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Research report

Changes in satiety hormone concentrations and feed intake in rats in response to lactic acid bacteria

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ABSTRACT

A negative energy balance can be accomplished by reducing the caloric intake which results in an increased feeling of hunger. This physiological state is regulated by secretion of satiety hormones. The secretion of these hormones can be influenced by ingestion of e.g. fat. Fat, dairy beverage and synbiotic mixture have been found to have satiety-inducing effects in humans and rats. Thus, the aim of this study was to investigate the change of satiety hormone concentration in rats in response to feeding of fermented milks containing lactic acid bacteria. Two studies were conducted with Wistar rats randomly allocated into groups receiving *Lactobacillus* fermented (2 *L. acidophilus*, *L. bulgaricus*, *L. salivarius* and *L. rhamnosus*) milk. A single isocaloric oral dose with the test item or control was given to the rats. Blood samples were taken after dosing with the test product and the satiety hormones were measured. For the test groups, significant changes could be detected in PYY concentrations after 60 min, although some groups had a significant lower feed intake. In conclusion, some probiotic *Lactobacillus* strains may modify satiety hormones production. However, more studies are needed to evaluate their potential of prolonging satiety.

Introduction

A slight imbalance in the energy equilibrium between intake and expenditure of energy, can lead to significant changes in body weight over time and eventually lead to obesity. Obesity is one of the major health problems facing all ages worldwide, and is a risk factor for several chronic disorders such as diabetes, cardiovascular disease, hypertension, osteoarthritis of weight-bearing joints, and asthma (Peeters et al., 2003; Rippe, 1998). Genetic, environmental, metabolic and behavioral issues may all contribute to the development of obesity (Rippe, 1998). However, the small changes in energy balance that may lead to weight gain might be prevented by slight modifications in feed intake, such as the inclusion of functional feeds for weight management. Some foods or food components, such as nuts (St-Onge, 2005), tea (Josic, Olsson, Wickeberg, Lindstedt, & Hlebowicz, 2010) and fiber (Hess, Birkett, Thomas, & Slavin, 2011; Mathern, Raatz, Thomas, & Slavin, 2009; Hull et al., 2012) have been studied for their effects on satiety, with mixed results.

Fermented milk represents an excellent source of nutrients such as calcium, protein, phosphorus and riboflavin. During the fermentation of milk, lactic acid and other organic acids are produced. The fermentation process of milk with lactic acid bacteria, adds taste and improves the aroma and digestibility of milk, in addition to an increase of the shelf-life of the product. Fermented milk may offer several health benefits, e.g. improvement of the immune system, promote or help in recovery from diarrhea, increase nutrient bioavailability and reduce blood pressure in hypertensive subjects. There could be an association of availability of nutrients with appetite suppression, since a higher nutrient availability may lead to a graduate release of glucose, which is involved in controlling appetite (Beausoleil et al., 2007; Jauhiainen et al., 2005; Silva, Dias, Ferreira, Franceschini, & Costa, 2008).

Ingestion of feed triggers a number of stimuli, such as the release of the gastrointestinal hormones cholecystokinin (CCK) and glucagon-like peptide 1 (GLP-1) within the gastrointestinal tract, modulating appetite sensations. Ingested nutrients stimulate CCK and GLP-1 secretion by indirect, duodenally activated, neurohumoral mechanisms, as well as by direct luminal exposure within the distal intestine. CCK is released in the duodenum in the presence of fats and proteins. GLP-1 is released by intestinal L-cells in response to carbohydrates and fats, although it is secretion may also

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be stimulated by the central nervous system (Orskov, Rabenhoj, Wettergren, Kofod, & Holst, 1994; Reimer, 2006). The hormone ghrelin is produced in the fundus of the stomach and its synthesis can be suppressed by carbohydrates, thereby reducing the feeling of hunger. After a meal, before the nutrients arrive into the ileum and colon, peptide YY (PYY) is secreted into the blood by the cells lining the ileum and colon. PYY decreases feed intake by inhibiting gut motility, acting as the so-called "ileal brake" to cause a sense of satiety (Aponte, Fink, Meyer, Tatemoto, & Taylor, 1985).

The aim of the present study was to investigate the effect of milk fermented by one of five *Lactobacillus* strains on feed intake and secretion of satiety hormones in rats.

Materials and methods

Two Experiments (Experiment 1 and Experiment 2, see Supplemental data) were conducted with a total of 230 male Wistar (HsdBrlHan:WIST) rats supplied by Harlan (Horst, the Netherlands). Further, Experiment 2 consisted of two subparts; referred to as Experiments 2a and 2b. The studies were reviewed and approved by the Animal Care and Use Committee of the State Provincial Office of Southern Finland, approval numbers 2007-07458 (Experiment 1) and 2008-03964 (Experiments 2a and 2b). The "Act on Use of Animals for Experimental Purposes (62/2006) and ordinance number 36/EEO/2006, Ministry of Agriculture and Forestry, Finland", "Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes (Text with EEA relevance) (Official Journal of the European Union L 276)", as well as the "Guidance document on the Recognition, Assessment and Use of Clinical Signs as Humane endpoints for Experimental Animals Used in Safety Evaluation" were followed. The animals, identifiable through their individual tail number, were housed in plastic cages (Makrolon 3, Bayer MaterialScience AG, Leverkusen, Germany). Two or three animals were housed in the same cage and kept in a conventional animal room with controlled lighting (12 h light, 12 h dark) and temperature 21 (SD 3) °C, and the relative humidity between 40% and 60%. Rats were fed a Formulab Diet (PMI Nutrition International, Richmond, IN, USA). The purpose of Experiments 1 and 2a was to investigate the changes in satiety hormone concentrations and glucose in rats in response to feeding various fermented dairy products containing lactic acid bacteria. Experiment 2b focused on feed intake measurement following the administration of the test items, feed accessibility and timing of feed access being the key elements.

Experiment 1

Over a period of 8–16 days (14–16 days for animals No. 1-147 and 8 days for No. 148-150, respectively), 150 animals with an initial body weight of 251 (SD 13) g, were subjected to a reversal of the normal diurnal light/dark cycle and trained to consume all their feed within 5 h from start of the dark cycle. The animals were randomly allocated to eight groups (*n* 20/group, except *n* 5/Group 1 and *n* 25/Group 2): Group 1; non-gavaged controls, Group 2; negative control group (acidified by lactic acid, low lactose, non-fat skimmed UHT milk (Valio, Helsinki, Finland), Group 3; positive control group (acidified by lactic acid, low lactose, UHT full fat milk 3.5% (Valio), with lactitol (Danisco), Group 4–8 received low lactose, non-fat skimmed UHT milk fermented with; *Lactobacillus acidophilus* MUH 41 fermented milk (Group 4); *Lactobacillus bulgaricus* MUH 192 (Group 5); *Lactobacillus rhamnosus* MUH 142 (Group 6); *L. acidophilus* NCFM (ATCC 700396; Group 7) or *Lactobacillus salivarius* MUH 1502 (Group 8). Weighing of the animals was performed the day before dosing and at dosing day, and the test or control items were administered by a single oral gavage in a dose volume of 2.5 ml/animal (a dose of ca. 10 ml/kg) (density of test items 1.1 g/ml) at the start of the dark cycle (8:00). Abnormal clinical signs of the rats were recorded until animals were euthanized at the respective time points. The animals were given feed one hour after the dosing (9:00). At each time point (40 min, 3 h, 5 h, 8 h and prior to dosing also in Group 2) five rats were anesthetized with 4% isoflurane and blood samples taken by a cardiac puncture into Venosafe™ EDTA K2 tubes (Terumo® Europe N.V., Leuven, Belgium). Immediately following the sampling, the collection tubes were placed in an ice-bath and DPP-IV inhibitor or aprotinin was added into the collection tubes for GLP-1 and CCK analysis respectively, both at a dose volume of 10 µl/ml blood. The non-gavaged animals in Group 1, were fasted prior to terminal blood sampling at time point 40 min. The plasma was separated from whole blood by centrifugation at 1600*g* for 15 min at 4 °C, frozen at −20 °C within 1 h from sampling and stored at same temperature until analyzed for the satiety hormones. The following satiety parameters were analyzed from the aliquots of the plasma samples according to the diagnostic kit manufacturers' instructions: cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1), ghrelin, PYY and insulin. CCK was analyzed by an ELISA method (DRG Diagnostics, Marburg, Germany). GLP-1, ghrelin, PYY and insulin were determined using a MILLIPLEX™ MAP kit (Millipore, Billerica, MA, USA). Plasma glucose was analyzed by the enzymatic photometric method using Konelab Glucose HK as reagent.

Experiment 2

Eighty animals, acclimatized for 14 day and with initial weight 301 (SD 18) g, were grouped (*n* 10/group) as follows: Group 1; non-gavaged controls, Group 2; negative control group (acidified by lactic acid, low lactose, non-fat skimmed UHT milk), Group 3; positive control group (acidified by lactic acid, low lactose, 3.5% fat, UHT milk with lactitol, 0.5% casamino acids, pH adj. to 4.2 by lactic acid), Group 4–8 received low lactose, non-fat skimmed UHT fermented with; *L. acidophilus* NCFM (Group 4); *L. acidophilus* MUH 41 (Group 5); *L. salivarius* 1502 (Group 6); *L. rhamnosus* MUH 142 (Group 7) or *L. bulgaricus* MUH 192 (Group 8). Skim milk powder (low lactose) was added to all milks after the fermentation. All gavages were isocaloric and contained 77 kcal per 100 ml. Test items were administrated by a single oral gavage of 19.5 g/kg in a dose volume 18.6 ml/kg (density of test items 1.1 g/ml). This Experiment had a shorter time span (0–180 min) compared with Experiment 1 (0–8 h).

Experiment 2a

The animals (two animals/cage) were weighed and then fasted for 10 h. Following the fasting period, rats in Group 2–8 were administrated the test or control items 1–3 h before the onset of the dark cycle. The subset of five animals in Group 2–8 were blood sampled from a lateral tail vein or heart by cardiac puncture (terminal samples) at time point 20 min, 40 min and 1 h (terminal samples), and another subset of five animals in the respective group at time point 20 min, 40 min, 1 h and 3 h (terminal samples). Rats in all groups were anesthetized with isoflurane (4%) prior to terminal blood sampling. Blood was collected into cooled Capiject® or Venosafe™ tubes (Terumo®). Immediately following the sampling, the collection tubes were placed in an ice-bath and DPP-IV inhibitor or aprotinin was added into the collection tubes for GLP-1 and CCK analysis respectively, both at a dose volume of 10 µl/ml blood. The plasma was separated from whole blood by centrifugation at 1600*g* for 15 min at RT, frozen at −20 °C within

2 h from sampling and stored at −70 °C until samples were analyzed. Satiety biomarkers as CCK, GLP-1, PYY and insulin were determined as described earlier in Experiment 1. Glucose from whole blood was measured using a HemoCue® Glucose 201+ analyzer (HemoCue AB, Ängelholm, Sweden).

Experiment 2b

Approximately 3 h before the onset of the dark cycle, the animals, kept in cages individually, were weighed and administrated with the test or control items. During this time period, animals did not have access to feed or tap water. When the dark cycle started, feed and water were provided and the individual feed intake was determined at 30 min, 1 h, 1.5 h, 2 h and 12 h (by the onset of the light cycle).

Statistics

Results are expressed as means ± SD. To quantify insulin resistance, the Homeostasis Model of Assessment–Insulin Resistance (HOMA–IR) was used. Statistical differences were determined by one-way ANOVA or Kruskall–Walls depending on the group variance, which was checked with the Shapiro–Wilks and Levene test. The level of significance was set at $P < 0.05$.

Results

Experiment 1

For PYY, no significant difference could be detected for the groups receiving fermented milks in comparison to the negative control group (Fig. 1a). GLP-1 levels did not differ from the negative control in any of the groups, Fig. 1b. However, the CCK levels significantly changed during the time points for the groups receiving fermented milk versus the negative control group (Fig. 1c). A significant increase (Kruskal–Wallis) could be detected at the 40 min time point for the groups receiving *L. acidophilus* MUH 41 ($P = 0.03$), *L. rhamnosus* MUH 142 ($P = 0.03$), and *L. acidophilus* NCFM ($P = 0.03$) fermented milks, as well as the 3 h time point for *L. acidophilus* MUH 41 ($P = 0.01$). For the group receiving *L. acidophilus* MUH 41 a significant increase ($P < 0.0001$) of CCK level, while a significant decrease ($P < 0.008$) of CCK levels for the groups receiving *L. bulgaricus* MUH 192 and *L. salivarius* MUH 1502 fermented milks, could be detected at the 5 h time point in comparison to the negative control group. During the 8 h time point a significant decrease ($P \leqslant 0.04$) of the CCK levels could be detected for the groups receiving *L. bulgaricus* MUH 192 and *L. salivarius* MUH 1502 fermented milks.

For the group consuming *L. salivarius* MUH 1502 fermented milk no significant difference in the serum glucose or insulin levels could be detected in comparison to the negative control group. HOMA–IR values were also compared between the groups, but no difference could be detected. The groups consuming *L. acidophilus* NCFM, *L. acidophilus* MUH 41 and *L. rhamnosus* MUH 142 fermented milk, had a significant decrease in serum glucose levels ($P < 0.04$) after 3 h (Fig. 2a), as well as decreased ($P < 0.006$) insulin levels after 5 h. In addition, a significant decrease of insulin level could be detected for the *L. acidophilus* MUH 41 ($P < 0.03$) and *L. bulgaricus* MUH 192 ($P < 0.003$) after 3 h and 5 h time points in comparison to the negative control, Fig. 2b. The *L. rhamnosus* 1502 group had a significant increase ($P < 0.02$), as compared to the control after 3 h.

No significant effect on the feed consumption (per 100 g body weight) could be detected between the groups (Fig. 3).

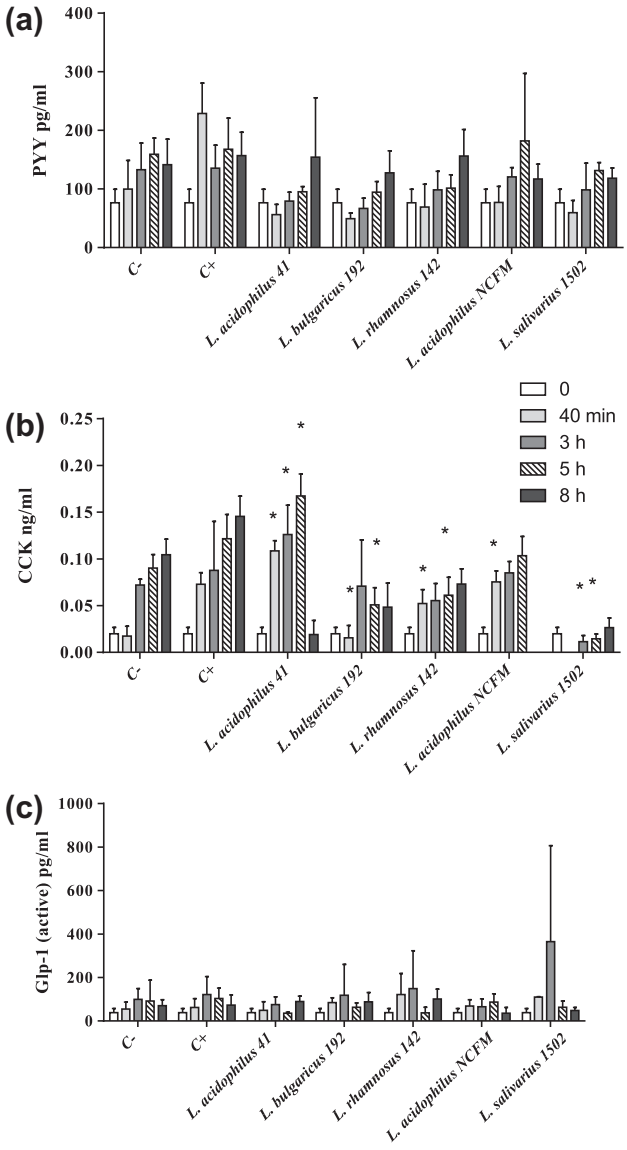

Fig. 1. Satiety hormone concentrations (a) PYY, (b) Glp-1 and (c) (CCK) as pg/ml or ng/ml (mean + SD) from Experiment 1 after dosage of fermented milk or negative (C−) or positive (C+) control milks. The 0 time point (base level, non-cavaged group) represents the average concentration for 5 rats. Asterisks (∗) indicate significant ($P < 0.05$) differences in relative to the negative control.

Experiment 2a

Although all the LAB fermented milks were associated with an increase in glucose levels; no significant difference could be detected between the groups receiving fermented milks or the negative control group (Fig. 4a). A trend ($P = 0.085$) of decrease could be seen 60 min after dosing in the *L. rhamnosus* MUH 142 group when compared to the positive control group. For insulin, no significant differences could be detected, Fig. 4b. No significant differences in HOMA–IR could be detected between the groups.

For the measured satiety hormones (Fig. 5), no significant difference could be seen between the groups receving fermentended milks and the negative control group during the first time points. At the 180 min time point, the PYY levels for all groups receiving fermented milks were significantly lower ($P < 0.009$) than the negative control, Fig. 5a. The GLP-1 levels were below detection limit for both the control groups as well as the groups receiving fermented milk at several time points, Fig. 5b. For CCK, the levels

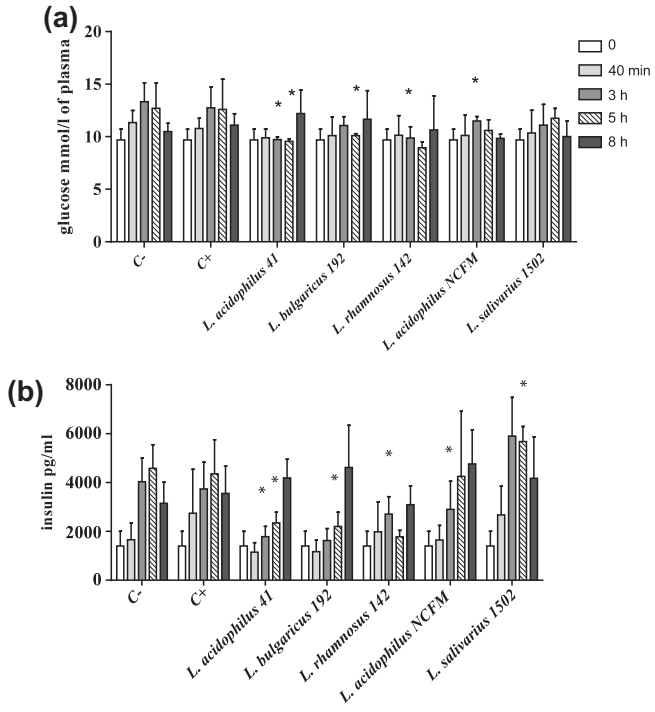

Fig. 2. Serum glucose (a) and insulin (b) concentrations (mean + SD) after dosage of fermented milk or negative (C−) or positive (C+) control milks (20 rats per group). The 0 time point (base level, non-cavaged group) represents the average concentration for 5 rats. Significant differences ($P < 0.05$) in comparison to the control are indicated by asterisks (∗).

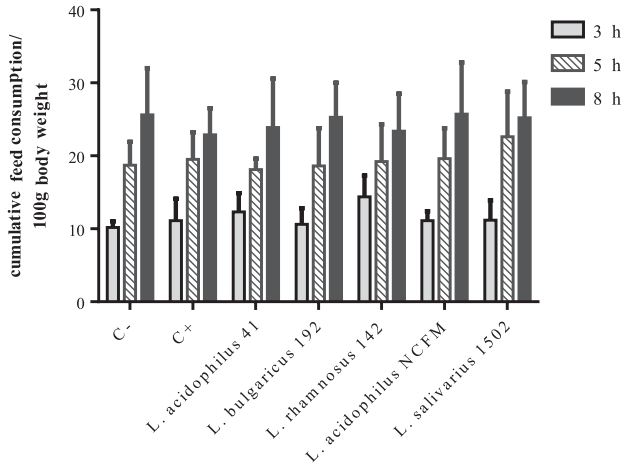

Fig. 3. Mean cumulative feed consumption per 100 g body weight for the different treatments; (C−) negative control, (C+) positive control (20 rats per group).

were mostly under detection limit, with measurable levels in only some animals in each treatment group. The highest increase was detected in the *L. rhamnosus* MUH 142 group, Fig. 5c.

Experiment 2b

A significant difference for feed consumption (per 100 g body weight) could be detected after 90 min between the negative control group and the groups receiving *L. salivarius* 1502 ($P = 0.023$) and *L. acidophilus* NCFM ($P = 0.052$) the fermented milks. The *L. acidophilus* NCFM group displayed a significant lower feed intake after 12 h ($P = 0.043$). The positive control group displayed a

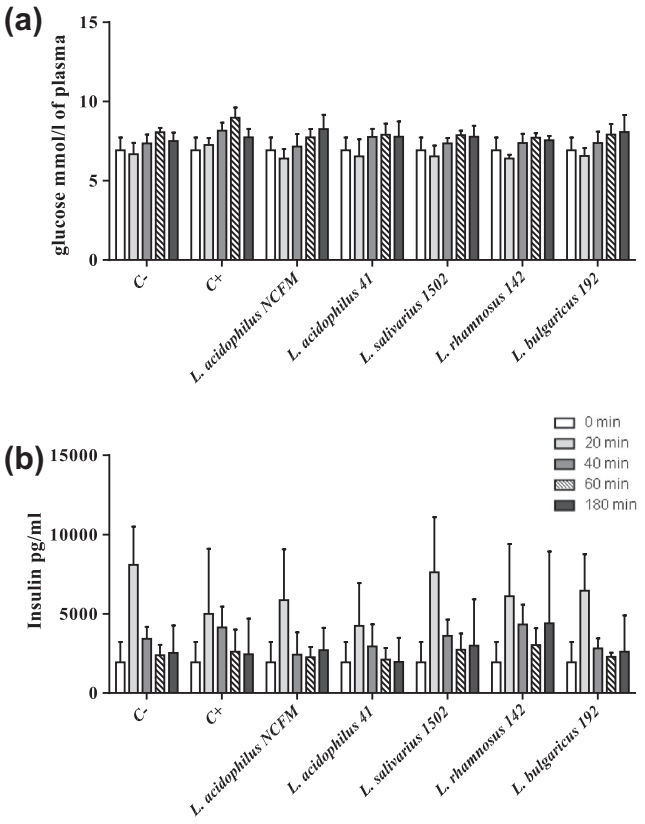

Fig. 4. Glucose (a) and insulin (b) concentrations as mean + SD in blood (Experiment 2a). After 40 and 60 min a significant difference ($P \leqslant 0.05$) was detected between the negative (C−) and positive (C+) controls. The 0 time point (base level, non-cavaged group) represents the average concentration for 10 rats. Each test group contained 10 rats.

significantly ($P = 0.0005$) lower consumption than the negative control group during all time points, Fig. 6.

Discussion

The gastrointestinal tract is equipped with specialized receptors monitoring physiological activity that pass information about the metabolic state, resulting from feed consumption to the brain in form of satiety signals, thus participating in the appetite control. Once the satiety hormones or signals are secreted in response to ingested food, they promote termination of a meal (Mathern et al., 2009). Although, all macronutrients contribute to satiety, a stronger short term effect is detected by proteins than by fat or carbohydrates (Batterham et al., 2002). Ingestion of high-protein meals induces satiety and fullness, and hunger, appetite, desire to eat, and estimated quantity to eat are suppressed by high-protein diets compared to normal-protein diets (Cummings et al., 2002; Urbienė & Leskauskaitė, 2006). Glucose is the major source of energy for the body, and is also considered a major contributor to satiety.

In a meta-analysis study (Million et al., 2012) where randomized controlled trials and comparative clinical studies in humans and animals or experimental models assessing the effect of *Lactobacillus*-containing probiotics on weight were analyzed, different *Lactobacillus* species were associated with different effects upon weight change. Therefore, further studies are needed to clarify the role of *Lactobacillus* species in energy harvest and weight regulation, and what the possible effects in different hosts are.

In Experiment 1, for groups receiving the *L. acidophilus* MUH 41, *L. acidophilus* NCFM and *L. rhamnosus* MUH 142 fermented milks a

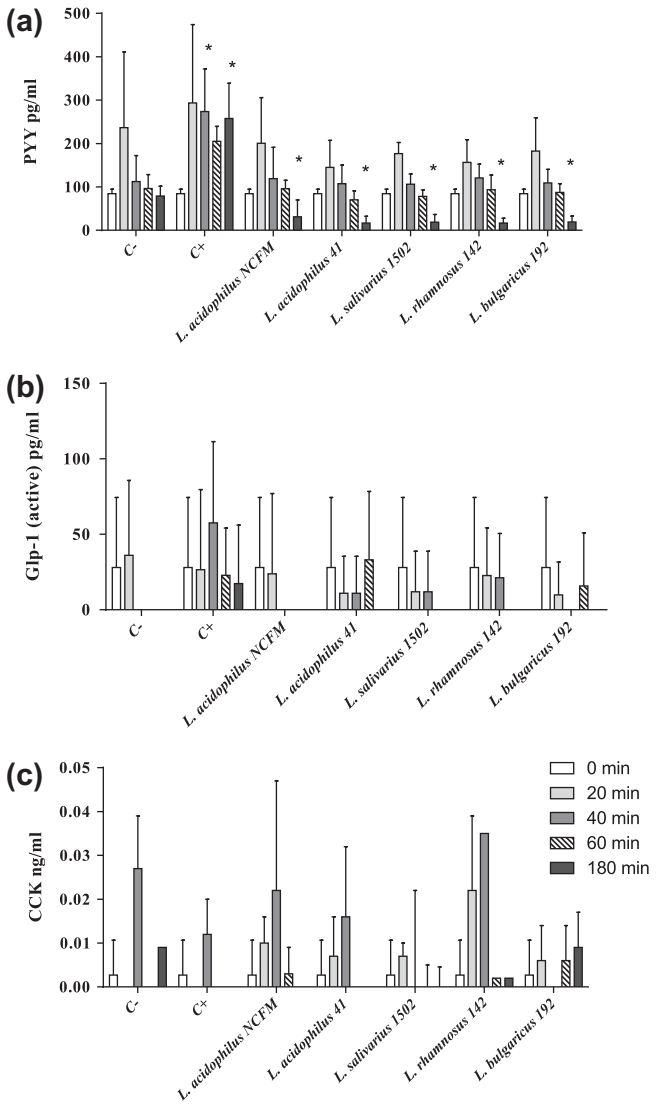

Fig. 5. Satiety hormone concentrations (a) PYY, (b) Glp-1 and (c) (CCK) as pg/ml, ng/ml or mmol/l (mean + SD) from Experiment 2a. The 0 time point (base level) represents the average concentration for 10 rats. Significant differences ($P \leqslant 0.05$) in comparison to the negative control are indicated by asterisks (*). Each test group contained 10 rats.

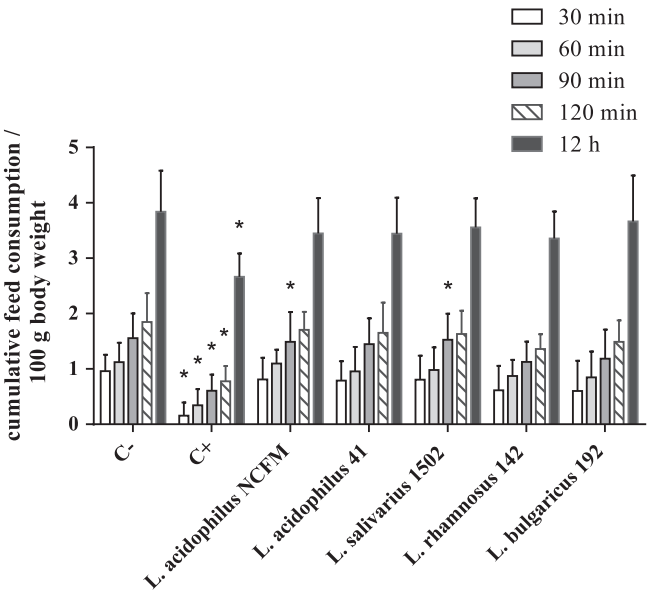

Fig. 6. Cumulative feed consumption as mean per 100 g body weight (+SD) (Experiment 2b). Asterisk (*) indicate significant difference ($P \leqslant 0.05$) between the group and the negative control. Each test group contained 10 rats.

significant decrease could be detected in serum glucose levels. Otherwise, no significant difference in the glucose levels was detected between the groups. Only a trend ($P < 0.08$) could be detected for *L. bulgaricus* MUH 192. A high insulin level increases liver metabolism of nutrients, thus promoting satiety. In this study, the *L. rhamnosus* 1502 group had a significant insulin increase as compared to the control after 3 h, while a significant decrease of insulin level could be detected for the *L. acidophilus* MUH 41 and *L. bulgaricus* MUH 192 groups after 3 h and 5 h time points in comparison to the negative control.

The measured satiety hormones participate in metabolism and hunger control, and CCK has been shown to dose dependently reduce the size of a meal (Gibbs, Young, & Smith, 1973). However, in the present study, CCK was measurable only from some animals, thus it is difficult to draw any statistical conclusions. Ghrelin and PYY, are peptides with opposing actions. PYY is associated with post-meal satiety, hence released predominantly after rather than during a meal (Batterham et al., 2002, 2003), while ghrelin is considered as a gut peptide with opposing action. Obese individuals have a higher plasma level of ghrelin as compared to lean individuals (Cummings et al., 2002) and it has been suggested that ghrelin is inversely related to calorie intake. The ghrelin levels were also measured in Experiment 1, however the levels were below the detection limit.

In Experiment 1 the first time point of blood sampling was after 40 min, followed by 3, 5 and 8 h. In Experiment 1 the animal had access to feed *ad libitum*, which subsequently can lead to continuous small increases of nutrients and gut hormones in the blood. Therefore, food deprivation during the Experiment is a requisite in a postprandial Experimental setup. Most of the hormonal responses will take place during the first 10–20 min (maximal 40 min) thus the blood sampling was mainly focused on the first hour in Experiment 2. The differences in hormone concentrations measured between Experiments 1 and 2 may be in addition to the feed consumption, also due to increase of energy content in Experiment 2.

PYY has been shown to be (Batterham et al., 2002, 2003) released from the gastrointestinal tract postprandially in proportion to the calorie content of a meal and directly affects feed intake. In the second part of this study, the levels of PYY were significantly lower after 60 min for the groups receiving fermented milks, when compared to the negative control. Interestingly, a significantly lower feed intake was detected for the *L. salivarius* 1502 and *L. acidophilus* NCFM groups. However, the measured satiety hormones are only indicators of satiety, thus it is the change in the actual feed intake that is the most relevant parameter. In the present study, significant differences in feed consumption could be detected for the negative and positive control groups, showing that the model is reliable and it is possible to detect the differences due to the fat content. However, although not significant, a trend for reduced feed consumption could be detected for two of the groups receiving fermented milk (*L. rhamnosus* MUH 142 and *L. bulgaricus* MUH 192). In addition to fat or proteins having a satiating effect, hippuric acid or benzoic acid could also have an effect on the feed intake. Hippuric acid is naturally present in milk, and it can be converted during fermentation to benzoic acid (Urbienė & Leskauskaitė, 2006). Thus, a minor study to investigate if it would be possible to increase the effect on feed intake in rats of fermentation

by *L. rhamnosus* MUH 142 with an increased amount of hippuric acid, or its metabolites was performed (Jensen, Korczynska, & Please provide more details for references 'Jensen et al., 2010). In this study it was shown that hippuric acid or its metabolites may have an effect on the feed intake.

Some of the tested *Lactobacillus* fermented milks induced a change in the level of some of the tested satiety hormones, small differences were detected in food intake within some groups when compared to the negative control. Satiety hormones have been shown to influence food intake. However, there are still conflicting results regarding the site of action or effect of the satiety hormones as the present study shows. In addition the effects may to some extent be host dependent (Kinzig, D'Alessio, & Seeley, 2002; Ritter, 2004; Vrang, Madsen, Tang-Christensen, Hansen, & Larsen, 2006; Zhang & Ritter, 2012). What role lactobacilli may play in appetite regulation, if any, is therefore still open. In contrast to a recent report (Million et al., 2012), they do in any case not seem to increase appetite and food intake. Thus, further animal and especially dietary intervention studies are needed to be able to make clear conclusions.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.appet.2013.06.093.

References

Aponte, G. W., Fink, A. S., Meyer, J. H., Tatemoto, K., & Taylor, I. L. (1985). Regional distribution and release of peptide YY with fatty acids of different chain length. *The American Journal of Physiology, 249*, G745–G750.

Batterham, R. L., Cohen, M. A., Ellis, S. M., Le Roux, C. W., Withers, D. J., Frost, G. S., et al. (2003). Inhibition of food intake in obese subjects by peptide YY3-36. *New England Journal of Medicine, 349*, 941–948.

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

Beausoleil, M., Fortier, N., Guenette, S., L'Ecuyer, A., Savoie, M., Franco, M., et al. (2007). Effect of a fermented milk combining *Lactobacillus acidophilus* CI1285 and *Lactobacillus casei* in the prevention of antibiotic-associated diarrhea. A randomized, double-blind, placebo-controlled trial. *Canadian Journal of Gastroenterology, 21*, 732–736.

Cummings, D. E., Weigle, D. S., Frayo, R. S., Breen, P. A., Ma, M. K., Dellinger, E. P., et al. (2002). Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *New England Journal of Medicine, 346*, 1623–1630.

Gibbs, J., Young, R. C., & Smith, G. P. (1973). Cholecystokinin decreases food intake in rats. *Obesity Research, 5*, 284–290.

Hess, J. R., Birkett, A. M., Thomas, W., & Slavin, J. L. (2011). Effects of short-chain fructooligosaccharides on satiety responses in healthy men and women. *Appetite, 56*, 128–134.

Hull, S., Re, R., Tiihonen, K., Viscione, L., & Wickham, M. (2012). Consuming polydextrose in a mid-morning snack increases acute satiety measurements and reduces subsequent energy intake at lunch in healthy human subjects. *Appetite, 59*, 706–712.

Jauhiainen, T., Vapaatalo, H., Poussa, T., Kyronpalo, S., Rasmussen, M., & Korpela, R. (2005). *Lactobacillus helveticus* fermented milk lowers blood pressure in hypertensive subjects in 24-h ambulatory blood pressure measurement. *American Journal of Hypertension, 18*, 1600–1605.

Jensen, H. M., Korczynska, M., Weinbreck, F., Schlatmann, J., Ouwehand, A. (2010). The influence of hippuric acid on the feed intakeof rats. Presented at the 1st International Diabetes and Obesity Forum, October 21-23.

Josic, J., Olsson, A., Wickeberg, J., Lindstedt, S., & Hlebowicz, J. (2010). Does green tea affect postprandial glucose, insulin and satiety in healthy subjects. A randomized controlled trial. *Nutrition Journal, 9*, 63.

Kinzig, K. P., D'Alessio, D. A., & Seeley, R. J. (2002). The diverse roles of specific GLP-1 receptors in the control of food intake and the response to visceral illness. *The Journal of Neuroscience, 22*, 10470–10476.

Mathern, J. R., Raatz, S. K., Thomas, W., & Slavin, J. L. (2009). Effect of fenugreek fiber on satiety, blood glucose and insulin response and energy intake in obese subjects. *Phytotherapy Research, 23*, 1543–1548.

Million, M., Angelakis, E., Paul, M., Armougom, F., Leibovici, L., & Raoult, D. (2012). Comparative meta-analysis of the effect of *Lactobacillus* species on weight gain in humans and animals. *Microbial Pathogenesis, 53*, 100–108.

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

Peeters, A., Barendregt, J., Willekens, F., Mackenbach, J., Mamun, A., Bonneux, L., et al. (2003). Obesity in adulthood and its consequences for life expectancy. A life-table analysis. *Annals of Internal Medicine, 138*, 24–32.

Reimer, R. A. (2006). Meat hydrolysate and essential amino acid-induced glucagon-like peptide-1 secretion, in the human NCI-H716 enteroendocrine cell line, is regulated by extracellular signal-regulated kinase1/2 and p38 mitogen-activated protein kinases. *Journal of Endocrinology, 191*, 159–170.

Rippe, J. (1998). Obesity as a chronic disease. Modern medical and lifestyle management. *Journal of American Dietitian Association, 98*, S9–S15.

Ritter, R. C. (2004). Increased food intake and CCK receptor antagonists. Beyond abdominal vagal afferents. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 286*, R991–R993.

Silva, M. R., Dias, G., Ferreira, C. L., Franceschini, S. C., & Costa, N. M. (2008). Growth of preschool children was improved when fed an iron-fortified fermented milk beverage supplemented with *Lactobacillus acidophilus*. *Nutrition Research, 28*, 226–232.

St-Onge, M.-P. (2005). Dietary fats, teas, dairy, and nuts. Potential functional foods for weight control? *The American Journal of Clinical Nutrition, 81*, 7–15.

Urbienė, S., & Leskauskaitė, D. (2006). Formation of some organic acids during fermentation of milk. *Polish Journal of Food and Nutrition Sciences, 15*(56), 277–281.

Vrang, N., Madsen, A. N., Tang-Christensen, M., Hansen, G., & Larsen, P. J. (2006). PYY(3-36) reduces food intake and body weight and improves insulin sensitivity in rodent models of diet-induced obesity. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 291*, R367–R375.

Zhang, J., & Ritter, R. C. (2012). Circulating GLP-1 and CCK-8 reduce food intake by capsaicin-insensitive, nonvagal mechanisms. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology, 302*, 26.