowers glucose and insulin after an oral glucose load. *Am J Clin Nutr* 53, 1425-1430.

Braden, B., Lembcke, B., Kuker, W. and Caspary, W.F. (2007). 13C-breath tests: current state of the art and future directions. *Dig Liver Dis* 39, 795-805.

Brand-Miller, J.C., Holt, S.H., Pawlak, D.B. and McMillan, J. (2002). Glycemic index and obesity. *Am J Clin Nutr* 76, 281S-285S.

Bray, G.A., Paeratakul, S. and Popkin, B.M. (2004). Dietary fat and obesity: a review of animal, clinical and epidemiological studies. *Physiol Behav* 83, 549-555.

Brennan, I.M., Otto, B., Feltrin, K.L., Meyer, J.H., Horowitz, M. and Feinle-Bisset, C. (2007). Intravenous CCK-8, but not GLP-1, suppresses ghrelin and stimulates PYY release in healthy men. *Peptides* 28, 607-611.

Broglio, F., Gottero, C., Prodam, F., Destefanis, S., Gauna, C., Me, E., Riganti, F., Vivenza, D., Rapa, A., Martina, V., et al. (2004). Ghrelin secretion is inhibited by glucose load and insulin-induced hypoglycaemia but unaffected by glucagon and arginine in humans. *Clin Endocrinol (Oxf)* 61, 503-509.

Brunstrom, J.M. (2011). The control of meal size in human subjects: a role for expected satiety, expected satiation and premeal planning. *Proc Nutr Soc* 70, 155-161.

Brunstrom, J.M., Brown, S., Hinton, E.C., Rogers, P.J. and Fay, S.H. (2011). 'Expected satiety' changes hunger and fullness in the inter-meal interval. *Appetite* 56, 310-315.

Brunstrom, J.M., Shakeshaft, N.G. and Alexander, E. (2010). Familiarity changes expectations about fullness. *Appetite* 54, 587-590.

Brunstrom, J.M., Shakeshaft, N.G. and Scott-Samuel, N.E. (2008). Measuring 'expected satiety' in a range of common foods using a method of constant stimuli. *Appetite* 51, 604-614.

Brynes, A.E., Frost, G.S., Edwards, C.M., Ghatei, M.A. and Bloom, S.R. (1998). Plasma glucagon-like peptide-1 (7-36) amide (GLP-1) response to liquid phase, solid phase, and meals of differing lipid composition. *Nutrition* 14, 433-436.

Burley, V.J., Leeds, A.R. and Blundell, J.E. (1987). The effect of high and low-fibre breakfasts on hunger, satiety and food intake in a subsequent meal. *Int J Obes* 11 Suppl 1, 87-93.

Burton-Freeman, B. (2000). Dietary fiber and energy regulation. *J Nutr* 130, 272S-275S.

Burton-Freeman, B. (2005). Sex and cognitive dietary restraint influence cholecystokinin release and satiety in response to preloads varying in fatty acid composition and content. *J Nutr* 135, 1407-1414.

Burton-Freeman, B., Davis, P.A. and Schneeman, B.O. (2002). Plasma cholecystokinin is associated with subjective measures of satiety in women. *Am J Clin Nutr* 76, 659-667.

Calame, W., Thomassen, F., Hull, S., Viebke, C. and Siemensma, A.D. (2011). Evaluation of satiety enhancement, including compensation, by blends of gum arabic. A methodological approach. *Appetite* 57, 358-64.

Calbet, J.A. and Holst, J.J. (2004). Gastric emptying, gastric secretion and enterogastrone response after administration of milk proteins or their peptide hydrolysates in humans. *Eur J Nutr* 43, 127-139.

Callahan, H.S., Cummings, D.E., Pepe, M.S., Breen, P.A., Matthys, C.C. and Weigle, D.S. (2004). Postprandial suppression of plasma ghrelin level is proportional to ingested caloric load but does not predict intermeal interval in humans. *J Clin Endocrinol Metab* 89, 1319-1324.

Camilleri, M., Malagelada, J.R., Brown, M.L., Becker, G. and Zinsmeister, A.R. (1985). Relation between antral motility and gastric emptying of solids and liquids in humans. *Am J Physiol* 249, G580-585.

Campfield, L.A. and Smith, F.J. (2003). Blood glucose dynamics and control of meal initiation: a pattern detection and recognition theory. *Physiol Rev* 83, 25-58.

Carbonnel, F., Lemann, M., Rambaud, J.C., Mundler, O. and Jian, R. (1994). Effect of the energy density of a solid-liquid meal on gastric emptying and satiety. *Am J Clin Nutr* 60, 307-311.

Castaneda, T.R., Tong, J., Datta, R., Culler, M. and Tschop, M.H. (2010). Ghrelin in the regulation of body weight and metabolism. *Front Neuroendocrinol* 31, 44-60.

Cecil, J.E., Francis, J. and Read, N.W. (1998). Relative contributions of intestinal, gastric, oro-sensory influences and information to changes in appetite induced by the same liquid meal. *Appetite* 31, 377-390.

Cecil, J.E., Francis, J. and Read, N.W. (1999). Comparison of the effects of a high-fat and high-carbohydrate soup delivered orally and intragastrically on gastric emptying, appetite, and eating behaviour. *Physiol Behav* 67, 299-306.

Chan, J.L., Stoyneva, V., Kelesidis, T., Raciti, P. and Mantzoros, C.S. (2006). Peptide YY levels are decreased by fasting and elevated following caloric intake but are not regulated by leptin. *Diabetologia* 49, 169-173.

Chandarana, K., Drew, M.E., Emmanuel, J., Karra, E., Gelegen, C., Chan, P., Cron, N.J. and Batterham, R.L. (2009). Subject standardization, acclimatization, and sample processing affect gut hormone levels and appetite in humans. *Gastroenterology* 136, 2115-2126.

Chapelot, D. and Payen, F. (2010). Comparison of the effects of a liquid yogurt and chocolate bars on satiety: a multidimensional approach. *Br J Nutr* 103, 760-767.

Charlton, K.E., Tapsell, L.C., Batterham, M.J., Thorne, R., O'Shea, J., Zhang, Q. and Beck, E.J. (2011). Pork, beef and chicken have similar effects on acute satiety and hormonal markers of appetite. *Appetite* 56, 1-8.

Chaudhri, O., Small, C. and Bloom, S. (2006). Gastrointestinal hormones regulating appetite. *Philos Trans R Soc Lond B Biol Sci* 361, 1187-1209.

Chen, C.Y., Asakawa, A., Fujimiya, M., Lee, S.D. and Inui, A. (2009). Ghrelin gene products and the regulation of food intake and gut motility. *Pharmacol Rev* 61, 430-481.

Codex, (2009). FAO/WHO Codex Alimentarius Commission. *Report of the 30th session of the Codex Committee on nutrition and foods for special dietary uses.* ALINORM 09/32/26. [online] Available at: <https://www.ccnfsdu.de/fileadmin/ user_upload/ PDF/2008/ al32_ 26e.pdf> [Accessed 5 September 2012]

Collier, G. and O'Dea, K. (1982). Effect of physical form of carbohydrate on the postprandial glucose, insulin, and gastric inhibitory polypeptide responses in type 2 diabetes. *Am J Clin Nutr* 36, 10-14.

Conlon, J.M. (2002). The origin and evolution of peptide YY (PYY) and pancreatic polypeptide (PP). *Peptides* 23, 269-278.

Cordain, L., Eaton, S.B., Sebastian, A., Mann, N., Lindeberg, S., Watkins, B.A., O'Keefe, J.H. and Brand-Miller, J. (2005). Origins and evolution of the Western diet: health implications for the 21st century. *Am J Clin Nutr* 81, 341-354.

Cornell, C.E., Rodin, J. and Weingarten, H. (1989). Stimulus-induced eating when satiated. *Physiol Behav* 45, 695-704.

Cox, H.M. (2007). Peptide YY: a neuroendocrine neighbor of note. *Peptides* 28, 345-351.

Crapo, P.A. and Henry, R.R. (1988). Postprandial metabolic responses to the influence of food form. *Am J Clin Nutr* 48, 560-564.

Creutzfeldt, W., Ebert, R., Willms, B., Frerichs, H. and Brown, J.C. (1978). Gastric inhibitory polypeptide (GIP) and insulin in obesity: increased response to stimulation and defective feedback control of serum levels. *Diabetologia* 14, 15-24.

Cummings, D.E. (2006). Ghrelin and the short- and long-term regulation of appetite and body weight. *Physiol Behav* 89, 71-84.

Cummings, D.E., Foster-Schubert, K.E. and Overduin, J. (2005). Ghrelin and energy balance: focus on current controversies. *Curr Drug Targets* 6, 153-169.

Cummings, D.E. and Overduin, J. (2007). Gastrointestinal regulation of food intake. *J Clin Invest* 117, 13-23.

Cummings, D.E., Purnell, J.Q., Frayo, R.S., Schmidova, K., Wisse, B.E. and Weigle, D.S. (2001). A preprandial rise in plasma ghrelin levels suggests a role in meal initiation in humans. *Diabetes* 50, 1714-1719.

Cummings, J.H. and Stephen, A.M. (2007). Carbohydrate terminology and classification. *Eur J Clin Nutr* 61 Suppl 1, S5-18.

Darwiche, G., Bjorgell, O. and Almer, L.O. (2003). The addition of locust bean gum but not water delayed the gastric emptying rate of a nutrient semisolid meal in healthy subjects. *BMC Gastroenterol* 3, 12.

de Castro, J.M. and Elmore, D.K. (1988). Subjective hunger relationships with meal patterns in the spontaneous feeding behavior of humans: evidence for a causal connection. *Physiol Behav* 43, 159-165.

de Graaf, C. (2011). Why liquid energy results in overconsumption. *Proc Nutr Soc* 70, 162-170.

de Graaf, C., Blom, W.A., Smeets, P.A., Stafleu, A. and Hendriks, H.F. (2004). Biomarkers of satiation and satiety. *Am J Clin Nutr* 79, 946-961.

de Graaf, C. and Hulshof, T. (1996). Effects of weight and energy content of preloads on subsequent appetite and food intake. *Appetite* 26, 139-151.

de Graaf, C. and Kok, F.J. (2010). Slow food, fast food and the control of food intake. *Nat Rev Endocrinol* 6, 290-293.

de Graaf, C., Schreurs, A. and Blauw, Y.H. (1993). Short-term effects of different amounts of sweet and nonsweet carbohydrates on satiety and energy intake. *Physiol Behav* 54, 833-843.

Deacon, C.F. (2004). Circulation and degradation of GIP and GLP-1. *Horm Metab Res* 36, 761-765.

Deacon, C.F., Johnsen, A.H. and Holst, J.J. (1995). Degradation of glucagon-like peptide-1 by human plasma in vitro yields an N-terminally truncated peptide that is a major endogenous metabolite in vivo. *J Clin Endocrinol Metab* 80, 952-957.

Degen, L., Drewe, J., Piccoli, F., Grani, K., Oesch, S., Bunea, R., D'Amato, M. and Beglinger, C. (2007). Effect of CCK-1 receptor blockade on ghrelin and PYY secretion in men. *Am J Physiol Regul Integr Comp Physiol* 292, R1391-1399.

Degen, L., Oesch, S., Casanova, M., Graf, S., Ketterer, S., Drewe, J. and Beglinger, C. (2005). Effect of peptide YY3-36 on food intake in humans. *Gastroenterology* 129, 1430-1436.

Delargy, H.J., Burley, V.J., O'Sullivan, K.R., Fletcher, R.J. and Blundell, J.E. (1995). Effects of different soluble: insoluble fibre ratios at breakfast on 24-h pattern of dietary intake and satiety. *Eur J Clin Nutr* 49, 754-766.

Delargy, H.J., O'Sullivan, K.R., Fletcher, R.J. and Blundell, J.E. (1997). Effects of amount and type of dietary fibre (soluble and insoluble) on short-term control of appetite. *Int J Food Sci Nutr* 48, 67-77.

Delzenne, N., Blundell, J., Brouns, F., Cunningham, K., De Graaf, K., Erkner, A., Lluch, A., Mars, M., Peters, H.P. and Westerterp-Plantenga, M. (2010). Gastrointestinal targets of appetite regulation in humans. *Obes Rev* 11, 234-250.

Di Lorenzo, C., Williams, C.M., Hajnal, F. and Valenzuela, J.E. (1988). Pectin delays gastric emptying and increases satiety in obese subjects. *Gastroenterology* 95, 1211-1215.

Diepvens, K., Haberer, D. and Westerterp-Plantenga, M. (2008). Different proteins and biopeptides differently affect satiety and anorexigenic/orexigenic hormones in healthy humans. *Int J Obes (Lond)* 32, 510-518.

Dikeman, C.L. and Fahey, G.C. (2006). Viscosity as related to dietary fiber: a review. *Crit Rev Food Sci Nutr* 46, 649-663.

Dikeman, C.L., Murphy, M.R. and Fahey, G.C.,Jr. (2006). Dietary fibers affect viscosity of solutions and simulated human gastric and small intestinal digesta. *J Nutr* 136, 913-919.

DiMeglio, D.P. and Mattes, R.D. (2000). Liquid versus solid carbohydrate: effects on food intake and body weight. *Int J Obes Relat Metab Disord* 24, 794-800.

Dove, E.R., Hodgson, J.M., Puddey, I.B., Beilin, L.J., Lee, Y.P. and Mori, T.A. (2009). Skim milk compared with a fruit drink acutely reduces appetite and energy intake in overweight men and women. *Am J Clin Nutr* 90, 70-75.

Drazen, D.L., Vahl, T.P., D'Alessio, D.A., Seeley, R.J. and Woods, S.C. (2006). Effects of a fixed meal pattern on ghrelin secretion: evidence for a learned response independent of nutrient status. *Endocrinology* 147, 23-30.

Drewnowski, A., Almiron-Roig, E., Marmonier, C. and Lluch, A. (2004). Dietary energy density and body weight: is there a relationship? *Nutr Rev* 62, 403-413.

Drucker, D.J. and Asa, S. (1988). Glucagon gene expression in vertebrate brain. *J Biol Chem* 263, 13475-13478.

Duca, F.A. and Covasa, M. (2012). Current and emerging concepts on the role of peripheral signals in the control of food intake and development of obesity. *Br J Nutr* , 1-16.

Eaton, S.B. (2006). The ancestral human diet: what was it and should it be a paradigm for contemporary nutrition? *Proc Nutr Soc* 65, 1-6.

Eaton, S.B. and Konner, M. (1985). Paleolithic nutrition. A consideration of its nature and current implications. *N Engl J Med* 312, 283-289.

Eaton, S.B., Konner, M. and Shostak, M. (1988). Stone agers in the fast lane: chronic degenerative diseases in evolutionary perspective. *Am J Med* 84, 739-749.

Eberlein, G.A., Eysselein, V.E., Schaeffer, M., Layer, P., Grandt, D., Goebell, H., Niebel, W., Davis, M., Lee, T.D. and Shively, J.E. (1989). A new molecular form of PYY: structural characterization of human PYY(3-36) and PYY(1-36). *Peptides* 10, 797-803.

El Khoury, D., Cuda, C., Luhovyy, B.L. and Anderson, G.H. (2012). Beta glucan: health benefits in obesity and metabolic syndrome. *J Nutr Metab* 2012, 851362.

El Khoury, D., El-Rassi, R., Azar, S. and Hwalla, N. (2010). Postprandial ghrelin and PYY responses of male subjects on low carbohydrate meals to varied balancing proportions of proteins and fats. *Eur J Nutr* 49, 493-500.

Elia, M. and Cummings, J.H. (2007). Physiological aspects of energy metabolism and gastrointestinal effects of carbohydrates. *Eur J Clin Nutr* 61 Suppl 1, S40-74.

Elliott, R.M., Morgan, L.M., Tredger, J.A., Deacon, S., Wright, J. and Marks, V. (1993). Glucagon-like peptide-1 (7-36)amide and glucose-dependent insulinotropic polypeptide secretion in response to nutrient ingestion in man: acute post-prandial and 24-h secretion patterns. *J Endocrinol* 138, 159-166.

Ello-Martin, J.A., Ledikwe, J.H. and Rolls, B.J. (2005). The influence of food portion size and energy density on energy intake: implications for weight management. *Am J Clin Nutr* 82, 236S-241S.

English, P.J., Ghatei, M.A., Malik, I.A., Bloom, S.R. and Wilding, J.P. (2002). Food fails to suppress ghrelin levels in obese humans. *J Clin Endocrinol Metab* 87, 2984.

Englyst, K.N., Liu, S. and Englyst, H.N. (2007). Nutritional characterization and measurement of dietary carbohydrates. *Eur J Clin Nutr* 61 Suppl 1, S19-39.

Ercili Cura, D., Lille, M., Partanen, R., Kruus, K., Buchert, J. and Lantto, R. (2010). Effect of *Trichoderma reesei* tyrosinase on rheology and microstructure of acidified milk gels. *Int Dairy J* 20, 830-837.

Erdmann, J., Leibl, M., Wagenpfeil, S., Lippl, F. and Schusdziarra, V. (2006). Ghrelin response to protein and carbohydrate meals in relation to food intake and glycerol levels in obese subjects. *Regul Pept* 135, 23-29.

Erdmann, J., Lippl, F. and Schusdziarra, V. (2003). Differential effect of protein and fat on plasma ghrelin levels in man. *Regul Pept* 116, 101-107.

Erdmann, J., Topsch, R., Lippl, F., Gussmann, P. and Schusdziarra, V. (2004). Postprandial response of plasma ghrelin levels to various test meals in relation to food intake, plasma insulin, and glucose. *J Clin Endocrinol Metab* 89, 3048-3054.

Essah, P.A., Levy, J.R., Sistrun, S.N., Kelly, S.M. and Nestler, J.E. (2007). Effect of macronutrient composition on postprandial peptide YY levels. *J Clin Endocrinol Metab* 92, 4052-4055.

EU, (2008). European Union. Comission directive 2008/100/EC.OffJEU.2008;L285:9–12. [online] Available at: <http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri= OJ:L:2008:285: 0009:0012:EN:PDF> [Accessed 5 September 2012]

Fardet, A. (2010). New hypotheses for the health-protective mechanisms of whole-grain cereals: what is beyond fibre? *Nutr Res Rev* 23, 65-134.

Feinle, C., O'Donovan, D., Doran, S., Andrews, J.M., Wishart, J., Chapman, I. and Horowitz, M. (2003). Effects of fat digestion on appetite, APD motility, and gut hormones in response to duodenal fat infusion in humans. *Am J Physiol Gastrointest Liver Physiol* 284, G798-807.

Feinle-Bisset, C., Patterson, M., Ghatei, M.A., Bloom, S.R. and Horowitz, M. (2005). Fat digestion is required for suppression of ghrelin and stimulation of peptide YY and pancreatic polypeptide secretion by intraduodenal lipid. *Am J Physiol Endocrinol Metab* 289, E948-53.

Feltrin, K.L., Little, T.J., Meyer, J.H., Horowitz, M., Rades, T., Wishart, J. and Feinle-Bisset, C. (2007). Effects of lauric acid on upper gut motility, plasma cholecystokinin and peptide YY, and energy intake are load, but not concentration, dependent in humans. *J Physiol* 581, 767-777.

Feltrin, K.L., Little, T.J., Meyer, J.H., Horowitz, M., Smout, A.J., Wishart, J., Pilichiewicz, A.N., Rades, T., Chapman, I.M. and Feinle-Bisset, C. (2004). Effects of intraduodenal fatty acids on appetite, antropyloroduodenal motility, and plasma CCK and GLP-1 in humans vary with their chain length. *Am J Physiol Regul Integr Comp Physiol* 287, R524-533.

Feltrin, K.L., Patterson, M., Ghatei, M.A., Bloom, S.R., Meyer, J.H., Horowitz, M. and Feinle-Bisset, C. (2006). Effect of fatty acid chain length on suppression of ghrelin and stimulation of PYY, GLP-2 and PP secretion in healthy men. *Peptides* 27, 1638-1643.

Field, B.C., Chaudhri, O.B. and Bloom, S.R. (2010). Bowels control brain: gut hormones and obesity. *Nat Rev Endocrinol* 6, 444-453.

Finucane, M.M., Stevens, G.A., Cowan, M.J., Danaei, G., Lin, J.K., Paciorek, C.J., Singh, G.M., Gutierrez, H.R., Lu, Y., Bahalim, A.N., et al. (2011). National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 377, 557-567.

Fischer, M.H., Yu, N., Gray, G.R., Ralph, J., Anderson, L. and Marlett, J.A. (2004). The gel-forming polysaccharide of psyllium husk (Plantago ovata Forsk). *Carbohydr Res* 339, 2009-2017.

Flint, A., Gregersen, N.T., Gluud, L.L., Moller, B.K., Raben, A., Tetens, I., Verdich, C. and Astrup, A. (2007). Associations between postprandial insulin and blood glucose responses, appetite sensations and energy intake in normal weight and overweight individuals: a meta-analysis of test meal studies. *Br J Nutr* 98, 17-25.

Flint, A., Raben, A., Blundell, J.E. and Astrup, A. (2000). Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *Int J Obes Relat Metab Disord* 24, 38-48.

Flood-Obbagy, J.E. and Rolls, B.J. (2009). The effect of fruit in different forms on energy intake and satiety at a meal. *Appetite* 52, 416-422.

Foltz, M., Maljaars, J., Schuring, E.A., van der Wal, R.J., Boer, T., Duchateau, G.S., Peters, H.P., Stellaard, F. and Masclee, A.A. (2009). Intragastric layering of lipids delays lipid absorption and increases plasma CCK but has minor effects on gastric emptying and appetite. *Am J Physiol Gastrointest Liver Physiol* 296, G982-991.

Ford, H. and Frost, G. (2010). Glycaemic index, appetite and body weight. *Proc Nutr Soc* 69, 199-203.

Foster-Schubert, K.E., Overduin, J., Prudom, C.E., Liu, J., Callahan, H.S., Gaylinn, B.D., Thorner, M.O. and Cummings, D.E. (2008). Acyl and total ghrelin are suppressed strongly by ingested proteins, weakly by lipids, and biphasically by carbohydrates. *J Clin Endocrinol Metab* 93, 1971-1979.

Freeland, K.R., Anderson, G.H. and Wolever, T.M. (2009). Acute effects of dietary fibre and glycaemic carbohydrate on appetite and food intake in healthy males. *Appetite* 52, 58-64.

French, S.J. and Cecil, J.E. (2001). Oral, gastric and intestinal influences on human feeding. *Physiol Behav* 74, 729-734.

French, S.J. and Read, N.W. (1994). Effect of guar gum on hunger and satiety after meals of differing fat content: relationship with gastric emptying. *Am J Clin Nutr* 59, 87-91.

Friedman, M.I., Edens, N.K. and Ramirez, I. (1983). Differential effects of medium- and long-chain triglycerides on food intake of normal and diabetic rats. *Physiol Behav* 31, 851-855.

Frost, G.S., Brynes, A.E., Dhillo, W.S., Bloom, S.R. and McBurney, M.I. (2003). The effects of fiber enrichment of pasta and fat content on gastric emptying, GLP-1, glucose, and insulin responses to a meal. *Eur J Clin Nutr* 57, 293-298.

Fujimiya, M., Asakawa, A., Ataka, K., Chen, C.Y., Kato, I. and Inui, A. (2010). Ghrelin, des-acyl ghrelin, and obestatin: regulatory roles on the gastrointestinal motility. *Int J Pept* 2010, 305192.

Gannon, M.C. and Nuttall, F.Q. (2010). Amino acid ingestion and glucose metabolism--a review. *IUBMB Life* 62, 660-668.

Garaiova, I., Guschina, I.A., Plummer, S.F., Tang, J., Wang, D. and Plummer, N.T. (2007). A randomised cross-over trial in healthy adults indicating improved absorption of omega-3 fatty acids by pre-emulsification. *Nutr J* 6, 4.

Georg Jensen, M., Kristensen, M., Belza, A., Knudsen, J.C. and Astrup, A. (2011). Acute Effect of Alginate-Based Preload on Satiety Feelings, Energy Intake, and Gastric Emptying Rate in Healthy Subjects. *Obesity (Silver Spring)* 20, 1851-1858.

Gerspach, A.C., Steinert, R.E., Schonenberger, L., Graber-Maier, A. and Beglinger, C. (2011). The role of the gut sweet taste receptor in regulating GLP-1, PYY, and CCK release in humans. *Am J Physiol Endocrinol Metab* 301, E317-325.

Gibbs, J., Young, R.C. and Smith, G.P. (1973). Cholecystokinin elicits satiety in rats with open gastric fistulas. *Nature* 245, 323-325.

Glerup, H., Bluhme, H., Villadsen, G.E., Rasmussen, K., Ejskjaer, N. and Dahlerup, J.F. (2007). Gastric emptying: a comparison of three methods. *Scand J Gastroenterol* 42, 1182-1186.

Goetze, O., Steingoetter, A., Menne, D., van der Voort, I.R., Kwiatek, M.A., Boesiger, P., Weishaupt, D., Thumshirn, M., Fried, M. and Schwizer, W. (2007). The effect of macronutrients on gastric volume responses and gastric emptying in humans: A magnetic resonance imaging study. *Am J Physiol Gastrointest Liver Physiol* 292, G11-17.

Gortmaker, S.L., Swinburn, B.A., Levy, D., Carter, R., Mabry, P.L., Finegood, D.T., Huang, T., Marsh, T. and Moodie, M.L. (2011). Changing the future of obesity: science, policy, and action. *Lancet* 378, 838-847.

Grandt, D., Schimiczek, M., Beglinger, C., Layer, P., Goebell, H., Eysselein, V.E. and Reeve, J.R.,Jr. (1994). Two molecular forms of peptide YY (PYY) are abundant in human blood: characterization of a radioimmunoassay recognizing PYY 1-36 and PYY 3-36. *Regul Pept* 51, 151-159.

Gray, R., French, S., Robinson, T. and Yeomans, M. (2002). Dissociation of the effects of preload volume and energy content on subjective appetite and food intake. *Physiol Behav* 76, 57-64.

Greenman, Y., Golani, N., Gilad, S., Yaron, M., Limor, R. and Stern, N. (2004). Ghrelin secretion is modulated in a nutrient- and gender-specific manner. *Clin Endocrinol (Oxf)* 60, 382-388.

Greenway, F., O'Neil, C.E., Stewart, L., Rood, J., Keenan, M. and Martin, R. (2007). Fourteen weeks of treatment with Viscofiber increased fasting levels of glucagon-like peptide-1 and peptide-YY. *J Med Food* 10, 720-724.

Gregersen, N.T., Flint, A., Bitz, C., Blundell, J.E., Raben, A. and Astrup, A. (2008). Reproducibility and power of ad libitum energy intake assessed by repeated single meals. *Am J Clin Nutr* 87, 1277-1281.

Gruendel, S., Garcia, A.L., Otto, B., Mueller, C., Steiniger, J., Weickert, M.O., Speth, M., Katz, N. and Koebnick, C. (2006). Carob pulp preparation rich in insoluble dietary fiber and polyphenols enhances lipid oxidation and lowers postprandial acylated ghrelin in humans. *J Nutr* 136, 1533-1538.

Gruendel, S., Otto, B., Garcia, A.L., Wagner, K., Mueller, C., Weickert, M.O., Heldwein, W. and Koebnick, C. (2007). Carob pulp preparation rich in insoluble dietary fibre and polyphenols increases plasma glucose and serum insulin responses in combination with a glucose load in humans. *Br J Nutr* 98, 101-105.

Guinard, J.X. and Brun, P. (1998). Sensory-specific satiety: comparison of taste and texture effects. *Appetite* 31, 141-157.

Guo, Y., Ma, L., Enriori, P.J., Koska, J., Franks, P.W., Brookshire, T., Cowley, M.A., Salbe, A.D., Delparigi, A. and Tataranni, P.A. (2006). Physiological evidence for the involvement of peptide YY in the regulation of energy homeostasis in humans. *Obesity (Silver Spring)* 14, 1562-1570.

Haber, G.B., Heaton, K.W., Murphy, D. and Burroughs, L.F. (1977). Depletion and disruption of dietary fibre. Effects on satiety, plasma-glucose, and serum-insulin. *Lancet* 2, 679-682.

Hagemann, D., Holst, J.J., Gethmann, A., Banasch, M., Schmidt, W.E. and Meier, J.J. (2007). Glucagon-like peptide 1 (GLP-1) suppresses ghrelin levels in humans via increased insulin secretion. *Regul Pept* 143, 64-68.

Hall, W.L., Millward, D.J., Long, S.J. and Morgan, L.M. (2003). Casein and whey exert different effects on plasma amino acid profiles, gastrointestinal hormone secretion and appetite. *Br J Nutr* 89, 239-248.

Hamedani, A., Akhavan, T., Samra, R.A. and Anderson, G.H. (2009). Reduced energy intake at breakfast is not compensated for at lunch if a high-insoluble-fiber cereal replaces a low-fiber cereal. *Am J Clin Nutr* 89, 1343-1349.

Harper, A., James, A., Flint, A. and Astrup, A. (2007). Increased satiety after intake of a chocolate milk drink compared with a carbonated beverage, but no difference in subsequent ad libitum lunch intake. *Br J Nutr* 97, 579-583.

Heath, R.B., Jones, R., Frayn, K.N. and Robertson, M.D. (2004). Vagal stimulation exaggerates the inhibitory ghrelin response to oral fat in humans. *J Endocrinol* 180, 273-281.

Heini, A.F., Lara-Castro, C., Schneider, H., Kirk, K.A., Considine, R.V. and Weinsier, R.L. (1998). Effect of hydrolyzed guar fiber on fasting and postprandial satiety and satiety hormones: a double-blind, placebo-controlled trial during controlled weight loss. *Int J Obes Relat Metab Disord* 22, 906-909.

Heinonen, M.V., Karhunen, L.J., Chabot, E.D., Toppinen, L.K., Juntunen, K.S., Laaksonen, D.E., Siloaho, M., Liukkonen, K.H., Herzig, K.H., Niskanen, L.K., et al. (2007). Plasma ghrelin levels after two high-carbohydrate meals producing different insulin responses in patients with metabolic syndrome. *Regul Pept* 138, 118-125.

Hellstrom, P.M., Gryback, P. and Jacobsson, H. (2006). The physiology of gastric emptying. *Best Pract Res Clin Anaesthesiol* 20, 397-407.

Helou, N., Obeid, O., Azar, S.T. and Hwalla, N. (2008). Variation of postprandial PYY 3-36 response following ingestion of differing macronutrient meals in obese females. *Ann Nutr Metab* 52, 188-195.

Henderson, M. and Freeman, C.P. (1987). A self-rating scale for bulimia. The 'BITE'. *Br J Psychiatry* 150, 18-24.

Henry, C.J., Lightowler, H.J. and Strik, C.M. (2007). Effects of long-term intervention with low- and high-glycaemic-index breakfasts on food intake in children aged 8-11 years. *Br J Nutr* 98, 636-640.

Hermans, R.C., Engels, R.C., Larsen, J.K. and Herman, C.P. (2009). Modeling of palatable food intake. The influence of quality of social interaction. *Appetite* 52, 801-804.

Hermans, R.C., Larsen, J.K., Herman, C.P. and Engels, R.C. (2012). How much should I eat? Situational norms affect young women's food intake during meal time. *Br J Nutr* 107, 588-594.

Herrmann, C., Goke, R., Richter, G., Fehmann, H.C., Arnold, R. and Goke, B. (1995). Glucagon-like peptide-1 and glucose-dependent insulin-releasing polypeptide plasma levels in response to nutrients. *Digestion* 56, 117-126.

Herzig, K.H. (1998). Cholecystokinin- and secretin-releasing peptides in the intestine--a new regulatory interendocrine mechanism in the gastrointestinal tract. *Regul Pept* 73, 89-94.

Herzig, K.H., Schon, I., Tatemoto, K., Ohe, Y., Li, Y., Folsch, U.R. and Owyang, C. (1996). Diazepam binding inhibitor is a potent cholecystokinin-releasing peptide in the intestine. *Proc Natl Acad Sci U S A* 93, 7927-7932.

Hetherington, M.M., Foster, R., Newman, T., Anderson, A.S. and Norton, G. (2006). Understanding variety: tasting different foods delays satiation. *Physiol Behav* 87, 263-271.

Hill, A.J., Rogers, P.J. and Blundell, J.E. (1995). Techniques for the experimental measurement of human eating behaviour and food intake: a practical guide. *Int J Obes Relat Metab Disord* 19, 361-375.

Himaya, A. and Louis-Sylvestre, J. (1998). The effect of soup on satiation. *Appetite* 30, 199-210.

Hipsley, E.H. (1953). Dietary "fibre" and pregnancy toxaemia. *Br Med J* 2, 420-422.

Hoad, C.L., Rayment, P., Spiller, R.C., Marciani, L., Alonso Bde, C., Traynor, C., Mela, D.J., Peters, H.P. and Gowland, P.A. (2004). In vivo imaging of intragastric gelation and its effect on satiety in humans. *J Nutr* 134, 2293-2300.

Hochstenbach-Waelen, A., Veldhorst, M.A., Nieuwenhuizen, A.G., Westerterp-Plantenga, M.S. and Westerterp, K.R. (2009a). Comparison of 2 diets with either 25% or 10% of energy as casein on energy expenditure, substrate balance, and appetite profile. *Am J Clin Nutr* 89, 831-838.

Hochstenbach-Waelen, A., Westerterp-Plantenga, M.S., Veldhorst, M.A. and Westerterp, K.R. (2009b). Single-protein casein and gelatin diets affect energy expenditure similarly but substrate balance and appetite differently in adults. *J Nutr* 139, 2285-2292.

Holst, J.J. (2007). The physiology of glucagon-like peptide 1. *Physiol Rev* 87, 1409-1439.

Holt, S.H., Brand-Miller, J.C. and Stitt, P.A. (2001). The effects of equal-energy portions of different breads on blood glucose levels, feelings of fullness and subsequent food intake. *J Am Diet Assoc* 101, 767-773.

Hopman, W.P., Jansen, J.B., Rosenbusch, G. and Lamers, C.B. (1984). Effect of equimolar amounts of long-chain triglycerides and medium-chain triglycerides on plasma cholecystokinin and gallbladder contraction. *Am J Clin Nutr* 39, 356-359.

Horowitz, M., Jones, K., Edelbroek, M.A., Smout, A.J. and Read, N.W. (1993). The effect of posture on gastric emptying and intragastric distribution of oil and aqueous meal components and appetite. *Gastroenterology* 105, 382-390.

Howarth, N.C., Saltzman, E. and Roberts, S.B. (2001). Dietary fiber and weight regulation. *Nutr Rev* 59, 129-139.

Hulshof, T., De Graaf, C. and Weststrate, J.A. (1993). The effects of preloads varying in physical state and fat content on satiety and energy intake. *Appetite* 21, 273-286.

Hunt, J.N. and Knox, M.T. (1972). The slowing of gastric emptying by four strong acids and three weak acids. *J Physiol* 222, 187-208.

Hunt, J.N., Knox, M.T. and Oginski, A. (1965). The Effect of Gravity on Gastric Emptying with various Test Meals. *J Physiol* 178, 92-97.

Hursel, R., van der Zee, L. and Westerterp-Plantenga, M.S. (2010). Effects of a breakfast yoghurt, with additional total whey protein or caseinomacropeptide-depleted alpha-lactalbumin-enriched whey protein, on diet-induced thermogenesis and appetite suppression. *Br J Nutr* 103, 775-780.

Hveem, K., Jones, K.L., Chatterton, B.E. and Horowitz, M. (1996). Scintigraphic measurement of gastric emptying and ultrasonographic assessment of antral area: relation to appetite. *Gut* 38, 816-821.

Hyde, R.J. and Witherly, S.A. (1993). Dynamic contrast: a sensory contribution to palatability. *Appetite* 21, 1-16.

IOM, (2001). Institute of Medicine. *Dietary Reference Intakes: Proposed Definition of Dietary Fiber.* Washington, DC: National Academies Press.

IOM, (2005). Institute of Medicine. *Dietary Reference Intakes: Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol.* National Academy of Sciences.

Isaksson, H., Rakha, A., Andersson, R., Fredriksson, H., Olsson, J. and Aman, P. (2011). Rye kernel breakfast increases satiety in the afternoon - an effect of food structure. *Nutr J* 10, 31.

Jahan-Mihan, A., Luhovyy, B.L., El Khoury, D. and Anderson, G.H. (2011). Dietary Proteins as Determinants of Metabolic and Physiologic Functions of the Gastrointestinal Tract. *Nutrients* 3, 574-603.

Janssen, P., Vanden Berghe, P., Verschueren, S., Lehmann, A., Depoortere, I. and Tack, J. (2011). Review article: the role of gastric motility in the control of food intake. *Aliment Pharmacol Ther* 33, 880-894.

Jeffery, R.W., Rydell, S., Dunn, C.L., Harnack, L.J., Levine, A.S., Pentel, P.R., Baxter, J.E. and Walsh, E.M. (2007). Effects of portion size on chronic energy intake. *Int J Behav Nutr Phys Act* 4, 27.

Jenkins, D.J., Wolever, T.M., Leeds, A.R., Gassull, M.A., Haisman, P., Dilawari, J., Goff, D.V., Metz, G.L. and Alberti, K.G. (1978). Dietary fibres, fibre analogues, and glucose tolerance: importance of viscosity. *Br Med J* 1, 1392-1394.

Jew, S., AbuMweis, S.S. and Jones, P.J. (2009). Evolution of the human diet: linking our ancestral diet to modern functional foods as a means of chronic disease prevention. *J Med Food* 12, 925-934.

Jones, K.L., Doran, S.M., Hveem, K., Bartholomeusz, F.D., Morley, J.E., Sun, W.M., Chatterton, B.E. and Horowitz, M. (1997). Relation between postprandial satiation and antral area in normal subjects. *Am J Clin Nutr* 66, 127-132.

Juntunen, K.S., Niskanen, L.K., Liukkonen, K.H., Poutanen, K.S., Holst, J.J. and Mykkanen, H.M. (2002). Postprandial glucose, insulin, and incretin responses to grain products in healthy subjects. *Am J Clin Nutr* 75, 254-262.

Juvonen, K.R., Purhonen, A.K., Salmenkallio-Marttila, M., Lahteenmaki, L., Laaksonen, D.E., Herzig, K.H., Uusitupa, M.I., Poutanen, K.S. and Karhunen, L.J. (2009). Viscosity of oat bran-enriched beverages influences gastrointestinal hormonal responses in healthy humans. *J Nutr* 139, 461-466.

Kamphuis, M.M., Mela, D.J. and Westerterp-Plantenga, M.S. (2003). Diacylglycerols affect substrate oxidation and appetite in humans. *Am J Clin Nutr* 77, 1133-1139.

Kanatani, A., Mashiko, S., Murai, N., Sugimoto, N., Ito, J., Fukuroda, T., Fukami, T., Morin, N., MacNeil, D.J., Van der Ploeg, L.H., et al. (2000). Role of the Y1 receptor in the regulation of neuropeptide Y-mediated feeding: comparison of wild-type, Y1 receptor-deficient, and Y5 receptor-deficient mice. *Endocrinology* 141, 1011-1016.

Karamanlis, A., Chaikomin, R., Doran, S., Bellon, M., Bartholomeusz, F.D., Wishart, J.M., Jones, K.L., Horowitz, M. and Rayner, C.K. (2007). Effects of protein on glycemic and incretin responses and gastric emptying after oral glucose in healthy subjects. *Am J Clin Nutr* 86, 1364-1368.

Karhunen, L.J., Juvonen, K.R., Huotari, A., Purhonen, A.K. and Herzig, K.H. (2008). Effect of protein, fat, carbohydrate and fibre on gastrointestinal peptide release in humans. *Regul Pept* 149, 70-78.

Karra, E., Chandarana, K. and Batterham, R.L. (2009). The role of peptide YY in appetite regulation and obesity. *J Physiol* 587, 19-25.

Keim, N.L. and Horn, W.F. (2004). Restrained eating behavior and the metabolic response to dietary energy restriction in women. *Obes Res* 12, 141-149.

Kenny, P.J. (2011). Reward mechanisms in obesity: new insights and future directions. *Neuron* 69, 664-679.

Kieffer, T.J., McIntosh, C.H. and Pederson, R.A. (1995). Degradation of glucose-dependent insulinotropic polypeptide and truncated glucagon-like peptide 1 in vitro and in vivo by dipeptidyl peptidase IV. *Endocrinology* 136, 3585-3596.

Kissileff, H.R. (1985). Effects of physical state (liquid-solid) of foods on food intake: procedural and substantive contributions. *Am J Clin Nutr* 42, 956-965.

Kissileff, H.R., Carretta, J.C., Geliebter, A. and Pi-Sunyer, F.X. (2003). Cholecystokinin and stomach distension combine to reduce food intake in humans. *Am J Physiol Regul Integr Comp Physiol* 285, R992-998.

Kissileff, H.R., Gruss, L.P., Thornton, J. and Jordan, H.A. (1984). The satiating efficiency of foods. *Physiol Behav* 32, 319-332.

Kissileff, H.R., Pi-Sunyer, F.X., Thornton, J. and Smith, G.P. (1981). C-terminal octapeptide of cholecystokinin decreases food intake in man. *Am J Clin Nutr* 34, 154-160.

Kissileff, H.R. and Van Itallie, T.B. (1982). Physiology of the control of food intake. *Annu Rev Nutr* 2, 371-418.

Koda, S., Date, Y., Murakami, N., Shimbara, T., Hanada, T., Toshinai, K., Niijima, A., Furuya, M., Inomata, N., Osuye, K., et al. (2005). The role of the vagal nerve in peripheral PYY3-36-induced feeding reduction in rats. *Endocrinology* 146, 2369-2375.

Kojima, M., Hosoda, H., Date, Y., Nakazato, M., Matsuo, H. and Kangawa, K. (1999). Ghrelin is a growth-hormone-releasing acylated peptide from stomach. *Nature* 402, 656-660.

Kokrashvili, Z., Mosinger, B. and Margolskee, R.F. (2009). Taste signaling elements expressed in gut enteroendocrine cells regulate nutrient-responsive secretion of gut hormones. *Am J Clin Nutr* 90, 822S-825S.

Koliaki, C., Kokkinos, A., Tentolouris, N. and Katsilambros, N. (2010). The effect of ingested macronutrients on postprandial ghrelin response: a critical review of existing literature data. *Int J Pept* 2010, 710852.

Kong, F. and Singh, R.P. (2008). Disintegration of solid foods in human stomach. *J Food Sci* 73, R67-80.

Kong, M.F., Chapman, I., Goble, E., Wishart, J., Wittert, G., Morris, H. and Horowitz, M. (1999). Effects of oral fructose and glucose on plasma GLP-1 and appetite in normal subjects. *Peptides* 20, 545-551.

Kopin, A.S., Mathes, W.F., McBride, E.W., Nguyen, M., Al-Haider, W., Schmitz, F., Bonner-Weir, S., Kanarek, R. and Beinborn, M. (1999). The cholecystokinin-A receptor mediates inhibition of food intake yet is not essential for the maintenance of body weight. *J Clin Invest* 103, 383-391.

Kral, T.V. and Rolls, B.J. (2004). Energy density and portion size: their independent and combined effects on energy intake. *Physiol Behav* 82, 131-138.

Kreymann, B., Williams, G., Ghatei, M.A. and Bloom, S.R. (1987). Glucagon-like peptide-1 7-36: a physiological incretin in man. *Lancet* 2, 1300-1304.

Kristek, B., Kurbel, S. and Banjari, I. (2010). Characteristics of dietary sugars compared with their roles in body metabolism. *Adv Physiol Educ* 34, 111-114.

Kristensen, M. and Jensen, M.G. (2011). Dietary fibres in the regulation of appetite and food intake. Importance of viscosity. *Appetite* 56, 65-70.

Kristensen, M., Jensen, M.G., Riboldi, G., Petronio, M., Bugel, S., Toubro, S., Tetens, I. and Astrup, A. (2010). Wholegrain vs. refined wheat bread and pasta. Effect on postprandial glycemia, appetite, and subsequent ad libitum energy intake in young healthy adults. *Appetite* 54, 163-169.

Kuipers, R.S., Luxwolda, M.F., Dijck-Brouwer, D.A., Eaton, S.B., Crawford, M.A., Cordain, L. and Muskiet, F.A. (2010). Estimated macronutrient and fatty acid intakes from an East African Paleolithic diet. *Br J Nutr* 104, 1666-1687.

Kwiatek, M.A., Menne, D., Steingoetter, A., Goetze, O., Forras-Kaufman, Z., Kaufman, E., Fruehauf, H., Boesiger, P., Fried, M., Schwizer, W., et al. (2009). Effect of meal volume and calorie load on postprandial gastric function and emptying: studies under physiological conditions by combined fiber-optic pressure measurement and MRI. *Am J Physiol Gastrointest Liver Physiol* 297, G894-901.

Laboure, H., Van Wymelbeke, V., Fantino, M. and Nicolaidis, S. (2002). Behavioral, plasma, and calorimetric changes related to food texture modification in men. *Am J Physiol Regul Integr Comp Physiol* 282, R1501-1511.

Laessle, R.G., Tuschl, R.J., Kotthaus, B.C. and Pirke, K.M. (1989). Behavioral and biological correlates of dietary restraint in normal life. *Appetite* 12, 83-94.

Lam, S.M., Moughan, P.J., Awati, A. and Morton, H.R. (2009). The influence of whey protein and glycomacropeptide on satiety in adult humans. *Physiol Behav* 96, 162-168.

Lang, V., Bellisle, F., Alamowitch, C., Craplet, C., Bornet, F.R., Slama, G. and Guy-Grand, B. (1999). Varying the protein source in mixed meal modifies glucose, insulin and glucagon kinetics in healthy men, has weak effects on subjective satiety and fails to affect food intake. *Eur J Clin Nutr* 53, 959-965.

Lang, V., Bellisle, F., Oppert, J.M., Craplet, C., Bornet, F.R., Slama, G. and Guy-Grand, B. (1998). Satiating effect of proteins in healthy subjects: a comparison of egg albumin, casein, gelatin, soy protein, pea protein, and wheat gluten. *Am J Clin Nutr* 67, 1197-1204.

Langhans, W. (1996). Metabolic and glucostatic control of feeding. *Proc Nutr Soc* 55, 497-515.

Larhammar, D. (1996). Structural diversity of receptors for neuropeptide Y, peptide YY and pancreatic polypeptide. *Regul Pept* 65, 165-174.

Larsson, L.I. and Rehfeld, J.F. (1979). Localization and molecular heterogeneity of cholecystokinin in the central and peripheral nervous system. *Brain Res* 165, 201-218.

Layman, D.K. (2009). Dietary Guidelines should reflect new understandings about adult protein needs. *Nutr Metab (Lond)* 6, 12.

le Roux, C.W. and Bloom, S.R. (2005). Peptide YY, appetite and food intake. *Proc Nutr Soc* 64, 213-216.

le Roux, C.W., Patterson, M., Vincent, R.P., Hunt, C., Ghatei, M.A. and Bloom, S.R. (2005). Postprandial plasma ghrelin is suppressed proportional to meal calorie content in normal-weight but not obese subjects. *J Clin Endocrinol Metab* 90, 1068-1071.

Ledikwe, J.H., Blanck, H.M., Kettel Khan, L., Serdula, M.K., Seymour, J.D., Tohill, B.C. and Rolls, B.J. (2006). Dietary energy density is associated with energy intake and weight status in US adults. *Am J Clin Nutr* 83, 1362-1368.

Ledoux, N., Mahe, S., Duarry, M., Bourras, M., Benamouzig, R. and Tome, D. (1999). Intraluminal immunoreactive caseinomacropeptide after milk protein ingestion in humans. *Nahrung* 43, 196-200.

Leidy, H.J., Apolzan, J.W., Mattes, R.D. and Campbell, W.W. (2010a). Food form and portion size affect postprandial appetite sensations and hormonal responses in healthy, nonobese, older adults. *Obesity (Silver Spring)* 18, 293-299.

Leidy, H.J., Armstrong, C.L., Tang, M., Mattes, R.D. and Campbell, W.W. (2010b). The influence of higher protein intake and greater eating frequency on appetite control in overweight and obese men. *Obesity (Silver Spring)* 18, 1725-1732.

Leidy, H.J., Bales-Voelker, L.I. and Harris, C.T. (2011). A protein-rich beverage consumed as a breakfast meal leads to weaker appetitive and dietary responses v. a protein-rich solid breakfast meal in adolescents. *Br J Nutr* 106, 37-41.

Leidy, H.J. and Campbell, W.W. (2011). The effect of eating frequency on appetite control and food intake: brief synopsis of controlled feeding studies. *J Nutr* 141, 154-157.

Leidy, H.J. and Racki, E.M. (2010). The addition of a protein-rich breakfast and its effects on acute appetite control and food intake in 'breakfast-skipping' adolescents. *Int J Obes (Lond)* 34, 1125-1133.

Lejeune, M.P., Westerterp, K.R., Adam, T.C., Luscombe-Marsh, N.D. and Westerterp-Plantenga, M.S. (2006). Ghrelin and glucagon-like peptide 1 concentrations, 24-h satiety, and energy and substrate metabolism during a high-protein diet and measured in a respiration chamber. *Am J Clin Nutr* 83, 89-94.

Lenard, N.R. and Berthoud, H.R. (2008). Central and peripheral regulation of food intake and physical activity: pathways and genes. *Obesity (Silver Spring)* 16 Suppl 3, S11-22.

Lentle, R.G. and Janssen, P.W. (2010). Manipulating digestion with foods designed to change the physical characteristics of digesta. *Crit Rev Food Sci Nutr* 50, 130-145.

Levin, F., Edholm, T., Schmidt, P.T., Gryback, P., Jacobsson, H., Degerblad, M., Hoybye, C., Holst, J.J., Rehfeld, J.F., Hellstrom, P.M., et al. (2006). Ghrelin stimulates gastric emptying and hunger in normal-weight humans. *J Clin Endocrinol Metab* 91, 3296-3302.

Li, P., Yin, Y.L., Li, D., Kim, S.W. and Wu, G. (2007). Amino acids and immune function. *Br J Nutr* 98, 237-252.

Liddle, R.A. (1989). Integrated actions of cholecystokinin on the gastrointestinal tract: use of the cholecystokinin bioassay. *Gastroenterol Clin North Am* 18, 735-756.

Liddle, R.A. (1997). Cholecystokinin cells. *Annu Rev Physiol* 59, 221-242.

Liddle, R.A., Goldfine, I.D., Rosen, M.S., Taplitz, R.A. and Williams, J.A. (1985). Cholecystokinin bioactivity in human plasma. Molecular forms, responses to feeding, and relationship to gallbladder contraction. *J Clin Invest* 75, 1144-1152.

Liddle, R.A., Morita, E.T., Conrad, C.K. and Williams, J.A. (1986). Regulation of gastric emptying in humans by cholecystokinin. *J Clin Invest* 77, 992-996.

Lieverse, R.J., Jansen, J.B., Masclee, A.A. and Lamers, C.B. (1995). Satiety effects of a physiological dose of cholecystokinin in humans. *Gut* 36, 176-179.

Lindeberg, S. (2012). Paleolithic diets as a model for prevention and treatment of Western disease. *Am J Hum Biol* 24, 110-115.

Lissner, L., Levitsky, D.A., Strupp, B.J., Kalkwarf, H.J. and Roe, D.A. (1987). Dietary fat and the regulation of energy intake in human subjects. *Am J Clin Nutr* 46, 886-892.

Little, T.J., Doran, S., Meyer, J.H., Smout, A.J., O'Donovan, D.G., Wu, K.L., Jones, K.L., Wishart, J., Rayner, C.K., Horowitz, M., et al. (2006). The release of GLP-1 and ghrelin, but not GIP and CCK, by glucose is dependent upon the length of small intestine exposed. *Am J Physiol Endocrinol Metab* 291, E647-655.

Little, T.J., Gopinath, A., Patel, E., McGlone, A., Lassman, D.J., D'Amato, M., McLaughlin, J.T. and Thompson, D.G. (2010). Gastric emptying of hexose sugars: role of osmolality, molecular structure and the CCK receptor. *Neurogastroenterol Motil* 22, 1183-1190.

Little, T.J., Russo, A., Meyer, J.H., Horowitz, M., Smyth, D.R., Bellon, M., Wishart, J.M., Jones, K.L. and Feinle-Bisset, C. (2007). Free fatty acids have more potent effects on gastric emptying, gut hormones, and appetite than triacylglycerides. *Gastroenterology* 133, 1124-1131.

Lorenzen, J., Frederiksen, R., Hoppe, C., Hvid, R. and Astrup, A. (2012). The effect of milk proteins on appetite regulation and diet-induced thermogenesis. *Eur J Clin Nutr* .

Ludwig, D.S. (2000). Dietary glycemic index and obesity. *J Nutr* 130, 280S-283S.

Lummela, N., Kekkonen, R.A., Jauhiainen, T., Pilvi, T.K., Tuure, T., Järvenpää, S., Eriksson, J.G. and Korpela, R. (2009). Effects of a fibre-enriched milk drink on insulin and glucose levels in healthy subjects. *Nutr J* 8, 45.

Lundin, L., Golding, M. and Wooster, T.J. (2008). Understanding food structure and function in developing food for appetite control. *Nutrition & Dietetics* 65, S79-S85.

Lyly, M., Liukkonen, K.H., Salmenkallio-Marttila, M., Karhunen, L., Poutanen, K. and Lahteenmaki, L. (2009). Fibre in beverages can enhance perceived satiety. *Eur J Nutr* 48, 251-258.

Lyly, M., Ohls, N., Lahteenmaki, L., Salmenkallio-Marttila, M., Liukkonen, K.H., Karhunen, L. and Poutanen, K. (2010). The effect of fibre amount, energy level and viscosity of beverages containing oat fibre supplement on perceived satiety. *Food Nutr Res* 54, 2149.

Maas, M.I., Hopman, W.P., Katan, M.B. and Jansen, J.B. (1998). Release of peptide YY and inhibition of gastric acid secretion by long-chain and medium-chain triglycerides but not by sucrose polyester in men. *Eur J Clin Invest* 28, 123-130.

MacIntosh, C.G., Andrews, J.M., Jones, K.L., Wishart, J.M., Morris, H.A., Jansen, J.B., Morley, J.E., Horowitz, M. and Chapman, I.M. (1999). Effects of age on concentrations of plasma cholecystokinin, glucagon-like peptide 1, and peptide YY and their relation to appetite and pyloric motility. *Am J Clin Nutr* 69, 999-1006.

Maffeis, C., Surano, M.G., Cordioli, S., Gasperotti, S., Corradi, M. and Pinelli, L. (2010). A high-fat vs. a moderate-fat meal in obese boys: nutrient balance, appetite, and gastrointestinal hormone changes. *Obesity (Silver Spring)* 18, 449-455.

Malik, S., McGlone, F., Bedrossian, D. and Dagher, A. (2008). Ghrelin modulates brain activity in areas that control appetitive behavior. *Cell Metab* 7, 400-409.

Maljaars, J., Romeyn, E.A., Haddeman, E., Peters, H.P. and Masclee, A.A. (2009). Effect of fat saturation on satiety, hormone release, and food intake. *Am J Clin Nutr* 89, 1019-1024.

Maljaars, P.W., Keszthelyi, D. and Masclee, A.A. (2010). An ileal brake-through? *Am J Clin Nutr* 92, 467-468.

Maljaars, P.W., Peters, H.P., Mela, D.J. and Masclee, A.A. (2008). Ileal brake: a sensible food target for appetite control. A review. *Physiol Behav* 95, 271-281.

Mann, J., Cummings, J.H., Englyst, H.N., Key, T., Liu, S., Riccardi, G., Summerbell, C., Uauy, R., van Dam, R.M., Venn, B., et al. (2007). FAO/WHO scientific update on carbohydrates in human nutrition: conclusions. *Eur J Clin Nutr* 61 Suppl 1, S132-137.

Marciani, L., Faulks, R., Wickham, M.S., Bush, D., Pick, B., Wright, J., Cox, E.F., Fillery-Travis, A., Gowland, P.A. and Spiller, R.C. (2009). Effect of intragastric acid stability of fat emulsions on gastric emptying, plasma lipid profile and postprandial satiety. *Br J Nutr* 101, 919-928.

Marciani, L., Gowland, P.A., Fillery-Travis, A., Manoj, P., Wright, J., Smith, A., Young, P., Moore, R. and Spiller, R.C. (2001). Assessment of antral grinding of a model solid meal with echo-planar imaging. *Am J Physiol Gastrointest Liver Physiol* 280, G844-849.

Marciani, L., Gowland, P.A., Spiller, R.C., Manoj, P., Moore, R.J., Young, P., Al-Sahab, S., Bush, D., Wright, J. and Fillery-Travis, A.J. (2000). Gastric response to increased meal viscosity assessed by echo-planar magnetic resonance imaging in humans. *J Nutr* 130, 122-127.

Marciani, L., Gowland, P.A., Spiller, R.C., Manoj, P., Moore, R.J., Young, P. and Fillery-Travis, A.J. (2001). Effect of meal viscosity and nutrients on satiety, intragastric dilution, and emptying assessed by MRI. *Am J Physiol Gastrointest Liver Physiol* 280, G1227-1233.

Marciani, L., Wickham, M., Singh, G., Bush, D., Pick, B., Cox, E., Fillery-Travis, A., Faulks, R., Marsden, C., Gowland, P.A., et al. (2007). Enhancement of intragastric acid stability of a fat emulsion meal delays gastric emptying and increases cholecystokinin release and gallbladder contraction. *Am J Physiol Gastrointest Liver Physiol* 292, G1607-1613.

Marciani, L., Wickham, M.S., Bush, D., Faulks, R., Wright, J., Fillery-Travis, A.J., Spiller, R.C. and Gowland, P.A. (2006). Magnetic resonance imaging of the behaviour of oil-in-water emulsions in the gastric lumen of man. *Br J Nutr* 95, 331-339.

Marlett, J.A. and Fischer, M.H. (2003). The active fraction of psyllium seed husk. *Proc Nutr Soc* 62, 207-209.

Mars, M., Stafleu, A. and de Graaf, C. (2012). Use of satiety peptides in assessing the satiating capacity of foods. *Physiol Behav* 105, 483-488.

Martens, M.J., Lemmens, S.G., Born, J.M. and Westerterp-Plantenga, M.S. (2011). A solid high-protein meal evokes stronger hunger suppression than a liquefied high-protein meal. *Obesity (Silver Spring)* 19, 522-527.

Martens, M.J. and Westerterp-Plantenga, M.S. (2012). Mode of consumption plays a role in alleviating hunger and thirst. *Obesity (Silver Spring)* 20, 517-524.

Martins, C., Morgan, L.M. and Robertson, M.D. (2009). Effects of restrained eating behaviour on insulin sensitivity in normal-weight individuals. *Physiol Behav* 96, 703-708.

Martins, C., Robertson, M.D. and Morgan, L.M. (2008). Effects of exercise and restrained eating behaviour on appetite control. *Proc Nutr Soc* 67, 28-41.

Martins, C., Robertson, M.D. and Morgan, L.M. (2010). Impact of restraint and disinhibition on PYY plasma levels and subjective feelings of appetite. *Appetite* 55, 208-213.

Mattes, R. (2005). Soup and satiety. *Physiol Behav* 83, 739-747.

Mattes, R.D. (2006). Fluid energy--Where's the problem? *J Am Diet Assoc* 106, 1956-1961.

Mattes, R.D. (2011). Spices and energy balance. *Physiol Behav* doi:10.1016/j.physbeh.2011.10.028.

Mattes, R.D. and Rothacker, D. (2001). Beverage viscosity is inversely related to postprandial hunger in humans. *Physiol Behav* 74, 551-557.

Matzinger, D., Degen, L., Drewe, J., Meuli, J., Duebendorfer, R., Ruckstuhl, N., D'Amato, M., Rovati, L. and Beglinger, C. (2000). The role of long chain fatty acids in regulating food intake and cholecystokinin release in humans. *Gut* 46, 688-693.

Mayer, J. (1953). Glucostatic mechanism of regulation of food intake. *N Engl J Med* 249, 13-16.

Mayer, J. (1955). Regulation of energy intake and the body weight: the glucostatic theory and the lipostatic hypothesis. *Ann N Y Acad Sci* 63, 15-43.

McClements, D.J., Decker, E.A. and Park, Y. (2009). Controlling lipid bioavailability through physicochemical and structural approaches. *Crit Rev Food Sci Nutr* 49, 48-67.

McLaughlin, J., Grazia Luca, M., Jones, M.N., D'Amato, M., Dockray, G.J. and Thompson, D.G. (1999). Fatty acid chain length determines cholecystokinin secretion and effect on human gastric motility. *Gastroenterology* 116, 46-53.

Mellinkoff, S.M., Frankland, M., Boyle, D. and Greipel, M. (1956). Relationship between serum amino acid concentration and fluctuations in appetite. *J Appl Physiol* 8, 535-538.

Merrill, E.P., Kramer, F.M., Cardello, A. and Schutz, H. (2002). A comparison of satiety measures. *Appetite* 39, 181-183.

Mishima, Y., Amano, Y., Takahashi, Y., Mishima, Y., Moriyama, N., Miyake, T., Ishimura, N., Ishihara, S. and Kinoshita, Y. (2009). Gastric emptying of liquid and solid meals at various temperatures: effect of meal temperature for gastric emptying. *J Gastroenterol* 44, 412-418.

Misra, M., Miller, K.K., Tsai, P., Gallagher, K., Lin, A., Lee, N., Herzog, D.B. and Klibanski, A. (2006). Elevated peptide YY levels in adolescent girls with anorexia nervosa. *J Clin Endocrinol Metab* 91, 1027-1033.

Mohlig, M., Koebnick, C., Weickert, M.O., Lueder, W., Otto, B., Steiniger, J., Twilfert, M., Meuser, F., Pfeiffer, A.F. and Zunft, H.J. (2005). Arabinoxylan-enriched meal increases serum ghrelin levels in healthy humans. *Horm Metab Res* 37, 303-308.

Mojsov, S., Heinrich, G., Wilson, I.B., Ravazzola, M., Orci, L. and Habener, J.F. (1986). Preproglucagon gene expression in pancreas and intestine diversifies at the level of post-translational processing. *J Biol Chem* 261, 11880-11889.

Monsivais, P., Carter, B.E., Christiansen, M., Perrigue, M.M. and Drewnowski, A. (2011). Soluble fiber dextrin enhances the satiating power of beverages. *Appetite* 56, 9-14.

Monteleone, P., Bencivenga, R., Longobardi, N., Serritella, C. and Maj, M. (2003). Differential responses of circulating ghrelin to high-fat or high-carbohydrate meal in healthy women. *J Clin Endocrinol Metab* 88, 5510-5514.

Moran, T.H. (2000). Cholecystokinin and satiety: current perspectives. *Nutrition* 16, 858-865.

Moran, T.H. (2009). Fructose and satiety. *J Nutr* 139, 1253S-1256S.

Moran, T.H. and Kinzig, K.P. (2004). Gastrointestinal satiety signals II. Cholecystokinin. *Am J Physiol Gastrointest Liver Physiol* 286, G183-188.

Morley, J.E., Levine, A.S., Grace, M. and Kneip, J. (1985). Peptide YY (PYY), a potent orexigenic agent. *Brain Res* 341, 200-203.

Mortensen, K., Christensen, L.L., Holst, J.J. and Orskov, C. (2003). GLP-1 and GIP are colocalized in a subset of endocrine cells in the small intestine. *Regul Pept* 114, 189-196.

Morton, G.J., Cummings, D.E., Baskin, D.G., Barsh, G.S. and Schwartz, M.W. (2006). Central nervous system control of food intake and body weight. *Nature* 443, 289-295.

Moss, C., Dhillo, W.S., Frost, G. and Hickson, M. (2012). Gastrointestinal hormones: the regulation of appetite and the anorexia of ageing. *J Hum Nutr Diet* 25, 3-15.

Mourao, D.M., Bressan, J., Campbell, W.W. and Mattes, R.D. (2007). Effects of food form on appetite and energy intake in lean and obese young adults. *Int J Obes (Lond)* 31, 1688-1695.

Mozaffarian, D., Hao, T., Rimm, E.B., Willett, W.C. and Hu, F.B. (2011). Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med* 364, 2392-2404.

Murphy, K.G. and Bloom, S.R. (2006). Gut hormones and the regulation of energy homeostasis. *Nature* 444, 854-859.

Murray, C.D., le Roux, C.W., Gouveia, C., Bassett, P., Ghatei, M.A., Bloom, S.R., Emmanuel, A.V. and Gabe, S.M. (2006). The effect of different macronutrient infusions on appetite, ghrelin and peptide YY in parenterally fed patients. *Clin Nutr* 25, 626-633.

Muurahainen, N., Kissileff, H.R., Derogatis, A.J. and Pi-Sunyer, F.X. (1988). Effects of cholecystokinin-octapeptide (CCK-8) on food intake and gastric emptying in man. *Physiol Behav* 44, 645-649.

Naslund, E., Bogefors, J., Gryback, P., Jacobsson, H. and Hellstrom, P.M. (2000). Gastric emptying: comparison of scintigraphic, polyethylene glycol dilution, and paracetamol tracer assessment techniques. *Scand J Gastroenterol* 35, 375-379.

Naslund, E., Bogefors, J., Skogar, S., Gryback, P., Jacobsson, H., Holst, J.J. and Hellstrom, P.M. (1999). GLP-1 slows solid gastric emptying and inhibits insulin, glucagon, and PYY release in humans. *Am J Physiol* 277, R910-916.

Naslund, E., King, N., Mansten, S., Adner, N., Holst, J.J., Gutniak, M. and Hellstrom, P.M. (2004). Prandial subcutaneous injections of glucagon-like peptide-1 cause weight loss in obese human subjects. *Br J Nutr* 91, 439-446.

Nauck, M.A., Heimesaat, M.M., Orskov, C., Holst, J.J., Ebert, R. and Creutzfeldt, W. (1993). Preserved incretin activity of glucagon-like peptide 1 [7-36 amide] but not of synthetic human gastric inhibitory polypeptide in patients with type-2 diabetes mellitus. *J Clin Invest* 91, 301-307.

Nedvidkova, J., Krykorkova, I., Bartak, V., Papezova, H., Gold, P.W., Alesci, S. and Pacak, K. (2003). Loss of meal-induced decrease in plasma ghrelin levels in patients with anorexia nervosa. *J Clin Endocrinol Metab* 88, 1678-1682.

Nieuwenhuizen, A.G., Hochstenbach-Waelen, A., Veldhorst, M.A., Westerterp, K.R., Engelen, M.P., Brummer, R.J., Deutz, N.E. and Westerterp-Plantenga, M.S. (2009). Acute effects of breakfasts containing alpha-lactalbumin, or gelatin with or without added tryptophan, on hunger, 'satiety' hormones and amino acid profiles. *Br J Nutr* 101, 1859-1866.

Nilsson, M., Stenberg, M., Frid, A.H., Holst, J.J. and Björck, I.M. (2004). Glycemia and insulinemia in healthy subjects after lactose-equivalent meals of milk and other food proteins: the role of plasma amino acids and incretins. *Am J Clin Nutr* 80, 1246-1253.

Nishi, Y., Hiejima, H., Hosoda, H., Kaiya, H., Mori, K., Fukue, Y., Yanase, T., Nawata, H., Kangawa, K. and Kojima, M. (2005). Ingested medium-chain fatty acids are directly utilized for the acyl modification of ghrelin. *Endocrinology* 146, 2255-2264.

Norton, G.N., Anderson, A.S. and Hetherington, M.M. (2006). Volume and variety: relative effects on food intake. *Physiol Behav* 87, 714-722.

Norton, I., Moore, S. and Fryer, P. (2007). Understanding food structuring and breakdown: engineering approaches to obesity. *Obes Rev* 8 Suppl 1, 83-88.

Oesch, S., Ruegg, C., Fischer, B., Degen, L. and Beglinger, C. (2006). Effect of gastric distension prior to eating on food intake and feelings of satiety in humans. *Physiol Behav* 87, 903-910.

O'Keefe, J.H.,Jr and Cordain, L. (2004). Cardiovascular disease resulting from a diet and lifestyle at odds with our Paleolithic genome: how to become a 21st-century hunter-gatherer. *Mayo Clin Proc* 79, 101-108.

Orskov, C., Rabenhoj, L., Wettergren, A., Kofod, H. and Holst, J.J. (1994). Tissue and plasma concentrations of amidated and glycine-extended glucagon-like peptide I in humans. *Diabetes* 43, 535-539.

Overduin, J., Frayo, R.S., Grill, H.J., Kaplan, J.M. and Cummings, D.E. (2005). Role of the duodenum and macronutrient type in ghrelin regulation. *Endocrinology* 146, 845-850.

Paddon-Jones, D., Short, K.R., Campbell, W.W., Volpi, E. and Wolfe, R.R. (2008a). Role of dietary protein in the sarcopenia of aging. *Am J Clin Nutr* 87, 1562S-1566S.

Paddon-Jones, D., Westman, E., Mattes, R.D., Wolfe, R.R., Astrup, A. and Westerterp-Plantenga, M. (2008b). Protein, weight management, and satiety. *Am J Clin Nutr* 87, 1558S-1561S.

Pal, S. and Ellis, V. (2010). The acute effects of four protein meals on insulin, glucose, appetite and energy intake in lean men. *Br J Nutr* 104, 1241-1248.

Pan, A. and Hu, F.B. (2011). Effects of carbohydrates on satiety: differences between liquid and solid food. *Curr Opin Clin Nutr Metab Care* 14, 385-390.

Panahi, S., Ezatagha, A., Temelli, F., Vasanthan, T. and Vuksan, V. (2007). Beta-glucan from two sources of oat concentrates affect postprandial glycemia in relation to the level of viscosity. *J Am Coll Nutr* 26, 639-644.

Papathanasopoulos, A. and Camilleri, M. (2010). Dietary fiber supplements: effects in obesity and metabolic syndrome and relationship to gastrointestinal functions. *Gastroenterology* 138, 65-72.

Parker, B.A., Sturm, K., MacIntosh, C.G., Feinle, C., Horowitz, M. and Chapman, I.M. (2004). Relation between food intake and visual analogue scale ratings of appetite and other sensations in healthy older and young subjects. *Eur J Clin Nutr* 58, 212-218.

Pedersen, N.L., Nagain-Domaine, C., Mahe, S., Chariot, J., Roze, C. and Tome, D. (2000). Caseinomacropeptide specifically stimulates exocrine pancreatic secretion in the anesthetized rat. *Peptides* 21, 1527-1535.

Pedersen-Bjergaard, U., Host, U., Kelbaek, H., Schifter, S., Rehfeld, J.F., Faber, J. and Christensen, N.J. (1996). Influence of meal composition on postprandial peripheral plasma concentrations of vasoactive peptides in man. *Scand J Clin Lab Invest* 56, 497-503.

Peracchi, M., Santangelo, A., Conte, D., Fraquelli, M., Tagliabue, R., Gebbia, C. and Porrini, M. (2000). The physical state of a meal affects hormone release and postprandial thermogenesis. *Br J Nutr* 83, 623-628.

Pereira, M.A. and Ludwig, D.S. (2001). Dietary fiber and body-weight regulation. Observations and mechanisms. *Pediatr Clin North Am* 48, 969-980.

Perrigue, M., Carter, B., Roberts, S.A. and Drewnowski, A. (2010). A low-calorie beverage supplemented with low-viscosity pectin reduces energy intake at a subsequent meal. *J Food Sci* 75, H300-305.

Perrigue, M.M., Monsivais, P. and Drewnowski, A. (2009). Added soluble fiber enhances the satiating power of low-energy-density liquid yogurts. *J Am Diet Assoc* 109, 1862-1868.

Peters, J.C. (2003). Dietary fat and body weight control. *Lipids* 38, 123-127.

Pilichiewicz, A.N., Little, T.J., Brennan, I.M., Meyer, J.H., Wishart, J.M., Otto, B., Horowitz, M. and Feinle-Bisset, C. (2006). Effects of load, and duration, of duodenal lipid on antropyloroduodenal motility, plasma CCK and PYY, and energy intake in healthy men. *Am J Physiol Regul Integr Comp Physiol* 290, R668-677.

Pollard, J., Kirk, S.F. and Cade, J.E. (2002). Factors affecting food choice in relation to fruit and vegetable intake: a review. *Nutr Res Rev* 15, 373-387.

Poppitt, S.D. and Prentice, A.M. (1996). Energy density and its role in the control of food intake: evidence from metabolic and community studies. *Appetite* 26, 153-174.

Poppitt, S.D., Strik, C.M., MacGibbon, A.K., McArdle, B.H., Budgett, S.C. and McGill, A.T. (2010). Fatty acid chain length, postprandial satiety and food intake in lean men. *Physiol Behav* 101, 161-167.

Porrini, M., Crovetti, R., Testolin, G. and Silva, S. (1995). Evaluation of satiety sensations and food intake after different preloads. *Appetite* 25, 17-30.

Potier, M., Darcel, N. and Tome, D. (2009). Protein, amino acids and the control of food intake. *Curr Opin Clin Nutr Metab Care* 12, 54-58.

Potier, M., Fromentin, G., Lesdema, A., Benamouzig, R., Tome, D. and Marsset-Baglieri, A. (2010). The satiety effect of disguised liquid preloads administered acutely and differing only in their nutrient content tended to be weaker for lipids but did not differ between proteins and carbohydrates in human subjects. *Br J Nutr* 104, 1406-1414.

Powley, T.L. and Phillips, R.J. (2004). Gastric satiation is volumetric, intestinal satiation is nutritive. *Physiol Behav* 82, 69-74.

Raben, A., Agerholm-Larsen, L., Flint, A., Holst, J.J. and Astrup, A. (2003). Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. *Am J Clin Nutr* 77, 91-100.

Raben, A., Christensen, N.J., Madsen, J., Holst, J.J. and Astrup, A. (1994a). Decreased postprandial thermogenesis and fat oxidation but increased fullness after a high-fiber meal compared with a low-fiber meal. *Am J Clin Nutr* 59, 1386-1394.

Raben, A., Tagliabue, A., Christensen, N.J., Madsen, J., Holst, J.J. and Astrup, A. (1994b). Resistant starch: the effect on postprandial glycemia, hormonal response, and satiety. *Am J Clin Nutr* 60, 544-551.

Radulescu, A., Gannon, M.C. and Nuttall, F.Q. (2010). The effect on glucagon, glucagon-like peptide-1, total and acyl-ghrelin of dietary fats ingested with and without potato. *J Clin Endocrinol Metab* 95, 3385-3391.

Ranganath, L.R., Beety, J.M., Morgan, L.M., Wright, J.W., Howland, R. and Marks, V. (1996). Attenuated GLP-1 secretion in obesity: cause or consequence? *Gut* 38, 916-919.

Raninen, K., Lappi, J., Mykkanen, H. and Poutanen, K. (2011). Dietary fiber type reflects physiological functionality: comparison of grain fiber, inulin, and polydextrose. *Nutr Rev* 69, 9-21.

Rasoamanana, R., Darcel, N., Fromentin, G. and Tome, D. (2012). Nutrient sensing and signalling by the gut. *Proc Nutr Soc* , 1-10.

Ratliff, J., Leite, J.O., de Ogburn, R., Puglisi, M.J., VanHeest, J. and Fernandez, M.L. (2010). Consuming eggs for breakfast influences plasma glucose and ghrelin, while reducing energy intake during the next 24 hours in adult men. *Nutr Res* 30, 96-103.

Rayner, C.K., Samsom, M., Jones, K.L. and Horowitz, M. (2001). Relationships of upper gastrointestinal motor and sensory function with glycemic control. *Diabetes Care* 24, 371-381.

Raynor, H.A. and Epstein, L.H. (2001). Dietary variety, energy regulation, and obesity. *Psychol Bull* 127, 325-341.

Read, N.W., McFarlane, A., Kinsman, R.I., Bates, T.E., Blackhall, N.W., Farrar, G.B., Hall, J.C., Moss, G., Morris, A.P. and O'Neill, B. (1984). Effect of infusion of nutrient solutions into the ileum on gastrointestinal transit and plasma levels of neurotensin and enteroglucagon. *Gastroenterology* 86, 274-280.

Rehfeld, J.F. (1998). Accurate measurement of cholecystokinin in plasma. *Clin Chem* 44, 991-1001.

Rehfeld, J.F. (2004). Clinical endocrinology and metabolism. Cholecystokinin. *Best Pract Res Clin Endocrinol Metab* 18, 569-586.

Rehfeld, J.F. and Hansen, H.F. (1986). Characterization of preprocholecystokinin products in the porcine cerebral cortex. Evidence of different processing pathways. *J Biol Chem* 261, 5832-5840.

Rehfeld, J.F., Sun, G., Christensen, T. and Hillingso, J.G. (2001). The predominant cholecystokinin in human plasma and intestine is cholecystokinin-33. *J Clin Endocrinol Metab* 86, 251-258.

Reynolds, K., Chin, A., Lees, K.A., Nguyen, A., Bujnowski, D. and He, J. (2006). A meta-analysis of the effect of soy protein supplementation on serum lipids. *Am J Cardiol* 98, 633-640.

Rigaud, D., Paycha, F., Meulemans, A., Merrouche, M. and Mignon, M. (1998). Effect of psyllium on gastric emptying, hunger feeling and food intake in normal volunteers: a double blind study. *Eur J Clin Nutr* 52, 239-245.

Ritter, R.C. and Ladenheim, E.E. (1985). Capsaicin pretreatment attenuates suppression of food intake by cholecystokinin. *Am J Physiol* 248, R501-504.

Rolls, B.J. (2009). The relationship between dietary energy density and energy intake. *Physiol Behav* 97, 609-615.

Rolls, B.J. (2010). Plenary Lecture 1: Dietary strategies for the prevention and treatment of obesity. *Proc Nutr Soc* 69, 70-79.

Rolls, B.J. and Bell, E.A. (1999). Intake of fat and carbohydrate: role of energy density. *Eur J Clin Nutr* 53 Suppl 1, S166-173.

Rolls, B.J., Bell, E.A. and Thorwart, M.L. (1999). Water incorporated into a food but not served with a food decreases energy intake in lean women. *Am J Clin Nutr* 70, 448-455.

Rolls, B.J., Bell, E.A. and Waugh, B.A. (2000). Increasing the volume of a food by incorporating air affects satiety in men. *Am J Clin Nutr* 72, 361-368.

Rolls, B.J., Castellanos, V.H., Halford, J.C., Kilara, A., Panyam, D., Pelkman, C.L., Smith, G.P. and Thorwart, M.L. (1998). Volume of food consumed affects satiety in men. *Am J Clin Nutr* 67, 1170-1177.

Rolls, B.J., Fedoroff, I.C., Guthrie, J.F. and Laster, L.J. (1990). Foods with different satiating effects in humans. *Appetite* 15, 115-126.

Rolls, B.J., Gnizak, N., Summerfelt, A. and Laster, L.J. (1988a). Food intake in dieters and nondieters after a liquid meal containing medium-chain triglycerides. *Am J Clin Nutr* 48, 66-71.

Rolls, B.J., Hetherington, M. and Burley, V.J. (1988b). Sensory stimulation and energy density in the development of satiety. *Physiol Behav* 44, 727-733.

Rolls, B.J., Morris, E.L. and Roe, L.S. (2002). Portion size of food affects energy intake in normal-weight and overweight men and women. *Am J Clin Nutr* 76, 1207-1213.

Rolls, B.J., Roe, L.S., Kral, T.V., Meengs, J.S. and Wall, D.E. (2004). Increasing the portion size of a packaged snack increases energy intake in men and women. *Appetite* 42, 63-69.

Rolls, B.J., Roe, L.S. and Meengs, J.S. (2006). Reductions in portion size and energy density of foods are additive and lead to sustained decreases in energy intake. *Am J Clin Nutr* 83, 11-17.

Rolls, B.J., Roe, L.S. and Meengs, J.S. (2007). The effect of large portion sizes on energy intake is sustained for 11 days. *Obesity (Silver Spring)* 15, 1535-1543.

Rolls, B.J., Rolls, E.T., Rowe, E.A. and Sweeney, K. (1981). Sensory specific satiety in man. *Physiol Behav* 27, 137-142.

Rolls, B.J., Rowe, E.A. and Rolls, E.T. (1982). How sensory properties of foods affect human feeding behavior. *Physiol Behav* 29, 409-417.

Rolls, B.J., Rowe, E.A., Rolls, E.T., Kingston, B., Megson, A. and Gunary, R. (1981). Variety in a meal enhances food intake in man. *Physiol Behav* 26, 215-221.

Rolls, E.T. and Rolls, J.H. (1997). Olfactory sensory-specific satiety in humans. *Physiol Behav* 61, 461-473.

Romero, A., Kirchner, H., Heppner, K., Pfluger, P.T., Tschop, M.H. and Nogueiras, R. (2010). GOAT: the master switch for the ghrelin system? *Eur J Endocrinol* 163, 1-8.

Rosen, L.A., Ostman, E.M. and Bjorck, I.M. (2011). Effects of cereal breakfasts on postprandial glucose, appetite regulation and voluntary energy intake at a subsequent standardized lunch; focusing on rye products. *Nutr J* 10, 7.

Sakata, I., Nakamura, K., Yamazaki, M., Matsubara, M., Hayashi, Y., Kangawa, K. and Sakai, T. (2002). Ghrelin-producing cells exist as two types of cells, closed- and opened-type cells, in the rat gastrointestinal tract. *Peptides* 23, 531-536.

Sakata, I. and Sakai, T. (2010). Ghrelin cells in the gastrointestinal tract. *Int J Pept* 2010, 945056.

Salvy, S.J., Howard, M., Read, M. and Mele, E. (2009). The presence of friends increases food intake in youth. *Am J Clin Nutr* 90, 282-287.

Samra RA. Fats and Satiety. In: Montmayeur JP, le Coutre J, editors. Fat Detection: Taste, Texture, and Post Ingestive EffectsBoca Raton (FL): Taylor & Francis Group, LLC; 2010.

Samra, R.A. and Anderson, G.H. (2007). Insoluble cereal fiber reduces appetite and short-term food intake and glycemic response to food consumed 75 min later by healthy men. *Am J Clin Nutr* 86, 972-979.

Sanaka, M. and Nakada, K. (2010). Stable isotope breath tests for assessing gastric emptying: A comprehensive review. *J Smooth Muscle Res* 46, 267-280.

Sanggaard, K.M., Holst, J.J., Rehfeld, J.F., Sandström, B., Raben, A. and Tholstrup, T. (2004). Different effects of whole milk and a fermented milk with the same fat and lactose content on gastric emptying and postprandial lipaemia, but not on glycaemic response and appetite. *Br J Nutr* 92, 447-459.

Santangelo, A., Peracchi, M., Conte, D., Fraquelli, M. and Porrini, M. (1998). Physical state of meal affects gastric emptying, cholecystokinin release and satiety. *Br J Nutr* 80, 521-527.

Savage, A.P., Adrian, T.E., Carolan, G., Chatterjee, V.K. and Bloom, S.R. (1987). Effects of peptide YY (PYY) on mouth to caecum intestinal transit time and on the rate of gastric emptying in healthy volunteers. *Gut* 28, 166-170.

Schneeman, B.O. (2002). Gastrointestinal physiology and functions. *Br J Nutr* 88 Suppl 2, S159-163.

Schroeder, N., Gallaher, D.D., Arndt, E.A. and Marquart, L. (2009). Influence of whole grain barley, whole grain wheat, and refined rice-based foods on short-term satiety and energy intake. *Appetite* 53, 363-369.

Schulze, K. (2006). Imaging and modelling of digestion in the stomach and the duodenum. *Neurogastroenterol Motil* 18, 172-183.

Schwartz, G.J. and Moran, T.H. (1994). CCK elicits and modulates vagal afferent activity arising from gastric and duodenal sites. *Ann N Y Acad Sci* 713, 121-128.

Schwartz, M.W., Woods, S.C., Porte, D.,Jr, Seeley, R.J. and Baskin, D.G. (2000). Central nervous system control of food intake. *Nature* 404, 661-671.

Seimon, R.V., Wooster, T., Otto, B., Golding, M., Day, L., Little, T.J., Horowitz, M., Clifton, P.M. and Feinle-Bisset, C. (2009). The droplet size of intraduodenal fat emulsions influences antropyloroduodenal motility, hormone release, and appetite in healthy males. *Am J Clin Nutr* 89, 1729-1736.

Sepple, C.P. and Read, N.W. (1989). Gastrointestinal correlates of the development of hunger in man. *Appetite* 13, 183-191.

Shiiya, T., Nakazato, M., Mizuta, M., Date, Y., Mondal, M.S., Tanaka, M., Nozoe, S., Hosoda, H., Kangawa, K. and Matsukura, S. (2002). Plasma ghrelin levels in lean and obese humans and the effect of glucose on ghrelin secretion. *J Clin Endocrinol Metab* 87, 240-244.

Shikany, J.M., Vaughan, L.K., Baskin, M.L., Cope, M.B., Hill, J.O. and Allison, D.B. (2010). Is dietary fat "fattening"? A comprehensive research synthesis. *Crit Rev Food Sci Nutr* 50, 699-715.

Shin, A.C., Zheng, H. and Berthoud, H.R. (2009). An expanded view of energy homeostasis: neural integration of metabolic, cognitive, and emotional drives to eat. *Physiol Behav* 97, 572-580.

Singh, H. and Sarkar, A. (2011). Behaviour of protein-stabilised emulsions under various physiological conditions. *Adv Colloid Interface Sci* 165, 47-57.

Slavin, J. and Green, H. (2007). Dietary fibre and satiety. *Nutrition Bulletin* 32, 32-42.

Slavin, J.L. (2005). Dietary fiber and body weight. *Nutrition* 21, 411-418.

Slavin, J.L. (2008). Position of the American Dietetic Association: health implications of dietary fiber. *J Am Diet Assoc* 108, 1716-1731.

Slavin, J.L., Savarino, V., Paredes-Diaz, A. and Fotopoulos, G. (2009). A review of the role of soluble fiber in health with specific reference to wheat dextrin. *J Int Med Res* 37, 1-17.

Sloth, B., Holst, J.J., Flint, A., Gregersen, N.T. and Astrup, A. (2007). Effects of PYY1-36 and PYY3-36 on appetite, energy intake, energy expenditure, glucose and fat metabolism in obese and lean subjects. *Am J Physiol Endocrinol Metab* 292, E1062-1068.

Smeets, A.J., Soenen, S., Luscombe-Marsh, N.D., Ueland, O. and Westerterp-Plantenga, M.S. (2008). Energy expenditure, satiety, and plasma ghrelin, glucagon-like peptide 1, and peptide tyrosine-tyrosine concentrations following a single high-protein lunch. *J Nutr* 138, 698-702.

Smeets, P.A., Erkner, A. and de Graaf, C. (2010). Cephalic phase responses and appetite. *Nutr Rev* 68, 643-655.

Soenen, S. and Westerterp-Plantenga, M.S. (2008). Proteins and satiety: implications for weight management. *Curr Opin Clin Nutr Metab Care* 11, 747-751.

Soffer, E.E. and Adrian, T.E. (1992). Effect of meal composition and sham feeding on duodenojejunal motility in humans. *Dig Dis Sci* 37, 1009-1014.

Solah, V.A., Kerr, D.A., Adikara, C.D., Meng, X., Binns, C.W., Zhu, K., Devine, A. and Prince, R.L. (2010). Differences in satiety effects of alginate- and whey protein-based foods. *Appetite* 54, 485-491.

Sorensen, L.B., Moller, P., Flint, A., Martens, M. and Raben, A. (2003). Effect of sensory perception of foods on appetite and food intake: a review of studies on humans. *Int J Obes Relat Metab Disord* 27, 1152-1166.

Spiegel, T.A., Fried, H., Hubert, C.D., Peikin, S.R., Siegel, J.A. and Zeiger, L.S. (2000). Effects of posture on gastric emptying and satiety ratings after a nutritive liquid and solid meal. *Am J Physiol Regul Integr Comp Physiol* 279, R684-694.

Spiegel, T.A., Hubert, C.D., Fried, H., Peikin, S.R., Siegel, J.A. and Zeiger, L.S. (1997). Contribution of gastric and postgastric feedback to satiation and satiety in women. *Physiol Behav* 62, 1125-1136.

Spiegel, T.A., Kaplan, J.M., Alavi, A., Kim, P.S. and Tse, K.K. (1994). Effects of soup preloads on gastric emptying and fullness ratings following an egg sandwich meal. *Physiol Behav* 56, 571-575.

Spiller, R.C., Trotman, I.F., Higgins, B.E., Ghatei, M.A., Grimble, G.K., Lee, Y.C., Bloom, S.R., Misiewicz, J.J. and Silk, D.B. (1984). The ileal brake--inhibition of jejunal motility after ileal fat perfusion in man. *Gut* 25, 365-374.

Steinert, R.E. and Beglinger, C. (2011). Nutrient sensing in the gut: interactions between chemosensory cells, visceral afferents and the secretion of satiation peptides. *Physiol Behav* 105, 62-70.

Steinert, R.E., Frey, F., Topfer, A., Drewe, J. and Beglinger, C. (2011a). Effects of carbohydrate sugars and artificial sweeteners on appetite and the secretion of gastrointestinal satiety peptides. *Br J Nutr* 105, 1320-1328.

Steinert, R.E., Gerspach, A.C., Gutmann, H., Asarian, L., Drewe, J. and Beglinger, C. (2011b). The functional involvement of gut-expressed sweet taste receptors in glucose-stimulated secretion of glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). *Clin Nutr* 30, 524-532.

Steinert, R.E., Meyer-Gerspach, A.C. and Beglinger, C. (2012). The role of the stomach in the control of appetite and the secretion of satiation peptides. *Am J Physiol Endocrinol Metab* 302, E666-673.

St-Onge, M.P., Ross, R., Parsons, W.D. and Jones, P.J. (2003). Medium-chain triglycerides increase energy expenditure and decrease adiposity in overweight men. *Obes Res* 11, 395-402.

Strik, C.M., Lithander, F.E., McGill, A.T., MacGibbon, A.K., McArdle, B.H. and Poppitt, S.D. (2010). No evidence of differential effects of SFA, MUFA or PUFA on post-ingestive satiety and energy intake: a randomised trial of fatty acid saturation. *Nutr J* 9, 24.

Stubbs, R.J. and Harbron, C.G. (1996). Covert manipulation of the ratio of medium- to long-chain triglycerides in isoenergetically dense diets: effect on food intake in ad libitum feeding men. *Int J Obes Relat Metab Disord* 20, 435-444.

Stubbs, R.J., Hughes, D.A., Johnstone, A.M., Rowley, E., Reid, C., Elia, M., Stratton, R., Delargy, H., King, N. and Blundell, J.E. (2000). The use of visual analogue scales to assess motivation to eat in human subjects: a review of their reliability and validity with an evaluation of new hand-held computerized systems for temporal tracking of appetite ratings. *Br J Nutr* 84, 405-415.

Stull, A.J., Apolzan, J.W., Thalacker-Mercer, A.E., Iglay, H.B. and Campbell, W.W. (2008). Liquid and solid meal replacement products differentially affect postprandial appetite and food intake in older adults. *J Am Diet Assoc* 108, 1226-1230.

Stunkard, A.J. and Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *J Psychosom Res* 29, 71-83.

Suortti, T. (1993). Size-exclusion chromatographic determination of beta-glucan with postcolumn reaction detection. *J Chromatogr* 632, 105-110.

Swinburn, B.A., Sacks, G., Hall, K.D., McPherson, K., Finegood, D.T., Moodie, M.L. and Gortmaker, S.L. (2011). The global obesity pandemic: shaped by global drivers and local environments. *Lancet* 378, 804-814.

Tannous dit El Khoury, D., Obeid, O., Azar, S.T. and Hwalla, N. (2006). Variations in postprandial ghrelin status following ingestion of high-carbohydrate, high-fat, and high-protein meals in males. *Ann Nutr Metab* 50, 260-269.

Tarini, J. and Wolever, T.M. (2010). The fermentable fibre inulin increases postprandial serum short-chain fatty acids and reduces free-fatty acids and ghrelin in healthy subjects. *Appl Physiol Nutr Metab* 35, 9-16.

Tatemoto, K. and Mutt, V. (1980). Isolation of two novel candidate hormones using a chemical method for finding naturally occurring polypeptides. *Nature* 285, 417-418.

Teff, K.L., Elliott, S.S., Tschop, M., Kieffer, T.J., Rader, D., Heiman, M., Townsend, R.R., Keim, N.L., D'Alessio, D. and Havel, P.J. (2004). Dietary fructose reduces circulating insulin and leptin, attenuates postprandial suppression of ghrelin, and increases triglycerides in women. *J Clin Endocrinol Metab* 89, 2963-2972.

Thomsen, C., Rasmussen, O., Lousen, T., Holst, J.J., Fenselau, S., Schrezenmeir, J. and Hermansen, K. (1999). Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. *Am J Clin Nutr* 69, 1135-1143.

Tieken, S.M., Leidy, H.J., Stull, A.J., Mattes, R.D., Schuster, R.A. and Campbell, W.W. (2007). Effects of solid versus liquid meal-replacement products of similar energy content on hunger, satiety, and appetite-regulating hormones in older adults. *Horm Metab Res* 39, 389-394.

Tiwary, C.M., Ward, J.A. and Jackson, B.A. (1997). Effect of pectin on satiety in healthy US Army adults. *J Am Coll Nutr* 16, 423-428.

Tolle, V., Kadem, M., Bluet-Pajot, M.T., Frere, D., Foulon, C., Bossu, C., Dardennes, R., Mounier, C., Zizzari, P., Lang, F., et al. (2003). Balance in ghrelin and leptin plasma levels in anorexia nervosa patients and constitutionally thin women. *J Clin Endocrinol Metab* 88, 109-116.

Tournier, A. and Louis-Sylvestre, J. (1991). Effect of the physical state of a food on subsequent intake in human subjects. *Appetite* 16, 17-24.

Tremblay, F., Lavigne, C., Jacques, H. and Marette, A. (2007). Role of dietary proteins and amino acids in the pathogenesis of insulin resistance. *Annu Rev Nutr* 27, 293-310.

Trowell, H., Southgate, D.A., Wolever, T.M., Leeds, A.R., Gassull, M.A. and Jenkins, D.J. (1976). Letter: Dietary fibre redefined. *Lancet* 1, 967.

Turnbull, W.H. and Thomas, H.G. (1995). The effect of a Plantago ovata seed containing preparation on appetite variables, nutrient and energy intake. *Int J Obes Relat Metab Disord* 19, 338-342.

Turton, M.D., O'Shea, D., Gunn, I., Beak, S.A., Edwards, C.M., Meeran, K., Choi, S.J., Taylor, G.M., Heath, M.M., Lambert, P.D., et al. (1996). A role for glucagon-like peptide-1 in the central regulation of feeding. *Nature* 379, 69-72.

Uhe, A.M., Collier, G.R. and O'Dea, K. (1992). A comparison of the effects of beef, chicken and fish protein on satiety and amino acid profiles in lean male subjects. *J Nutr* 122, 467-472.

Van Citters, G.W. and Lin, H.C. (1999). The ileal brake: a fifteen-year progress report. *Curr Gastroenterol Rep* 1, 404-409.

van Dam, R.M. and Seidell, J.C. (2007). Carbohydrate intake and obesity. *Eur J Clin Nutr* 61 Suppl 1, S75-99.

Van Wymelbeke, V., Himaya, A., Louis-Sylvestre, J. and Fantino, M. (1998). Influence of medium-chain and long-chain triacylglycerols on the control of food intake in men. *Am J Clin Nutr* 68, 226-234.

Van Wymelbeke, V., Louis-Sylvestre, J. and Fantino, M. (2001). Substrate oxidation and control of food intake in men after a fat-substitute meal compared with meals supplemented with an isoenergetic load of carbohydrate, long-chain triacylglycerols, or medium-chain triacylglycerols. *Am J Clin Nutr* 74, 620-630.

Veldhorst, M., Smeets, A., Soenen, S., Hochstenbach-Waelen, A., Hursel, R., Diepvens, K., Lejeune, M., Luscombe-Marsh, N. and Westerterp-Plantenga, M. (2008). Protein-induced satiety: effects and mechanisms of different proteins. *Physiol Behav* 94, 300-307.

Veldhorst, M.A., Nieuwenhuizen, A.G., Hochstenbach-Waelen, A., van Vught, A.J., Westerterp, K.R., Engelen, M.P., Brummer, R.J., Deutz, N.E. and Westerterp-Plantenga, M.S. (2009a). Dose-dependent satiating effect of whey relative to casein or soy. *Physiol Behav* 96, 675-682.

Veldhorst, M.A., Nieuwenhuizen, A.G., Hochstenbach-Waelen, A., Westerterp, K.R., Engelen, M.P., Brummer, R.J., Deutz, N.E. and Westerterp-Plantenga, M.S. (2009b). A breakfast with alpha-lactalbumin, gelatin, or gelatin + TRP lowers energy intake at lunch compared with a breakfast with casein, soy, whey, or whey-GMP. *Clin Nutr* 28, 147-155.

Veldhorst, M.A., Nieuwenhuizen, A.G., Hochstenbach-Waelen, A., Westerterp, K.R., Engelen, M.P., Brummer, R.J., Deutz, N.E. and Westerterp-Plantenga, M.S. (2009c). Comparison of the effects of a high- and normal-casein breakfast on satiety, 'satiety' hormones, plasma amino acids and subsequent energy intake. *Br J Nutr* 101, 295-303.

Veldhorst, M.A., Nieuwenhuizen, A.G., Hochstenbach-Waelen, A., Westerterp, K.R., Engelen, M.P., Brummer, R.J., Deutz, N.E. and Westerterp-Plantenga, M.S. (2009d). Effects of complete whey-protein breakfasts versus whey without GMP-breakfasts on energy intake and satiety. *Appetite* 52, 388-395.

Veldhorst, M.A., Nieuwenhuizen, A.G., Hochstenbach-Waelen, A., Westerterp, K.R., Engelen, M.P., Brummer, R.J., Deutz, N.E. and Westerterp-Plantenga, M.S. (2009e). Effects of high and normal soyprotein breakfasts on satiety and subsequent energy intake, including amino acid and 'satiety' hormone responses. *Eur J Nutr* 48, 92-100.

Verdich, C., Toubro, S., Buemann, B., Lysgard Madsen, J., Juul Holst, J. and Astrup, A. (2001). The role of postprandial releases of insulin and incretin hormones in meal-induced satiety--effect of obesity and weight reduction. *Int J Obes Relat Metab Disord* 25, 1206-1214.

Vickery, H.B. (1950). The origin of the word protein. *Yale J Biol Med* 22, 387-393.

Vitaglione, P., Lumaga, R.B., Montagnese, C., Messia, M.C., Marconi, E. and Scalfi, L. (2010). Satiating effect of a barley beta-glucan-enriched snack. *J Am Coll Nutr* 29, 113-121.

Vitaglione, P., Lumaga, R.B., Stanzione, A., Scalfi, L. and Fogliano, V. (2009). beta-Glucan-enriched bread reduces energy intake and modifies plasma ghrelin and peptide YY concentrations in the short term. *Appetite* 53, 338-344.

Vrang, N., Phifer, C.B., Corkern, M.M. and Berthoud, H.R. (2003). Gastric distension induces c-Fos in medullary GLP-1/2-containing neurons. *Am J Physiol Regul Integr Comp Physiol* 285, R470-478.

Vuksan, V., Panahi, S., Lyon, M., Rogovik, A.L., Jenkins, A.L. and Leiter, L.A. (2009). Viscosity of fiber preloads affects food intake in adolescents. *Nutr Metab Cardiovasc Dis* 19, 498-503.

Wanders, A.J., van den Borne, J.J., de Graaf, C., Hulshof, T., Jonathan, M.C., Kristensen, M., Mars, M., Schols, H.A. and Feskens, E.J. (2011). Effects of dietary fibre on subjective appetite, energy intake and body weight: a systematic review of randomized controlled trials. *Obes Rev* 12, 724-739.

Wansink, B. (2004). Environmental factors that increase the food intake and consumption volume of unknowing consumers. *Annu Rev Nutr* 24, 455-479.

Wansink, B. (2010). From mindless eating to mindlessly eating better. *Physiol Behav* 100, 454-463.

Weickert, M.O. and Pfeiffer, A.F. (2008). Metabolic effects of dietary fiber consumption and prevention of diabetes. *J Nutr* 138, 439-442.

Weickert, M.O., Spranger, J., Holst, J.J., Otto, B., Koebnick, C., Mohlig, M. and Pfeiffer, A.F. (2006). Wheat-fibre-induced changes of postprandial peptide YY and ghrelin responses are not associated with acute alterations of satiety. *Br J Nutr* 96, 795-798.

Westerterp, K.R., Wilson, S.A. and Rolland, V. (1999). Diet induced thermogenesis measured over 24h in a respiration chamber: effect of diet composition. *Int J Obes Relat Metab Disord* 23, 287-292.

Westerterp-Plantenga, M.S. (2001). Analysis of energy density of food in relation to energy intake regulation in human subjects. *Br J Nutr* 85, 351-361.

Westerterp-Plantenga, M.S. (2004a). Effects of energy density of daily food intake on long-term energy intake. *Physiol Behav* 81, 765-771.

Westerterp-Plantenga, M.S. (2004b). Fat intake and energy-balance effects. *Physiol Behav* 83, 579-585.

Westerterp-Plantenga, M.S., Nieuwenhuizen, A., Tome, D., Soenen, S. and Westerterp, K.R. (2009). Dietary protein, weight loss, and weight maintenance. *Annu Rev Nutr* 29, 21-41.

WHO, (2003). *Diet, Nutrition and the Prevention of Chronic Diseases. Report of a Joint WHO/ FAO Expert Consultation.* WHO Technical Report Series, No. 916. World Health Organization, Geneva.

Willems, M., Quartero, A.O. and Numans, M.E. (2001). How useful is paracetamol absorption as a marker of gastric emptying? A systematic literature study. *Dig Dis Sci* 46, 2256-2262.

Williams, D.L., Cummings, D.E., Grill, H.J. and Kaplan, J.M. (2003). Meal-related ghrelin suppression requires postgastric feedback. *Endocrinology* 144, 2765-2767.

Williamson, D.A., Geiselman, P.J., Lovejoy, J., Greenway, F., Volaufova, J., Martin, C.K., Arnett, C. and Ortego, L. (2006). Effects of consuming mycoprotein, tofu or chicken upon subsequent eating behaviour, hunger and safety. *Appetite* 46, 41-48.

Willis, H.J., Thomas, W., Eldridge, A.L., Harkness, L., Green, H. and Slavin, J.L. (2010). Increasing doses of fiber do not influence short-term satiety or food intake and are inconsistently linked to gut hormone levels. *Food Nutr Res* 54, 5135.

Willis, H.J., Thomas, W., Willis, D.J. and Slavin, J.L. (2011). Feasibility of measuring gastric emptying time, with a wireless motility device, after subjects consume fiber-matched liquid and solid breakfasts. *Appetite* 57, 38-44.

Witte, A.B., Gryback, P., Holst, J.J., Hilsted, L., Hellstrom, P.M., Jacobsson, H. and Schmidt, P.T. (2009). Differential effect of PYY1-36 and PYY3-36 on gastric emptying in man. *Regul Pept* 158, 57-62.

Wolf, A., Bray, G.A. and Popkin, B.M. (2008). A short history of beverages and how our body treats them. *Obes Rev* 9, 151-164.

Wolf, B.W., Wolever, T.M., Lai, C.S., Bolognesi, C., Radmard, R., Maharry, K.S., Garleb, K.A., Hertzler, S.R. and Firkins, J.L. (2003). Effects of a beverage containing an enzymatically induced-viscosity dietary fiber, with or without fructose, on the postprandial glycemic response to a high glycemic index food in humans. *Eur J Clin Nutr* 57, 1120-1127.

Wong, J.M., de Souza, R., Kendall, C.W., Emam, A. and Jenkins, D.J. (2006). Colonic health: fermentation and short chain fatty acids. *J Clin Gastroenterol* 40, 235-243.

Wood, P.J., Braaten, J.T., Scott, F.W., Riedel, K.D., Wolynetz, M.S. and Collins, M.W. (1994). Effect of dose and modification of viscous properties of oat gum on plasma glucose and insulin following an oral glucose load. *Br J Nutr* 72, 731-743.

Woods, S.C. (2009). The control of food intake: behavioral versus molecular perspectives. *Cell Metab* 9, 489-498.

Wren, A.M. and Bloom, S.R. (2007). Gut hormones and appetite control. *Gastroenterology* 132, 2116-2130.

Wynne, K., Stanley, S. and Bloom, S. (2004). The gut and regulation of body weight. *J Clin Endocrinol Metab* 89, 2576-2582.

Wynne, K., Stanley, S., McGowan, B. and Bloom, S. (2005). Appetite control. *J Endocrinol* 184, 291-318.

Yao, M. and Roberts, S.B. (2001). Dietary energy density and weight regulation. *Nutr Rev* 59, 247-258.

Yeomans, M.R. (1998). Taste, palatability and the control of appetite. *Proc Nutr Soc* 57, 609-615.

Yeomans, M.R. (2000). Rating changes over the course of meals: what do they tell us about motivation to eat? *Neurosci Biobehav Rev* 24, 249-259.

Yvon, M., Beucher, S., Guilloteau, P., Le Huerou-Luron, I. and Corring, T. (1994). Effects of caseinomacropeptide (CMP) on digestion regulation. *Reprod Nutr Dev* 34, 527-537.

Zheng, H., Lenard, N.R., Shin, A.C. and Berthoud, H.R. (2009). Appetite control and energy balance regulation in the modern world: reward-driven brain overrides repletion signals. *Int J Obes (Lond)* 33 Suppl 2, S8-13.

Zijlstra, N., de Wijk, R.A., Mars, M., Stafleu, A. and de Graaf, C. (2009a). Effect of bite size and oral processing time of a semisolid food on satiation. *Am J Clin Nutr* 90, 269-275.

Zijlstra, N., Mars, M., de Wijk, R.A., Westerterp-Plantenga, M.S., Holst, J.J. and de Graaf, C. (2009b). Effect of viscosity on appetite and gastro-intestinal hormones. *Physiol Behav* 97, 68-75.

Zwirska-Korczala, K., Konturek, S.J., Sodowski, M., Wylezol, M., Kuka, D., Sowa, P., Adamczyk-Sowa, M., Kukla, M., Berdowska, A., Rehfeld, J.F., et al. (2007). Basal and postprandial plasma levels of PYY, ghrelin, cholecystokinin, gastrin and insulin in women with moderate and morbid obesity and metabolic syndrome. *J Physiol Pharmacol* 58 Suppl 1, 13-35.

APPENDICES

Appendix 1. Postprandial studies on dietary protein and appetite, food intake and gastrointestinal (GI) hormone responses.

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Hall et al. 2003	Preloads: - whey (48 g) - casein (48 g)	Liquid	1) 16 (8 F, 8 M) NW 2) 9 (8 F, 1 M) NW	3 h	1) Fullness / hunger / desire to eat: ns 2) Fullness: whey > casein Desire to eat: whey < casein	CCK: increased after whey GLP-1: increased after whey	Ad lib EI: 1) whey < casein
Anderson et al. 2004	1) Drinks: - egg albumen, whey protein, soy, sucrose - water control - sucrose and protein provided with 0.65 g/kg - *ad lib* meal 1 h later 2) 50 g whey protein, egg albumen - water control - *ad lib* meal 1 h later 3) 50 g whey protein, whey protein hydrolysate - water control - *ad lib* meal 2 h later 4) soy protein (50 g), soy protein (25 g) with amylose (25 g) or glucose (25 g) - ad lib lunch 1 h later	Liquid	1) 13 M, NW 2) 22 M, NW 3) 10 M, NW, OW 4) 13 M, NW	1) 1h 2) 1 h 3) 2 h 4) 1 h	..	..	1) *Ad lib*: whey, soy < egg, control 2) *Ad lib*: whey < egg, control 3) *Ad lib*: whey protein & hydrolysate < control 4) *Ad lib*: soy < soy/amylose, control
Calbet and Holst 2004	Solutions - whey whole protein - casein whole protein - whey peptide hydrolysate - casein hydrolysate	Liquid	6 M, NW	2 h	..	GLP-1: ns PYY: ns	..
Sanggaard et al. 2004	Milk-based meals: - whole milk (M, 48g protein) - fermented whole milk (A-38, 52 g protein)	Liquid	8 M, NW	8 h	Hunger / desire to eat: ns Satiety, fullness: ns	CCK, GLP-1, PYY: after A-38 greater increase and quicker decrease of CCK, PYY, GLP-1 vs M	..

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Bowen et al. 2006a	Preload, soup: - whey 51 g (71E%) - soy 50 g (71E%) - gluten 51 g (71 E%) - glucose 63 g (87E%) - ad lib meal 3 h later	Liquid	38 M (18 NW, 20 OW)	3 h	Hunger, ns	CCK: whey, soy, gluten > glucose Total ghrelin decrease: whey, soy, gluten > glucose GLP-1: whey, soy, gluten > glucose	*Ad lib* EI: gluten < glucose
Bowen et al. 2006b	Isoenergetic preload: - whey (55 g) - casein (55 g) - lactose(56 g) - glucose(60 g)	Liquid	19 M, OW	3 h	Hunger: ns Desire to eat: ns Satiation: ns Overall appetite: glucose > proteins, lactose	CCK: proteins > glucose, lactose Total ghrelin decrease: proteins, lactose > glucose	*ad lib* EI: proteins, lactose < glucose
Tannous dit El Khoury et al. 2006	Meals: - high-carbohydrate (HC, 60% CHO) - high-fat (HF, 50% fat) - high-protein (HP, 50% protein) - prot source, soy / whey protein	Liquid	10 M, NW, OW	3 h	..	Acylated ghrelin decrease: HC > HF, HP longer suppression after HP vs HC, HF	..
Harper et al. 2007	Drinks: - cola (protein 0 g) - chocolate milk, protein (13 g) - *ad lib* lunch 30 min later	Liquid	22 M, NW	4 h	Hunger: milk < cola Satiety, fullness: milk > cola	..	EI: ns
Karamanlis et al. 2007	Drinks: - 30 g gelatin - 50 g glucose - 50 g glucose with 30 g gelatin	Liquid	9 M, NW, OW	3 h	..	GLP-1: ns	..
Bertenshaw et al. 2008	Dairy fruit drinks: - carbohydrate-enriched (CHO) - protein-enriched (whey, 50 E% protein, 38 g) - low-energy control - 30 and 120 min before *ad lib* lunch	Liquid	18 M, NW	2 h	Hunger: ns Fullness: ns	..	EI, protein < CHO, control preload timing; no effect

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Diepvens et al. 2008	Shake: - whey protein, 15 g (WP) - pea protein hydrolysate, 15 g (PPH) - combination, 7.5 g WP and 7.5 g PPH (WP+PPH) - milk protein, 15 g (MP) - 25 E% protein level	Liquid	39 (20 F, 19 M) OW	1) 4 h (appetite , blood samples) 2) 7 h (appetite, EI at 180 min)	Hunger: PPH < MP, PPH < WP , PPH < WP+PPH Satiety, fullness: PPH > MP 2) Satiety, fullness: PPH > MP, WP+PPH WP > MP, WP+PPH Desire to eat: PPH < MP, WP+PPH	CCK: WP, PPH, WP+PPH < MP Active ghrelin decrease: WP+PPH > MP GLP-1: WP, PPH, WP+PPH < MP PYY: WP+PPH > MP, others	*ad lib* EI: 2) ns
Bertenshaw et al. 2009	Dairy fruit drinks: - low-protein (13 E%, 9 g) - medium protein (25 E%, 17 g) - high-protein (50 E%, 34 g) - low-energy control - after 30 min *ad lib* meal	Liquid	28 M, NW		Hunger: ns Fullness: ns	..	EI: medium / high protein < control Dose response effect of protein level on intake
Dove et al. 2009	Drinks: - skim milk (25 g protein) - fruit drink (< 1 g protein)	Liquid	34 (21 , 13 M) OW	4 h	Satisfaction: milk < fruit drink Fullness: milk < fruit drink	..	EI: milk < fruit drink
Lam et al. 2009	Milkshake: - whey protein isolate (WPI) without GMP (46 g protein) - WPI with 21% GMP (45 g protein) - WPI with 21% GMP plus added GMP (43 g protein) - carbohydrate control (10 g protein) - *ad lib* lunch 30 min later	Liquid	50 (19 M, 31 F) NW	90 min	Fullness: WPI with 21% GMP > others Hunger: ns	..	EI: ns

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Perrigue et al. 2009	Yoghurt with or without inulin (6g) - low-energy-density (12 g protein) - high-energy-density (12 g protein) - orange juice control	Liquid	38 (20 F, 18M) NW, OW	2 h	Hunger: all yogurt < juice Desire to eat: high-ED yogurts, low-ED high-fibre < juice Satiety: High-ED yogurts > low-ED no fibre Fullness: All yogurt > juice High-ED yogurts, low-ED high-fibre > low-ED no fibre	..	EI (*ad lib*): ns among yogurts
Akhavan et al. 2010	1) whey protein - 10, 20, 30, 40 g - water control 2) whey protein - 5, 10, 20, 40 g - 10 g whey prot hydrolysate - water control	Liquid	1) 16 M, NW 2) 12 M, 9 F, NW	30 min	Appetite, 1) and 2): ns	..	EI (*ad lib*): 1) 40 g < 20, 30 g WP < control
Astbury et al. 2010	Drinks: 1) Whey protein based drinks - 13, 25 and 50 g protein 2) Whey protein based drinks - 7, 13 and 25 g protein - *ad lib* lunch 90 min later	Liquid	1) 24 (12 F, 12 M) 2) 26 (13 F, 13 M)	1.5 h	Fullness: ns Hunger: ns	..	EI, 1) 50 , 25 g < 13 g 2) ns
Boelsma et al. 2010	Meal: - high-protein (35 E%) /low CHO (35 E%) (HP/LC) - low-protein (10 E%) / high CHO (60 E%) (LP/HC) - whey protein as source	Liquid	21 M, NW	4 h	Satisfaction: HP/LC > LP/HC Fullness: HP/LC > LP/HC Hunger: ns Desire to eat: HP/LC < LP/HC	CCK: HP/LC > LP/HC Total ghrelin decrease: HP/LC > LP/HC	*ad lib* EI: ns

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
El Khoury et al. 2010	- high-protein low fat (HPLF, 40% protein, 25% fat) - low-protein high fat (LPHF, 10% protein, 55% fat) - medium-protein medium-fat (MPMF, 25% protein, 40% fat) - CHO content 35%	Liquid	8M, NW	4 h	..	Acyl ghrelin: ns PYY3-36: HPLF, LPHF > MPMF	..
Hursel et al. 2010	Yoghurt drink: - normal-protein (NP), whole milk (15% protein) - high-protein (HP) with whey (41% protein) - HP with caseinomacropeptide-depleted alpha-lactalbumin - enriched whey protein (alpha-lac) (41% protein)	Liquid	35 (18 F, 17 M) NW	4 h	Hunger, desire to eat: alpha-lac < HP whey Fullness: ns	..	..
Pal and Ellis 2010	Meal: - high-protein (51 g) meals, whey, tuna, turkey, egg albumin - ad lib meal 4 h later	Liquid	22 M, NW	4 h	Hunger: whey < tuna < turkey, egg Fullness: whey, tuna > turkey, egg	..	Ad lib EI: whey < tuna < turkey, egg
Solah et al. 2010	Drinks: - low viscosity whey protein (30 g) (LVHP) - high viscosity low protein alginate-based (0.25 g) (HVLP) - low viscosity low protein alginate-based drink (LVLP)	Liquid	33, NW	4 h	Hunger: LVHP < LVLP HVLP < LVLP HVLP < LVHP	..	..
Acheson et al. 2011	Isocaloric meals: - 3 protein-rich meals (50% protein, ~57.4 g) of whey, casein, soy - CHO meal 95.5% (maltodextrin, dextrose monohydrate) - glucose meal, 40% (184 kcal, 46 g)	Liquid	23, NW	5.5 h	Hunger: Whey > cas, soy Desire to eat: Whey > cas, soy Satiety score: Cas, soy > whey Fullness: Cas, soy > whey	..	..

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Nilsson et al. 2004	Meals: - white wheat bread - milk (liquid) - cheese (solid) - whey (liquid) - cod (solid) - wheat gluten low (liquid), - wheat gluten high (liquid) - in all meals 18.2 g prot, except GL, WWB 2.8 g prot	Liquid / solid	12 (6 M, 6 F) NW	2 h	..	GLP-1: ns	..
Lang et al. 1998	Protein-modified lunches: -egg white (albumin) protein 61.4 g (modified 40.1 g) - casein, 71.1(43.6) - gelatin, 73.0 (46.4) - soy protein, 66.9 (47.0) - pea protein, 74.1 (47.5) - wheat gluten, 74.4 (47.1)	Solid / liquid	12 M, NW	8 h	Hunger: ns Satiety: ns Fullness: ns Desire to eat: ns	..	EI: ns
Lang et al. 1999	Protein-modified lunches (65% manipulated) - lunch 1.8 MJ, casein-low, prot 24.4 g (15.1 g, modified) gelatin-low, 25.2 (16.4) soy-low, 24.2 (16.4) - lunch 3.6 MJ, casein-high, 49.3 (30.6) gelatin-high, 50.8 (33.1) soy-high, 49.3 (33.5)	Solid / liquid	9 M, NW	8 h	Hunger (energy level): ns Satiety (prot type): ns Satiety (energy level): 3.6 MJ > 1.8 MJ	..	EI: ns
Erdmann et al. 2003	Meals: 1) CHO-rich (62% CHO) 2) 75 g glucose in water 3) fat-rich (85% fat) 4) protein-rich (250 g turkey (99% protein)	Solid, liquid	10 (3 M, 7 F) NW	3 h	..	Total ghrelin: decreased after solid CHO-rich meal and liquid glucose - decreased after fat-rich meal towards the end of the study period - increased to plateau after protein-rich meal	..

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Akhavan et al. 2011	Preload: 1) gelatin 6 g - gelatin solid - gelatin liquid - sweet gelatin liquid 2) 50g whey - acid whey solid - sweet whey solid - acid whey liquid - sweet whey liquid - water control	Solid/ liquid	1) 14 M, NW 2) 14 M, NW	1 h	Appetite: 1) solid gelatin < liquid gelatin 2) all whey < water sweet whey solid < sweet whey liquid	..	EI (*ad lib*): 1) ns 2) all whey < water among the whey meals, ns
Uhe et al. 1992	Meal: - 50 g protein from beef, chicken, fish	Solid	6 M, NW	3 h	Satiety: fish > chicken, beef	..	..
Blom et al. 2006a	Isocaloric dairy meals: - high-carbohydrate (CHO, 47 E%) - high-protein (HP, 58 E%, whey protein isolate)	Solid	15 M, NW	3 h	Hunger: ns Desire to eat: ns Fullness: ns	CCK: increased after HP Total ghrelin decrease: HP > HC Acyl ghrelin: ns GLP-1: HP tended to increase GLP-1 vs HC	*ad lib* EI: ns
Borzoei et al. 2006	Meal: - isoenergetic protein-rich (64 g) fish or beef (minced) dish - ad lib meal 4 h after	Solid	23 M, NW	4 h	Hunger, satiety: ns	..	*ad lib* EI: fish < beef
Williamson et al. 2006	Preload meal: - mycoprotein - tofu - chicken - 17 E% (~20 g) protein - sandwiches 20 min later	Solid	42 F, OW	4 h	Hunger: ns Fullness: ns	..	EI: mycoprotein, tofu < chicken
Smeets et al. 2008	Lunch: - adequate protein (AP, 10 E%) - high-proetin (HP, 25E%)	Solid	30 (19F, 11M) NW - obese	3 h	Satiety, HP > AP	Active ghrelin: ns GLP-1: HP < AP Total PYY: ns	..

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Hochstenbach-Waelen et al. 2009a	Custard: - isoenergetic 10% or 25% energy from casein	Solid	24 (12F, 12M) NW, OW	4 h (after breakfast)	Satiety: 25E% > 10E% Fullness: 25E% > 10E% Hunger: 25E% < 10E% Desire to eat: 25E% < 10E%	Total ghrelin: ns GLP-1: 25E% < 10E% PYY: 25E% < 10E%	..
Hochstenbach-Waelen et al. 2009b	Custards: - 4 isoenergetic, casein or gelatin at 10 E% or 25 E% protein	Solid	23 (11 M, 12 F) NW	4 h	Hunger: gelatin 10E% < casein 10 E%	Ghrelin: ns GLP-1: ns PYY: ns	..
Nieuwenhuizen et al. 2009	Custard: - alpha-lactalbumin ((α -lact), high tryptophan, TRP) - gelatin (low TRP) - gelatin with added TRP (gelatin+TRP) - 10 E% protein	Solid	24 (11 M, 13F) NW, OW	4 h	Hunger: α -lact < gelatin, gelatin + TRP	GLP-1: ns Active ghrelin: ns	*ad lib* EI: ns
Veldhorst et al. 2009a	Custards: - casein, soy or whey protein at 10 E% or 25 E% protein level	Solid	25 (11 M, 14 F) NW	4 h (appetite) 3 h (GLP-1, active ghrelin)	Hunger: At 10E%, whey < casein/ soy At 25E%, no differences in appetite ratings	GLP-1: at 25 E%, whey > casein Active ghrelin decrease: 10 E%, casein > soy	*ad lib* EI: ns
Veldhorst et al. 2009b	Custard: - casein - soy - whey - whey without glycomacropeptide (whey-GMP) - alpha-lactalbumin (a-lact) - gelatin - gelatin+ tryptophan (TRP) - at 10 E% or 25 E% protein - ad lib lunch 180 min after	Solid	24 (14 F, 10 M)	3 h	Satiety, hunger suppression: a-lact, gelatin, and/or gelatin+TRP > casein, soy, whey, and/or whey-GMP, both at 10 and 25 E%	Ghrelin 10 / 25 E %: ns GLP-1: 10E %, ns	EI at 10 / 25 E% protein: a-lact, gelatin (+TRP) < casein, soy, whey-GMP at 25 E% protein a-lact, gelatin +TRP < whey

(cont.)

Reference	Protein type / source / content	Physical state	Study subjects	Duration / Follow-up period	Appetite	GI hormone responses	Energy / food intake (EI)
Veldhorst et al. 2009c	Custard: - casein 10% or 25 E% protein	Solid	25 (11 M, 14F) NW - obese	4 h	Satiety, fullness: 25 E% > 10 E%	GLP- 1: ns Active ghrelin: ns	*ad lib* EI: ns
Veldhorst et al. 2009d	Custards: - whey or whey without glycomacropeptide GMP (WhGMP) at protein level 10% or 25%	Solid	25 (11M, 14 F) NW	4 h	Satiety: 10E% > 25E% irrespective of protein type	GLP-1: 25E% > 10E% Active ghrelin decrease: 25E% >10E% 25E% WhGMP > 10E% WhGMP	*ad lib* EI: whey < WhGMP irrespective of protein level
Veldhorst et al. 2009e	Custards: - 10 E% soy - 25E% soy	Solid	25 (14 F, 11 M) NW	4 h	Satiety: 25 E% > 10E%	Total ghrelin: ns GLP-1: ns	EI at lunch: ns
Ratliff et al. 2010	Isoenergetic breakfasts: - egg-based meal (23E% protein) - bagel-based meal (16E% protein)	Solid	21 M, NW, OW	3 h	Hunger: egg < bagel Desire to eat: ns Satisfaction: egg > bagel Fullness: ns	Total ghrelin: bagel > egg GLP-1: ns PYY: ns	*ad lib* EI: bagel > egg
Blatt et al. 2011	*ad lib* lunch and dinner: - covertly varied protein content, 10%, 15%, 20%, 25%, or 30E%	Solid	18 F, NW	24 h	Hunger: ns Fullness: ns	..	EI: ns
Charlton et al. 2011	Meals: - pork - beef - chicken - protein ~ 42g	Solid	30 F (19 NW, 8 obese)	3 h	Hunger: ns Desire to eat: ns Satiety/fullness: ns	Ghrelin: ns CCK: ns Total PYY: pork > chicken	EI (*ad lib* lunch): ns

Ad lib, *ad libitum* meal; CCK, cholecystokinin; CHO, carbohydrate; DF, dietary fibre; E%, percentage of total energy; F, female; GLP-1, glucagon-like peptide 1; M, male; ns, non-significant; NW, normal weight; OW, overweight; PYY, peptide YY; vs, versus, ..; not measured / no information available.

Appendix 2. Postprandial studies on dietary fibre (DF) and appetite, food intake and gastrointestinal (GI) hormone responses.

Reference	Fibre type / fibre source	Physical state	Study subjects	Duration/ Follow-up period	Appetite	GI hormone responses	Energy/ food intake (EI)
Bergmann et al. 1992	Psyllium 10.8 g in 100 ml water - one minute later a standard solid meal	Liquid	12 (3 M, 9 F), OW	6 h	Psyllium increased satiety, decreased hunger	..	..
French and Read 1994	Soup: - 3% guar gum in high- and low-fat soups	Liquid	8 M, NW, OW	3 h	Hunger: reduced after high-fat soup + guar Fullness: increased after high-fat soup + guar	..	..
Turnbull and Thomas 1995	Preload: - psyllium 20 g - placebo 20 g - water (200 ml) - 3 h premeal and same dose immediately pre-meal - lunch 3 h after	Liquid	17 F	3 h	Fullness: psyllium > placebo, water	..	Total fat intake: psyllium < water
Tiwary et al. 1997	Drink: - pectin; 5,10,15 and 20 g with orange juice (~450 ml)	Liquid	74 (49 M / 25 F) NW	4 h	Satiety: increased already after the lowest dose	..	..
Rigaud et al. 1998	Preload: - psyllium, 7.4 g or placebo - after 15 min solid test meal	Liquid	14 (7 M, 7 F) NW	6 h	Hunger: psyllium < placebo Fullness: ns	..	EI: psyllium < placebo
Hoad et al. 2004	Drinks: - milk-based drinks with weak-gelling alginate, strong-gelling alginate, and viscous guar (1 % by weight) - milk-based control drink	Liquid	12 (3 M, 9 F) NW	4 h	Hunger: strong-gelling alginate > control Fullness: strong-gelling alginate, guar > control	..	..
Adam and Westerterp-Plantenga 2005	Preload: - galactose (50 g)/guar gum (2.5 g) + standard breakfast (GG) - water + standard breakfast (W)	Liquid	30 (15 M, 15 F) NW	2 h	Satiety related to GLP-1 after GG	GLP-1: GG > W	..

(cont.)

Reference	Fibre type / fibre source	Physical state	Study subjects	Duration/ Follow-up period	Appetite	GI hormone responses	Energy/ food intake (EI)
Gruendel et al. 2006	Isocaloric meals: - 0, 5, 10 or 20 g of insoluble carob pulp fibre	Liquid	20 (11 F, 9 M) NW	5 h	..	Total ghrelin: ns Lowered acyl ghrelin vs control No dose-dependent effect	..
Gruendel et al. 2007	Drink: - 0, 5, 10 or 20 g of insoluble carob pulp fibre with 50 g glucose	Liquid	20 (12 F, 8 M) NW	3 h	..	Total ghrelin decrease: 10 g carob fibre > control Acyl ghrelin: ns	..
Lummela et al. 2009	Milk drink: - no fibre - fibre-enriched (polydextrose, 3 g) - normal fat-free milk	Liquid	26 (16 F, 10 M) NW, OW	3 h	Satiety: ns	..	..
Lyly et al. 2009	Beverages: - no fibre - guar gum, 7.8 g - oat beta-glucan, 10.5 g - wheat bran, 10.5 g	Liquid	19, NW, OW	2 h	Satiety: guar > no fibre Fullness: beta-glucan > no fibre	..	..
Lyly et al. 2010	Beverages: 1) fibre set: 0, 5 and 10 g fibre at 700 kJ 2) energy set: 700 or 1400 kJ at fibre level 0 and 10 g 3) viscosity set: 0, 10 and 10 g with reduced viscosity (10/LV) at 700 kJ - DF from oat bran	Liquid	29 (18 F, 11 M) NW, OW	3 h	1) Satiety: 5, 10 g > 0 g Hunger: 5, 10 g < 0 g at both energy levels 2) Satiety: 10 g > 0 g Hunger: 10 g < 0 g at both energy levels 3) Satiety: 10 g <10/LV < 0 g Hunger: 10, 10/LV < 0 g	..	..

(cont.)

Reference	Fibre type / fibre source	Physical state	Study subjects	Duration/ Follow-up period	Appetite	GI hormone responses	Energy/ food intake (EI)
Tarini and Wolever 2010	Drinks: - 80 g high-fructose corn syrup (80HFCS) - 56 g HFCS - 56 g HFCS + 24 g inulin	Liquid	12 (7 F, 5 M) NW	4 h + std meal + 2h	..	Total ghrelin: Inulin < 56HFCS Inulin < 80HFCS GLP-1: Inulin, 80HFCS > 56HFCS	..
Calame et al. 2011	Blends of gum arabic (EmulGold, EG), (PreVitae, PV) 1) 10, 20, 40 g of EF or PV 2) 5 and 10 g of EG - water as control - ad lib meal 3 h after	Liquid	1) 12 M, NW, OW 2) 58 (42 F, 16 M)	3 h	1) Satiety: after EG 40, PV 20 and 10 most increase in satiety vs control 2) Satiety: 5, 10 g of EG > control	..	*ad lib* EI: 1) EG and PV at 40 g < control 2) 5, 10 g of EG < control
Barone Lumaga et al. 2012	Beverages: - 3 g barley β-glucan or 2.5 g dietary fibre (DF) from fruit - no DF (control)	Liquid	14	3 h	Satiety, fullness: beverages with DF > control	Ghrelin suppression: fruit-based, β-glucan > control	Ad lib lunch EI: β-glucan < control
Hulshof et al. 1993	Preloads - liquid, solid with locust bean gum, and solid with gelatin at energy levels 0.42, 1.67 and 3.35 MJ	Liquid / solid	33 F, NW	3.5 h	Satiety: solid preloads with fibre > without fibre	..	EI: ns
Monsivais et al. 2011	Preload: - soluble fibre dextrin (12 g) - soluble corn fibre (11.8 g) - polydextrose (11.8 g) - resistant starch (11.2g) - 20 -24 g fibre before lunch - 2 control meals, - isoenergetic, low-fibre(1.9 g) - lower-energy, low-fibre (0.5g)	Solid, liquid	36 (14 M, 22 F) NW	220 min	Fullness: higher-energy preloads > low-energy control Hunger: higher-energy preloads < low-energy control Desire to eat: higher-energy preloads < low-energy control		*ad lib* EI: soluble fibre dextrin < isoenergetic control

(cont.)

Reference	Fibre type / fibre source	Physical state	Study subjects	Duration/ Follow-up period	Appetite	GI hormone responses	Energy/ food intake (EI)
Raben et al. 1994a	Isoenergetic meals: - high-fibre (HF, 4.7 g/MJ, ~ 25.5 g) - low-fibre (LF, 1.7 g/MJ, ~ 9.2 g) - DF: pea fibre, cellulose, pectin, hemicellulose	Solid	10 M, NW	6 h	Hunger, desire to eat: decreased after HF Fullness: increased after HF	GLP-1: ns	..
Delargy et al. 1995	Cereals: 1) - low-energy, - low-fibre 3 g, - high-fibre 20 g (50:50, soluble:insoluble) 2) 4 isoenergetic breakfasts, 20 g fibre in ratios of soluble: insoluble fibre (8:2, 6:4, 4:6, 2:8) - soluble (psyllium), insoluble (wheat bran)	Solid	1) 12 M 2) 16 M	24 h	Insoluble DF, greatest satiety shortly after meal Soluble DF, greatest satiety 13.5 h after meal	..	1) *ad lib* EI: 20 g < low-energy total daily EI: ns 2) lunch or total daily EI: ns
Delargy et al. 1997	Cereals: - 2 isoenergetic high fibre (psyllium, wheat bran, 22 g) - isoenergetic low fibre (3 g) - low energy - *ad lib* snack 1.5 h after	Solid	16 M, NW	24 h	Trend for lower hunger at snack after wheat bran vs. psyllium Trend for reduced hunger after psyllium vs. wheat bran 9.5-13.5 after	..	*Ad lib* EI**:** wheat bran < psyllium - low-fibre< psyllium - low energy > low-fibre, wheat bran Total daily EI: ns
Bourdon et al. 1999	Meal: - high-fibre (total DF 15.7 g; ~5g beta-glucan, flour naturally high in beta-glucan) - high-fibre (total DF 15.7 g; ~5g beta-glucan, flour enriched with beta-glucan) - low-fibre (total DF 4.6g, no beta-glucan)	Solid	11 M, NW, OW	6 h	..	CCK: remained elevated longer after high-fibre meals	..

(cont.)

Reference	Fibre type / fibre source	Physical state	Study subjects	Duration/ Follow-up period	Appetite	GI hormone responses	Energy/ food intake (EI)
Juntunen et al. 2002	Meals: - pasta (P, total DF 5.6 g, soluble 1.3 g) - whole-kernel rye bread (RB, 12.8 g, 3.8 g) - β-glucan rye bread (βRB, 17.1g, 6.8 g) - white wheat bread (WWB, 3.1 g, 0.9 g)	Solid	20 (10 F, 10 M) NW, OW	3 h	..	GLP-1: P, RB < WWB	..
Frost et al. 2003	Meals: - pasta meal with psyllium (PP, 1.7 g) - pasta meal with fat (PF, 30 g sunflower oil) - pasta meal with psyllium and fat (PPF) - pasta meal (P)	Solid	10 (6 F, 4 M) NW, OW	4 h	Hunger: ns Fullness: ns	GLP-1: PP vs P, ns GLP-1 increased after PF	*ad lib* EI**:** ns
Nedvídková et al. 2003	Breakfast: - solid mixed meal - psyllium (4 g)	Solid	6 F, NW	2 h	..	Total ghrelin: decreased equally after solid meal and psyllium	..
Möhlig et al. 2005	Breakfast: - arabinoxylan fibre (AX, 6 g) - control	Solid	11 (7 F, 4 M)	2 h	..	Ghrelin: less decreased after AX	..
Weickert et al. 2006	Bread: - wheat-fibre (10.5 g) - oat-fibre (10.6 g) - low-fibre white bread (control)	Solid	14 F	5 h	Hunger: ns	Total ghrelin: blunted after wheat fibre Total PYY: blunted after wheat fibre	..
Hamedani et al. 2009	Cereal: - high-insoluble fibre (HF) cereal (26 g) - low-fibre (LF) cereal (1 g)	Solid	32 (16 F, 16 M) NW	3 h	Appetite: ns	..	*ad lib* EI**:** ns

(cont.)

Reference	Fibre type / fibre source	Physical state	Study subjects	Duration/ Follow-up period	Appetite	GI hormone responses	Energy/ food intake (EI)
Vitaglione et al. 2009	Isocaloric breakfasts: - barley β-gluc bread (βGB, 3 %) - control bread (CB)	Solid	14 (7 M, 7 F) NW	3 h	Satiety, fullness: βGB > CB Hunger: βGB < B	Acyl ghrelin decrease: βGB > CB PYY: βGB > CB	*ad lib* EI: βGB < CB
Vitaglione et al. 2010	Biscuit: - low (2 g) or high (6 g) barley beta-glucan-enriched (BB) biscuits - low (L) or high (H) energy control biscuits (CB) - lunch 2 h after	Solid	16 (7 M, 9 F) NW, OW	2 h	Satiety, fullness: L-BB > L-CB Desire to eat: L-BB < L-CB	..	*ad lib* EI: ns
Willis et al. 2010	Mixed fibre muffins: - 0 g, 4 g (soluble/insoluble 2.5 /3.2g), 8 g (4.0/4.9 g), 12 g (6.1/6.7g) of mixed fibres - DF types; pectin, barley b-glucan, guar gum, pea fibre, citrus fibre	Solid	20, (10 F, 10M) NW, OW	3 h	Satisfaction, fullness: 4g > 0g Hunger: ns	Ghrelin decrease: 12 g < 4 and 8 g GLP-1: 0 g > 12 and 4 g PYY 3-36: ns	*ad lib* EI: ns

Ad lib, *ad libitum* meal; CCK, cholecystokinin; DF, dietary fibre; EI, energy intake; E%, percentage of total energy; F, female; GLP-1, glucagon-like peptide 1; M, male; ns, non-significant; NW, normal weight; OW, overweight; PYY, peptide YY; vs, versus; ..; not measured / no information available.

Kristiina Juvonen

Appetite Control

The Role of Food Composition and Structure

The physicochemical properties of dietary fibre and protein delineate their postprandial physiological and appetite responses. This thesis focused on the postprandial effects of selected dietary fibres and proteins and their structural modification on appetite and appetite-related gastrointestinal responses in healthy individuals. The results emphasize the marked role of viscous dietary fibres and physical food form in the control of short-term physiological and appetite responses.

UNIVERSITY OF
EASTERN FINLAND

Publications of the University of Eastern Finland
Dissertations in Health Sciences

ISBN 978-952-61-0886-5