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RESEARCH ARTICLE | *Nutrient Sensing, Nutrition, and Metabolism*

Oatmeal particle size alters glycemic index but not as a function of gastric emptying rate

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Mackie AR, Bajka BH, Rigby NM, Wilde PJ, Alves-Pereira F, Mosleth EF, Rieder A, Kirkhus B, Salt LJ. Oatmeal particle size alters glycemic index but not as a function of gastric emptying rate. *Am J Physiol Gastrointest Liver Physiol* 313: G239–G246, 2017. First published June 1, 2017; doi:10.1152/ajpgi.00005.2017.—The aim of this study was to determine the extent to which oat particle size in a porridge could alter glucose absorption, gastric emptying, gastrointestinal hormone response, and subjective feelings of appetite and satiety. Porridge was prepared from either oat flakes or oat flour with the same protein, fat, carbohydrate, and mass. These were fed to eight volunteers on separate days in a crossover study, and subjective appetite ratings, gastric contents, and plasma glucose, insulin, and gastrointestinal hormones were determined over a period of 3 h. The flake porridge gave a lower glucose response than the flour porridge, and there were apparent differences in gastric emptying in both the early and late postprandial phases. The appetite ratings showed similar differences between early- and late-phase behavior. The structure of the oat flakes remained sufficiently intact to delay their gastric emptying, leading to a lower glycemic response, even though initial gastric emptying rates were similar for the flake and flour porridge. This highlights the need to take food structure into account when considering relatively simple physiological measures and offering nutritional guidance.

NEW & NOTEWORTHY The impact of food structure on glycemic response even in simple foods such as porridge is dependent on both timing of gastric emptying and the composition of what is emptied as well as duodenal starch digestion. Thus structure should be accounted for when considering relatively simple physiological measures and offering nutritional guidance.

oats; glycemic response; particle size; gastric emptying, appetite

THE FOOD INDUSTRY is faced with the task of producing highly palatable foods that meet consumer preferences and comply with their nutritional needs. However, the overabundance of very nutritious food has brought with it a number of challenges associated with adverse health outcomes. Of special concern is the dramatic increase in obesity and metabolic diseases. Therefore now more than ever we need to understand the mechanisms through which rates of nutrient release may be controlled, affecting physiological responses to food as well as sensations of appetite and satiety. The way that dietary components and food structure modify digestion kinetics may reveal foods with the potential to reduce risk factors associated with metabolic diseases such as type 2 diabetes, e.g., hyperglycemia and elevated blood pressure.

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Recent research indicates that oats (*Avena sativa*) contain bioactive components that have a range of positive health benefits, including effects on lipidemic and glycemic control (14, 31), as well as satiety (3). Soluble fiber may promote satiety by slowing down digestion, resulting in increased gastric retention and feelings of fullness (15). The presence of soluble fiber has also been shown to alter the secretion of gastrointestinal hormones (4) and aid body weight regulation (33).

During the digestion of food there are two modes of gastric emptying, first by eroding the solid bolus of food in the stomach from the outside, where the food has been most exposed to acid and enzymes. The chime may then be squeezed through the pylorus into the duodenum if the particle size is sufficiently small (22, 23). When the gastric contents are more fluid or semisolid (e.g., soup or porridge), emptying occurs primarily during periods of quiescence in antral pressure activity and, by implication, in antral contractile activity (13) and thus may empty from the center of the stomach, a zone that has not been subjected to significant pH change or exposed to gastric enzymes (29). In the antrum, selective "sieving" permits the rapid passage of liquids and smaller food particles while the larger particles are retained for further processing, although this is affected by the viscosity of the gastric contents (24). The size cut-off means that particles larger than ~3 mm (17) tend to be retained longer, although not indefinitely (34). The rate at which food is emptied from the stomach depends on a number of factors, but one is the energy density of the food (11, 12). As far back as the 1970s it was shown that energy density has an inverse effect on gastric emptying. However, in addition, the rheological properties of the gastric content play an important role on gastric processing (9) and emptying rate. Although both are important, increasing the viscosity is considered less effective than increasing the energy density in slowing gastric emptying (7).

A number of foods have traditionally been eaten because they are perceived as healthy, and this includes oat porridge. However, studies have shown that the way that the oats are processed has a strong influence on glycemic index (36). In particular, the modern trend toward quick cook oats is likely to have a significant effect on the glycemic index of the final product. It is not clear, though, whether this difference is a result of alterations in gastric residence time or intestinal starch hydrolysis. Indeed given the high beta-glucan content of oats it could be that release of this polymer significantly alters intestinal viscosity, or has a similar influence on gastric residence time because although energy density affects gastric emptying, it is also affected by viscosity (7). The milling process of oat flakes increases the accessibility of nutrients and fiber, including beta-glucan, and this may influence gastric emptying dynamics and glycemic response. Thus our study investigated the effect of oat grain processing upon gastric emptying rates, glycemic response, and satiety. Study participants consumed two isocaloric porridges prepared from finely milled oats and flaked oats, and MRI imaging was used to study gastric volumes and layering. Subjective feelings of appetite and satiety were recorded, as well as levels of blood glucose, insulin, and GI hormones. The overall aim was to understand how food structure is involved with some of the mechanisms that regulate hunger, appetite, and satiety. Our hypothesis was that greater release of starch and soluble fiber from the finely milled porridge would generate a higher viscosity in the stomach than the flaked porridge. In combination with the more effective nutrient release from the finely ground porridge this would lead to a lower glycemic response, slower gastric emptying, and greater feelings of fullness for longer.

MATERIALS AND METHODS

The meals. The two meals used in this crossover were based on the same porridge recipe. The composition of the two meals is given in Table 1. Both oat samples had the same composition as they were produced from the same batch of Norwegian Belinda oats. The oat flakes were of commercial quality, provided by Lantmännen Cerealia, Moss, Norway. The oat flakes were milled into flour using a hammer mill (Retsch ZM 200, Dale, Norway) with a 0.5-mm screen. The β-glucan content of the oats was 4.52 g/100 g dry wt as determined by an enzymatic method using a mixed linkage beta-glucan assay kit from Megazyme (Megazyme International, Bray, Ireland). Oat flake or oat flour porridge was prepared on the morning of the study using the following protocol: Skimmed milk, water, and margarine were gently heated until the margarine melted. Then either oat flakes or oat flour were added and well mixed. The mixture was brought to the boil (constant stirring), then sugar and salt added, and boiled for 1 min. The porridge was then transferred to an insulated container and transported (~10 min) to a room set aside for its consumption, adjacent to the MRI facility.

Table 1. *Composition and nutritional information of the two porridge meals*

Ingredient	Oat Flakes	Oat Flour
Flakes or flour, g	35.2	35.2
Skimmed milk, g	110	110
Water, g	110	110
Margarine, g	6.6	6.6
Sugar, g	1.98	1.98
Salt, g	0.11	0.11
Total amount, g	264	264
Kcal for 264 g portion	237.6	237.6

Nutrition	g/100 g	g/264 g	g/100 g	g/264 g
Fat	2.94	7.76	2.94	7.76
Carbohydrate	11.7	30.9	11.7	30.9
Fiber	1.66	4.38	1.66	4.38
Beta-glucan	0.54	1.43	0.54	1.43
Protein	3.36	8.87	3.36	8.87
*Salt	0.80	2.11	0.80	2.11

*Salt content estimated using http://nutritiondata.self.com/.

Imaging of gastric contents. The gastric contents of the volunteers was determined using a conventional 3T magnetic resonance imaging (MRI) scanner (GE Discovery MR750w). Imaging used a FIESTA (Fast Imaging Employing Steady-state Acquisition) protocol developed to scan the stomach in a breath-hold of the order of 15–20 s depending on the fullness of the stomach (TR/TE 3.73/1.19 ms, field of view 450 mm, matrix 512 × 512, slice thickness 5 mm). This yields contiguous 5-mm axial slices through the stomach enabling calculation of total stomach volume. Both transverse and coronal images were acquired to ensure that the gastric volume could be accurately defined. Total volumes of gastric contents (excluding gas) and the nature of layers formed as a result of sedimentation were determined at each time point using freehand tracings of the region of interest around the stomach contents for each 5-mm-thick slice and from this the total stomach volume was calculated using Image-Pro Plus v7.1 software (Media Cybernetics, San Diego, CA) (20). This involved assessment of the position of the pylorus. Each set of scans took ~5 min and between scans the volunteers remained seated upright close to the scanner. From the variation of the gastric volume with time we deduced an apparent emptying rate, which provides the estimated rate at which the food emptied from the stomach, due to the inhomogeneous distribution of the food material inside the stomach and because of the simultaneous addition of gastric secretion.

Visual analog scales. We assessed volunteer satiety with a self-reported visual analog scale technique (35). Before the meal and at specific time intervals postmeal (see Table 3), the volunteers completed a five-question satiety questionnaire with a visual-analog scale (VAS) for each of the following questions: *1*) "How hungry are you?"; *2*) "How full do you feel?"; *3*) "How satisfied do you feel?"; *4*) "How big is your desire to eat?"; and *5*) "How thirsty are you?". The analog scores for each question were then converted to numeric scores based on the following: *1*) 1 = "not at all hungry" and 10 = "very hungry"; *2*) 1 = "not full at all" and 10 = "very full"; *3*) 1 = "not satisfied at all" and 10 = "very satisfied"; *4*) 1 = "no desire to eat at all" and 10 = "very big desire to eat"; and *5*) 1 = "not thirsty at all" and 10 = "very thirsty." The individual participant data were normalized by subtracting the mean value and dividing by the standard deviation of each time course. The data are presented as the difference from baseline and show the mean ± standard error of the mean (SE).

Determination of glucose, insulin, and GI hormones. At the start of each study session volunteers were fitted with a cannula so that blood could be drawn periodically. At each required time point 4 ml of blood was drawn and stored on ice for <2 h before being centrifuged. Blood was collected into tubes (Vacutainer K2 EDTA, Becton Dickenson) containing 170.9 μl (2,000 KIU) of aprotinin (Sigma-Aldrich, UK), and after centrifugation for 10 min at 1,500 *g* and 4°C, the plasma was removed and stored in prelabeled tubes at −80°C. The plasma analysis was performed by the Core Biochemical Assay Laboratory of Cambridge University Hospitals. The plasma was analyzed for insulin, GIP (glucose-dependent insulinotropic peptide), and GLP-1 (*Glucagon-like peptide 1)* by Diasorin Liaison XL auto analyzer. The insulin concentrations were determined using a one-step chemiluminescence immunoassay also from Diasorin (Diasorin, Saluggia, Italy). The GLP-1 and GIP concentrations were determined using electrochemical luminescence immunoassay kits from MesoScale Discovery (Gaithersburg, MD). The plasma samples were also analyzed for glucose using a Randox DatoNa$^+$ (Randox Laboratories, Crumlin, UK) and a colorimetric GL 8318 glucose kit.

Determination of viscosity and available β-glucan during in vitro digestion. A simulated digestion model (28) was used to digest porridge samples (2 g) in duplicates. Pepsin (P7000 from porcine gastric mucosa (EC 3.4.23.1, Sigma-Aldrich, St. Louis, MO), pancreatin (P1750 from porcine pancreas, Sigma-Aldrich), and bile salts

Table 2. *Participant clinical characteristics*

Participant ID	Age, yr	Height, cm	Weight, kg	Body Mass Index, kg/m^2	Blood Pressure, mmHg	Resting Heart Rate, beats/min
OM01	48	176.6	81.2	26	138/82	57
OM02	48	179.6	89.1	27.6	120/84	61
OM03	53	188.9	94.9	26.6	124/79	53
OM04	48	178.8	75.7	23.7	129/84	70
OM06	38	178.7	94.5	29.6	129/78	63
OM07	46	173.6	78.7	26.1	137/82	60
OM08	53	188.9	92.3	25.9	123/73	56
OM09	37	193.8	96.4	25.7	137/88	61

(B8381 bile from bovine and ovine, Sigma-Aldrich) were used at concentrations of 2,000 U/ml, 100 U/ml (based on trypsin activity), and 10 mM, respectively, in the final digestion mixtures. The digestion was performed in 50-ml centrifuge tubes placed horizontally in a shaking incubator (Innova 40, Incubator Shaker Series, New Brunswick Scientific, Edison, NJ) at 175 rpm and 37°C. Incubation in the intestinal phase was 2 h, after which the samples were centrifuged at 4,000 rpm for 10 min (Heraeus Multifuge 4 KR). An aliquot of the supernatant was boiled for 5 min, diluted, filtered through a 0.8-μm syringe filter, and injected into a HPSEC system with calcofluor detection to determine β-glucan M_w as previously described (30). The β-glucan concentrations were calculated from the area under the chromatographic peak using β-glucan standards of known concentration as reference. The viscosity of the supernatants was measured at constant shear (10 s^{-1}) using a Physica MCR 301 rheometer (Anton Paar, Stuttgart, Germany) fitted with a double gap geometry (DG26.7).

Methodology. The crossover study was designed to assess differences in gastric emptying, satiety indicators, and levels of glucose, insulin, and GI hormones glucose-dependent insulinotropic peptide (GIP) and glucogon like peptide 1 (GLP-1). The study included only male volunteers aged between 37 and 53 yr and with a body mass index (BMI; kg/m^2) between 23 and 30. The mean age of the cohort was 46 ± 6 yr and the mean BMI was 26.4 ± 1.7. The clinical details of the participants are given in Table 2. All 8 volunteers recruited to the study were apparently healthy and provided written informed consent before taking part in the study, which was approved by an NHS research ethics committee (approval 15/SW/0165). Each volunteer attended the study center on two occasions, at least 7 days apart, consuming a different meal on each occasion. The order in which the meals were consumed was randomly allocated. All volunteers were able to consume all of the test meals within 5 min.

On each study day volunteers were asked to fast overnight, with the last consumption of a meal before 2200 the day previous to the study. They were allowed to drink as much water as they needed but only until 0700. After this time no further consumption was allowed. The experimental protocol was started between 0830 and 0900, which corresponds to the first time point in Table 3. After initial formalities each volunteer had a cannula inserted into an arm ready for blood drawing. They then underwent the first MRI scan, a 4 ml sample of blood was drawn, and they were asked to complete a VAS questionnaire (baseline measurements). The volunteer consumed the meal, allocated at random. Immediately after the meal was consumed the second MRI scan was performed with subsequent scans being undertaken as laid out in Table 3. The volunteers were asked to repeatedly complete a VAS satiety questionnaire and have a 4 ml sample of blood drawn, and the timing for these is also given in Table 3.

Table 3. *Timing of the study protocol*

Time Point	MRI Scan	Blood Sampling	VAS Questionnaire
1	−15	−10	−5
2	5	10	15
3	25	20	30
4	45	35	50
5	65	60	70
6	90	85	100
7	115	110	130
8	145	140	160
9	180	170	190

All times are given in minutes after completion of meal consumption with the exception of the first row, which indicates the time before meal consumption of the porridge.

Statistics. The study was powered based on the primary outcome, glycemic response, which in healthy participants is most significantly shown with insulin. Using the data from a previous study (32) as a guide, to see a significant difference ($P < 0.05$) of at least 18 pmol/l (106 pg/ml) insulin between treatments, the current study requires 8 volunteers (power = 95%). The data are multivariate by nature, which calls the need to be analyzed as such. For overview and validation multivariate data analysis using Partial Least Squares Discriminant Analysis (PLS-DA) (2) was performed with product type (flakes vs. flour) as response variable. The features were standardized to unit variance. The PLS-DA model was performed by Unscramble (version 10.3, Camo Software) and plotted in the setup using the data programming language R (http://www.r-project.org/version 3.2.2). Validation of the model is given as percentage of correctly classified response (flour, flakes) in a cross-validation test where one sample at a time is left out from the calibration and used for the validation. The results are presented first for one feature at the time using error bars as guidelines.

RESULTS

The primary aim of the study was to determine whether oat porridge produced from flaked oats gave a different glycemic response and remained in the stomach for longer than porridge

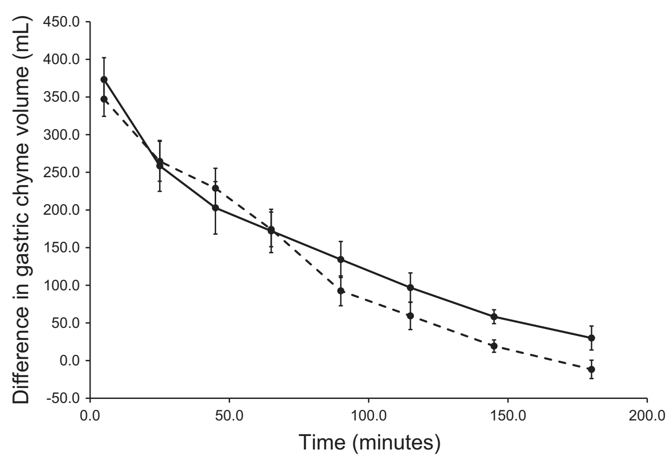

Fig. 1. Total volume of gastric content (excluding gas) after consumption of porridge made from either oat flakes (continuous line) or oat flour (dashed line). The error bars represent the standard error of the mean (SE); n = 8.

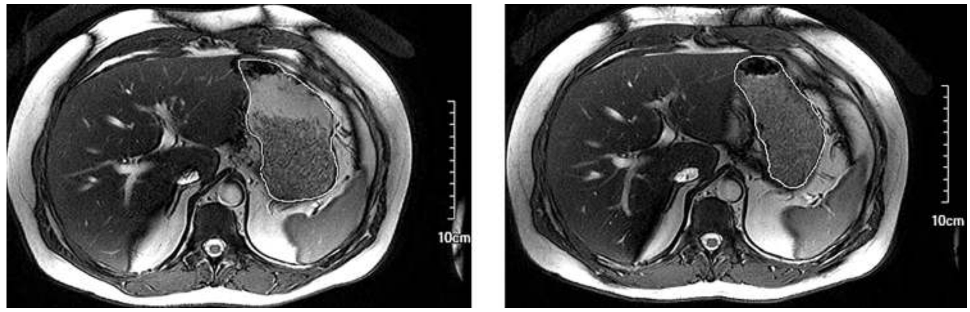

Fig. 2. Axial FIESTA MRI images of the stomach (outlined) taken 5 min (left) and 25 min (right) postconsumption. The left image shows a layer above the oat flake porridge that is not apparent after 25 min.

made from oat flour. Participants were fed 264 g of porridge along with 175 ml of water making a total of ~440 ml, which was consumed in <10 min. Analysis of the MRI images yielded the volume of gastric chyme for all participants as a function of time. These data, shown in Fig. 1, indicate an initial gastric volume slightly higher than the meal volume after 5 min, which is most likely due to the fasting secretion present before the meal was consumed. The data demonstrate very little difference between the two meals. However, toward the end of the gastric cycle it is clear that more of the flakes remained in the stomach.

Using a simple Elashoff equation (8) to fit the gastric chyme volume data gives emptying half-time ($t_{1/2}$) values of 74 ± 17 and 84 ± 11 min for the flour and flake porridge, respectively. A simple shape factor of 1 was used to fit the data assuming no lag phase. This then gives mean emptying rates of 3.3 ± 0.7 and 2.7 ± 0.5 ml/min, respectively, for the flour and flake porridge. Thus, given that the final caloric density of what was consumed in both cases, i.e., the porridge and water, was 0.54 kcal/ml, the caloric emptying rate was 1.8 and 1.5 kcal/min for the flour and flake porridge, respectively.

The data for the oat flakes suggest an initial faster rate of emptying followed by a slower rate. This is also confirmed by images of the gastric content shown in Fig. 2. After 5 min, clear layering (phase separation) was seen in the flake porridge but the layering was no longer visible 20 min later, indicating that the liquid layer on the top of the stomach contents had been emptied. The mean volume of this clear layer was 107 ±

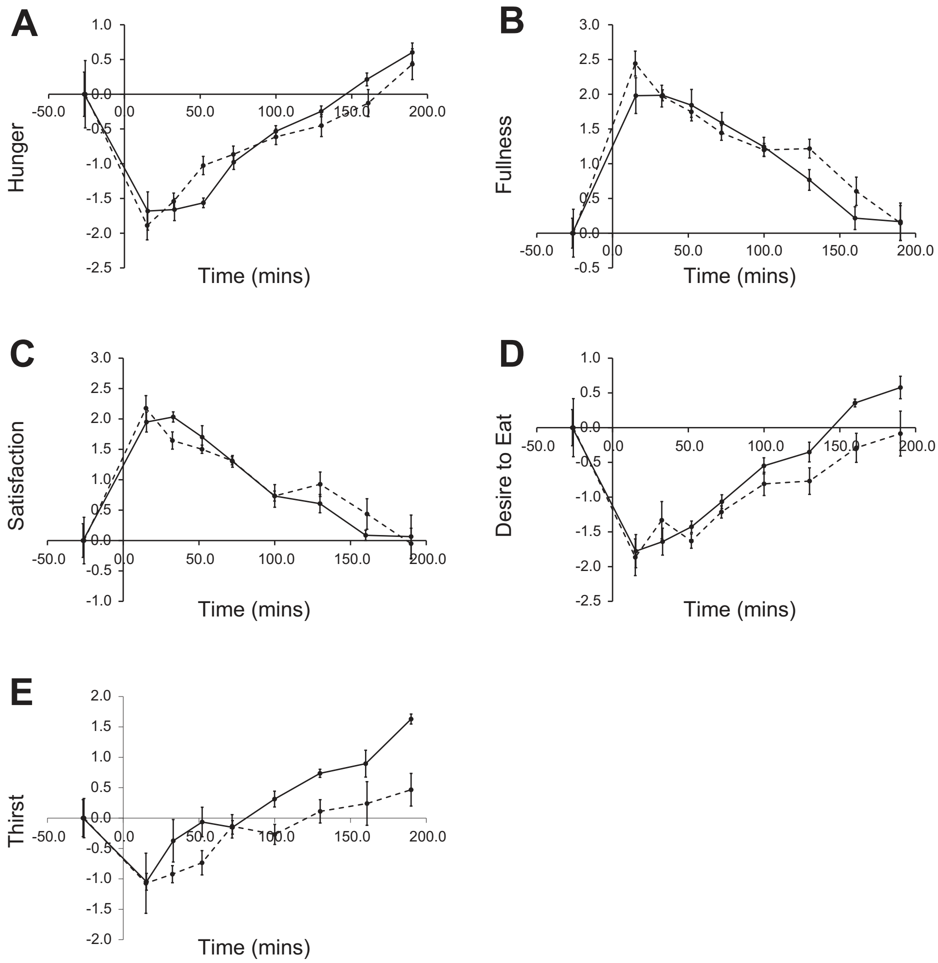

Fig. 3. Normalized visual analog scale questionnaire results shown as the mean value for hunger (*A*), fullness (*B*), satisfaction (*C*), desire to eat (*D*), and thirst (*E*) after consumption of either oat flakes (continuous line) or oat flour (dashed line) porridge. The error bars shown represent the SE; $n = 8$.

24 ml, which closely corresponds to the 115 ± 30 ml emptied between 5 and 25 min after consumption of the meal. This strongly suggests that the initial emptying of the flaked porridge meal was almost entirely the liquid part and not the oat flakes themselves.

In addition to measuring the volume of gastric contents, the participants were asked to complete a VAS questionnaire associated with appetite. In particular, the sensation of fullness is normally closely associated with gastric volume and also inversely associated with hunger. The data for hunger, fullness, satisfaction, desire to eat, and thirst are shown in Fig. 3, *A–E*. In this case the fullness, hunger, and satisfaction ratings were similar for both meals at all time points, whereas the flakes showed higher scores for desire to eat from 50 min after intake. The ratings for thirst showed marked differences after 90 min with the flake giving more pronounced feelings of thirst. Interestingly all of the data except thirst showed a crossover at ~100 min.

Both gastric emptying and appetite-related sensations are linked to nutrient absorption and gastrointestinal hormone secretion. The results of the analysis of the blood samples taken are shown in Figs. 4 and 5. The data show that there was a small difference in peripheral glucose with the flakes giving a smaller peak at ~35 min after meal consumption. The incremental area under the curve (iAUC) for the glucose as calculated by the method of Brouns et al. (6) is 65.9 ± 21.4

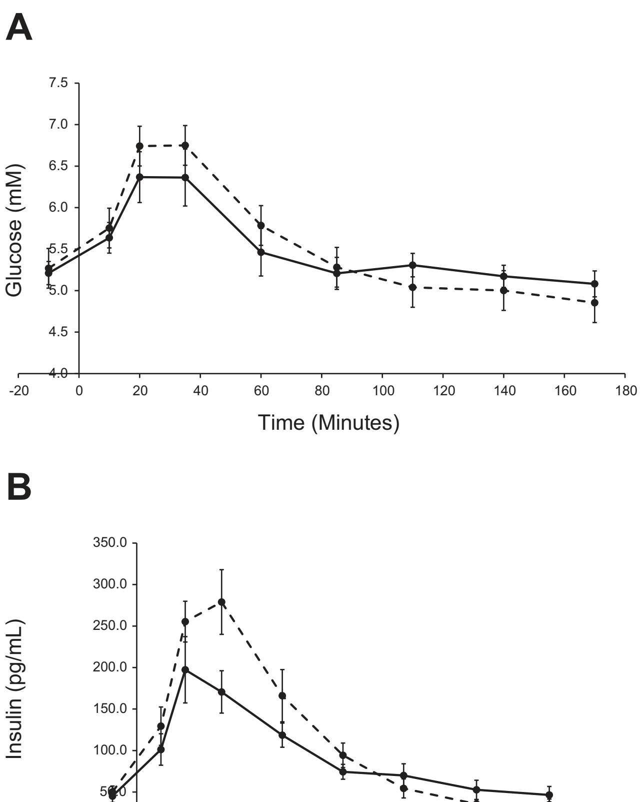

Fig. 4. The average concentrations of glucose (*A*) and insulin (*B*) found in plasma after consumption of porridge made from either oat flakes (continuous line) or oat flour (dashed line). The error bars represent the SE; $n = 8$.

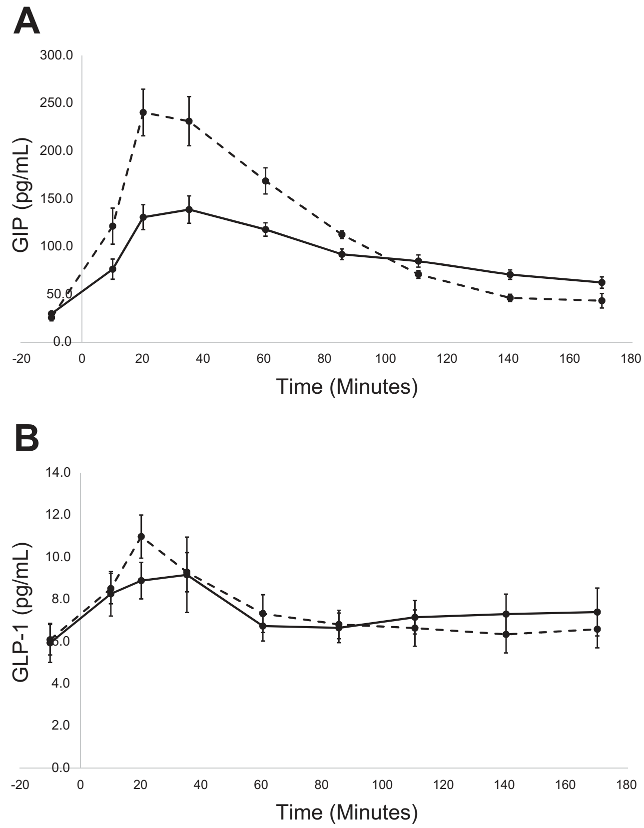

Fig. 5. The average concentrations of GIP (*A*) and GLP-1 (*B*) found in plasma after consumption of porridge made from either oat flakes (continuous line) or oat flour (dashed line). The error bars represent the SE; $n = 8$.

mM·min/l for the flour porridge and 46.0 ± 37.7 mM·min/l for the flakes. The difference in insulin response was larger with the peak at 35 min markedly higher for the flour than the flakes. Although the small apparent drop of the plasma glucose below the fasted (initial) value in the latter stage of the study day was within the random error of the experiment, such a drop has also been seen in similar studies (5, 16).

The data for the GIP and GLP-1 responses are shown in Fig. 5. As both of these hormones are incretins, they both follow similar patterns. The patterns for the change in plasma concentrations of GIP and insulin are very similar after consumption of both meals, with a peak at ~30 min. In the case of GIP the difference between the meals is very marked, in particular at 35 min. The greater response was generated by the flour at all post consumption time points up to 85 min with the flakes giving the greater response thereafter. The GLP-1 concentration showed a difference between the two meals at 20 min, with the flour giving the larger response at that time. Interestingly, the crossover in all the plasma data was at ~90–100 min, which is slightly after a crossover in the gastric volume curves and may indicate the time at which most of the flour porridge had been digested but when there was still glucose from the flake porridge being absorbed.

To investigate the role of β-glucan in the late period of digestion, when the crossover was observed in blood parameters and VAS measures, simulated intestinal viscosity and β-glucan release were obtained after in vitro digestion. The two porridge samples did not differ in β-glucan M_w with values of 1,097 ± 14 and 1,107 ± 17 for the flour and flakes, respectively. However, more β-glucan was solubilized in the flour porridge (37.5 ± 1.8%) compared with the flake porridge (28.5 ± 1.5%) and the viscosity of the extract was also slightly higher for the flour porridge (1.38 ± 0.02 mPa·s) compared with the flake porridge (1.17 ± 0.01 mPa·s).

An overview and validation of the effects produced by the digestion of the two porridge meals is provided by PLS-DA discriminant analysis performed at an early time point, i.e., 35 min after consumption of the porridge (Fig. 6, *A* and *B*), and a later time point, i.e., 180 min after consumption (Fig. 6, *C* and *D*).

In the score plots of the samples, displayed in Fig. 6*A* (35 min) and Fig. 6*C* (180 min), the flour is located toward the upper right corner and the flakes are located toward the lower left corner. The loading plot at 35 min (Fig. 6*B*) reflects the higher levels of glucose, insulin, and GIP, as well as higher ratings of hunger observed for the flour porridge at this time point. All these features are located toward the righthand side in the loading plot, and so is the response variable "flour." At the later time point (180 min) (Fig. 6, *C* and *D*), this pattern is changed, with the flake porridge associated with the highest ratings of hunger and desire to eat, and the flour porridge with higher fullness and satisfaction. The plasma levels of glucose, insulin, and GIP, as well as the gastric volume, were highest for the flake porridge at this time point.

DISCUSSION

Once consumed, food passes into the stomach, where it stays until it is emptied into the duodenum. In the time that it resides in the stomach a number of changes can take place including digestion by gastric and oral enzymes depending on local pH and phase separation (25). In this case the oat flake porridge showed significant signs of sedimentation of the flakes immediately postconsumption (Fig. 2*A*). The absence of the liquid phase above the flakes in the image taken 20 min later shows that the flakes remained sufficiently intact to be prevented from passing through the pylorus into the duodenum. This confirms that a good proportion of the original flake porridge meal remained in the stomach longer than flour porridge meal. However, does this mean that the starch in that porridge remained associated with the flakes and thus was not emptied into the duodenum? The lower peak in plasma glucose, insulin, and GIP certainly suggests that this was the case.

The most significant difference in the plasma components that were measured was seen in glucose-dependent insulinotropic peptide (GIP). The secretion of GIP by K-cells is driven by the rate of nutrient absorption in the proximal small intestine, especially glucose or fat (1). The primary role of GIP is in the pancreas where it binds to its specific receptor (GIPR) on β-cells and enhances glucose-dependent insulin secretion. Thus it is no surprise that the GIP response is mirrored by the insulin response to both meals but to a lesser extent. In a recent study, Trahair et al. sought to determine the effect of two different rates of intraduodenal glucose infusions (1 or 3 kcal/min) on glycemic, insulinemic, and incretin hormone responses in lean and obese subjects, and compare the effects of oral and intraduodenal glucose in obese subjects (37). This was done to mimic different rates of gastric emptying. Unsurprisingly, the faster delivery of glucose in their study gave higher responses in glucose, insulin, and GIP. In the healthy control group, the pattern was very similar to that seen in this study with the GIP response the largest followed by the insulin and then the plasma glucose. This was not the case in the obese group, where the GIP response was less significant than either the insulin or glucose responses. The authors concluded that the rate of duodenal delivery of glucose is a major determinant of glycemia in obese subjects and that "strategies that slow

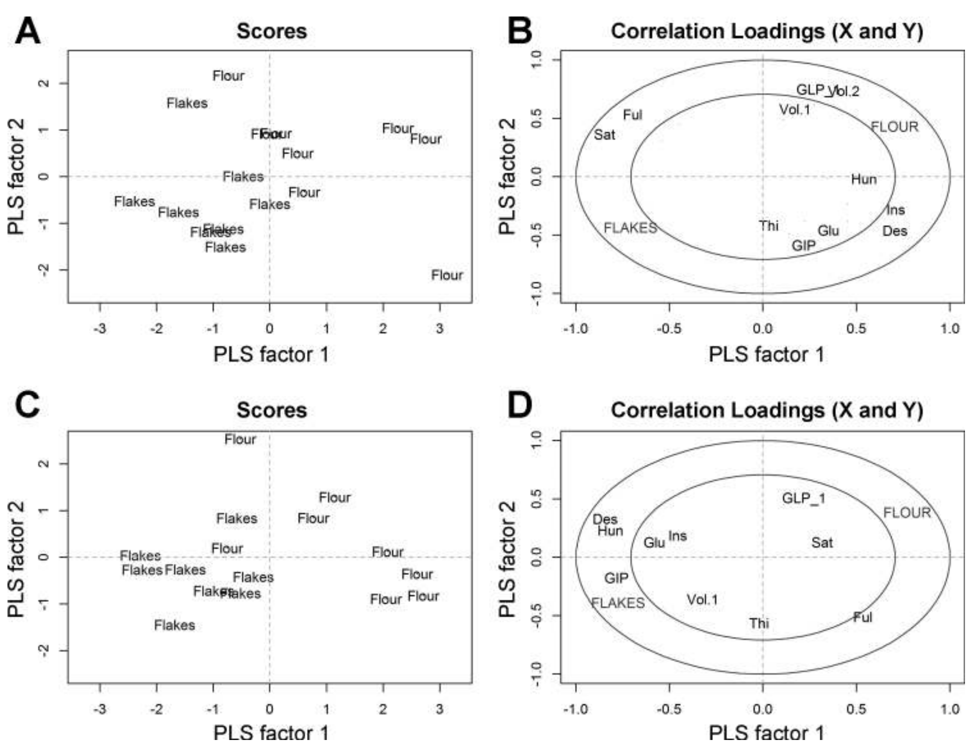

Fig. 6. Multivariate data analysis (PLS-DA) of the observed data on glucose, insulin, GIP, gastric volume, and satiety sensations, with porridge type (flakes and flour) as two response classes. *A* and *B* show the results 35 min after intake of porridge, and *C* and *D* show the results 180 min after intake. *A* and *C* are score plots of the samples, and *B* and *D* show the corresponding loadings of the input variables and the responses; $n = 8$.

gastric emptying may prevent progression to type 2 diabetes in obesity warrants exploration." In the work presented here we have started that exploration.

The particle size (flour vs. flakes) in oat porridge significantly influenced the glycemic response. The peaks in blood glucose, insulin, and GIP observed 30–40 min after intake were significantly higher for the flour porridge compared with the flake porridge. The MRI analyses indicate that this was not due to a more rapid gastric emptying after intake of flour porridge. However, the composition of what was emptied from the stomach could have been very different because of the gastric sieving effect. The higher glycemic response is therefore more likely reflecting increased starch hydrolysis in the intestine due to more easily available starch in the flour than the flakes.

In an attempt to unify all of the data including the subjective appetite scores, a multivariate analysis was undertaken. Results from the PLS-DA also reflect the differences in glycemic response. Over the time course, the plasma levels of glucose, insulin, and GIP declined for both porridges, resulting in a shift after ~2 h when the flour porridge showed slightly lower levels of glucose, insulin, and GIP than the flake porridge. Similarly, the satiety data changed with time. At 35 min after ingestion the flake porridge was associated with lower hunger, whereas at 180 min the flake porridge got the highest ratings of hunger and desire to eat. Although the satiety data correlated well with the levels of plasma glucose, insulin, and GIP at both time points (low levels were associated with higher fullness and satisfaction), there may not be any cause and effect relationship. It is unlikely that the glycemic or insulin response can explain the shift in satiety taking place from 35 to 180 min after ingestion. Neither were there any strong correlations between satiety ratings and gastric volume. Hence, there must be other explanations for the differences in satiety.

At the early time point (35 min) the flake porridge was considered as more satiating than the flour porridge. MRI analysis indicated that the liquid layer on the top of the stomach content is rapidly emptied during this period. The flake porridge also gave a more pronounced feeling of thirst, which may indicate that the flake porridge was more viscous in the stomach than the flour porridge (26, 27). Viscosity has been shown to have an effect on satiety and fullness in many studies but may not affect fullness through delayed gastric emptying (10, 18). Hence, the increased perceived fullness observed after ingestion of flake porridge in the present study may be due to increased viscosity in the stomach, not generated by the starch and β-glucan but rather the persistent structure of the flakes. At later time points, the flour porridge was associated with higher fullness and satisfaction. This may be due to the higher release of β-glucan from the flour porridge (37.5%) compared with the flake porridge (28.5%) as measured after in vitro digestion. Hence, the smaller particle size in flour compared with flakes makes the β-glucan more available and resulted in a higher viscosity in the intestinal phase for the porridge made from flour compared with the porridge made with flakes. Increased viscosity may have an effect on nutrient digestion and uptake, and, hence, the stimulation of release of satiety hormones. However, it should be noted that the viscosity difference between the two porridge samples ($P = 0.053$) was very small (0.21 mPa·s). It is therefore unlikely that the viscosity difference alone can explain the different outcomes for the two porridges at later time points of digestion, and other mechanisms may be involved. It is possible that the higher amount of solubilized β-glucan in the flour porridge still plays a role, for example by decreasing the permeability of the intestinal mucus layer (19). Previous studies have shown that increasing amounts of β-glucan lower postprandial blood glucose and insulin levels (21). In the present study, a potential inhibiting effect of β-glucan on the uptake of glucose seemed minor compared with the effect of more available starch in the duodenum.

In summary, the results suggest that there are two main phenomena taking place. First, decreased gastric emptying of flakes in comparison to the increased availability of starch in the flour porridge resulted in a more pronounced glycemic response from the flour. Second, increased availability of β-glucan caused increased perceived satiety in the flour after 2 h. Neither satiety nor glycemic response appeared to be related to gastric emptying rate.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

A.R.M. and B.K. conceived and designed research; A.R.M., L.J.S., B.H.B. and N.M.R. performed the experiments; A.R.M., BHB and EFM analyzed data; A.R.M., B.K., and E.F.M. interpreted results of experiments; A.R.M. and E.F.M. prepared figures; A.R.M. drafted the manuscript; A.R.M., P.J.W., E.F.M. and B.K. edited and revised manuscript; A.R.M., PJ.W., P.M. and B.K. approved final version of manuscript.

REFERENCES

1. **Baggio LL, Drucker DJ.** Biology of incretins: GLP-1 and GIP. *Gastroenterology* 132: 2131–2157, 2007. doi:10.1053/j.gastro.2007.03.054.
2. **Barker M, Rayens W.** Partial least squares for discrimination. *J Chemometr* 17: 166–173, 2003. doi:10.1002/cem.785.
3. **Beck EJ, Tosh SM, Batterham MJ, Tapsell LC, Huang XF.** Oat beta-glucan increases postprandial cholecystokinin levels, decreases insulin response and extends subjective satiety in overweight subjects. *Mol Nutr Food Res* 53: 1343–1351, 2009. doi:10.1002/mnfr.200800343.
4. **Behall KM, Scholfield DJ, Hallfrisch J.** Comparison of hormone and glucose responses of overweight women to barley and oats. *J Am Coll Nutr* 24: 182–188, 2005. doi:10.1080/07315724.2005.10719464.
5. **Brand-Miller JC, Stockmann K, Atkinson F, Petocz P, Denyer G.** Glycemic index, postprandial glycemia, and the shape of the curve in healthy subjects: analysis of a database of more than 1,000 foods. *Am J Clin Nutr* 89: 97–105, 2009. doi:10.3945/ajcn.2008.26354.
6. **Brouns F, Bjorck I, Frayn KN, Gibbs AL, Lang V, Slama G, Wolever TMS.** Glycaemic index methodology. *Nutr Res Rev* 18: 145–171, 2005. doi:10.1079/NRR2005100.
7. **Camps G, Mars M, de Graaf C, Smeets PA.** Empty calories and phantom fullness: a randomized trial studying the relative effects of energy density and viscosity on gastric emptying determined by MRI and satiety. *Am J Clin Nutr* 104: 73–80, 2016. doi:10.3945/ajcn.115.129064.
8. **Elashoff JD, Reedy TJ, Meyer JH.** Analysis of gastric emptying data. *Gastroenterology* 83: 1306–1312, 1982.

9. **Ferrua MJ, Singh RP.** Modeling the fluid dynamics in a human stomach to gain insight of food digestion. *J Food Sci* 75: R151–R162, 2010. doi:10.1111/j.1750-3841.2010.01748.x.
10. **Hoad CL, Rayment P, Spiller RC, Marciani L, Alonso BC, Traynor C, Mela DJ, Peters HPF, Gowland PA.** In vivo imaging of intragastric gelation and its effect on satiety in humans. *J Nutr* 134: 2293–2300, 2004.
11. **Hunt JN, Cash R, Newland P.** Energy density of food, gastric emptying, and obesity. *Lancet* 306: 905–906, 1975. doi:10.1016/S0140-6736(75)92133-9.
12. **Hunt JN, Stubbs DF.** The volume and energy content of meals as determinants of gastric emptying. *J Physiol* 245: 209–225, 1975. doi:10.1113/jphysiol.1975.sp010841.
13. **Indireshkumar K, Brasseur JG, Faas H, Hebbard GS, Kunz P, Dent J, Feinle C, Li M, Boesiger P, Fried M, Schwizer W.** Relative contributions of "pressure pump" and "peristaltic pump" to gastric emptying. *Am J Physiol Gastrointest Liver Physiol* 278: G604–G616, 2000.
14. **Jenkins AL, Jenkins DJA, Zdravkovic U, Würsch P, Vuksan V.** Depression of the glycemic index by high levels of beta-glucan fiber in two functional foods tested in type 2 diabetes. *Eur J Clin Nutr* 56: 622–628, 2002. doi:10.1038/sj.ejcn.1601367.
15. **Jiménez-Cruz A, Manuel Loustaunau-López V, Bacardi-Gascón M.** The use of low glycemic and high satiety index food dishes in Mexico: a low cost approach to prevent and control obesity and diabetes. *Nutr Hosp* 21: 353–356, 2006.
16. **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* 21: 748–756, 2011. doi:10.1016/j.numecd.2010.02.002.
17. **Kong F, Singh RP.** Disintegration of solid foods in human stomach. *J Food Sci* 73: R67–R80, 2008. doi:10.1111/j.1750-3841.2008.00766.x.
18. **Lavin JH, Read NW.** The effect on hunger and satiety of slowing the absorption of glucose: relationship with gastric emptying and postprandial blood glucose and insulin responses. *Appetite* 25: 89–96, 1995. doi:10.1006/appe.1995.0043.
19. **Mackie A, Rigby N, Harvey P, Bajka B.** Increasing dietary oat fibre decreases the permeability of intestinal mucus. *J Funct Foods* 26: 418–427, 2016. doi:10.1016/j.jff.2016.08.018.
20. **Mackie AR, Rafiee H, Malcolm P, Salt L, van Aken G.** Specific food structures supress appetite through reduced gastric emptying rate. *Am J Physiol Gastrointest Liver Physiol* 304: G1038–G1043, 2013. doi:10.1152/ajpgi.00060.2013.
21. **Mäkeläinen H, Anttila H, Sihvonen J, Hietanen RM, Tahvonen R, Salminen E, Mikola M, Sontag-Strohm T.** The effect of beta-glucan on the glycemic and insulin index. *Eur J Clin Nutr* 61: 779–785, 2007. doi:10.1038/sj.ejcn.1602561.
22. **Marciani L, Gowland PA, Fillery-Travis A, Manoj P, Wright J, Smith A, Young P, Moore R, Spiller RC.** Assessment of antral grinding of a model solid meal with echo-planar imaging. *Am J Physiol Gastrointest Liver Physiol* 280: G844–G849, 2001.
23. **Marciani L, Gowland PA, Spiller RC, Manoj P, Moore RJ, Young P, Fillery-Travis AJ.** Effect of meal viscosity and nutrients on satiety, intragastric dilution, and emptying assessed by MRI. *Am J Physiol Gastrointest Liver Physiol* 280: G1227–G1233, 2001.
24. **Marciani L, Hall N, Pritchard SE, Cox EF, Totman JJ, Lad M, Hoad CL, Foster TJ, Gowland PA, Spiller RC.** Preventing gastric sieving by blending a solid/water meal enhances satiation in healthy humans. *J Nutr* 142: 1253–1258, 2012. doi:10.3945/jn.112.159830.
25. **Marciani L, Wickham M, Singh G, Bush D, Pick B, Cox E, Fillery-Travis A, Faulks R, Marsden C, Gowland PA, Spiller RC.** Delaying gastric emptying and enhancing cholecystokinin release and satiety by using acid stable fat emulsions. *Gastroenterology* 130: A227, 2006.
26. **Martens MJI, Lemmens SGT, Born JM, Westerterp-Plantenga MS.** Satiating capacity and post-prandial relationships between appetite parameters and gut-peptide concentrations with solid and liquefied carbohydrate. *PLoS One* 7: e42110, 2012. doi:10.1371/journal.pone.0042110.
27. **Martens MJI, Westerterp-Plantenga MS.** Mode of consumption plays a role in alleviating hunger and thirst. *Obesity (Silver Spring)* 20: 517–524, 2012. doi:10.1038/oby.2011.345.
28. **Minekus M, Alminger M, Alvito P, Ballance S, Bohn T, Bourlieu C, Carrière F, Boutrou R, Corredig M, Dupont D, Dufour C, Egger L, Golding M, Karakaya S, Kirkhus B, Le Feunteun S, Lesmes U, Macierzanka A, Mackie A, Marze S, McClements DJ, Ménard O, Recio I, Santos CN, Singh RP, Vegarud GE, Wickham MSJ, Weitschies W, Brodkorb A.** A standardised static in vitro digestion method suitable for food - an international consensus. *Food Funct* 5: 1113–1124, 2014. doi:10.1039/C3FO60702J.
29. **Pal A, Brasseur JG, Abrahamsson B.** A stomach road or "Magenstrasse" for gastric emptying. *J Biomech* 40: 1202–1210, 2007. doi:10.1016/j.jbiomech.2006.06.006.
30. **Rieder A, Ballance S, Lovaas A, Knutsen SH.** Minimizing molecular weight reduction of beta-glucan during barley bread making. *Lebensm Wiss Technol* 64: 767–774, 2015. doi:10.1016/j.lwt.2015.06.034.
31. **Ripsin CM, Keenan JM, Jacobs DR Jr, Elmer PJ, Welch RR, Van Horn L, Liu K, Turnbull WH, Thye FW, Kestin M, Hegsted M, Davidson DM, Davidson MH, Dugan LD, Demarkwahnefried W, Beling S.** Oat products and lipid lowering. A meta-analysis. *JAMA* 267: 3317–3325, 1992. doi:10.1001/jama.1992.03480240079039.
32. **Rosén LAH, Silva LOB, Andersson UK, Holm C, Ostman EM, Björck IME.** Endosperm and whole grain rye breads are characterized by low post-prandial insulin response and a beneficial blood glucose profile. *Nutr J* 8: 42, 2009. doi:10.1186/1475-2891-8-42.
33. **Schuster J, Benincá G, Vitorazzi R, Morelo Dal Bosco S.** Effects of oats on lipid profile, insulin resistance and weight loss. *Nutr Hosp* 32: 2111–2116, 2015. doi:10.3305/nh.2015.32.5.9590.
34. **Stotzer PO, Abrahamsson H.** Human postprandial gastric emptying of indigestible solids can occur unrelated to antral phase III. *Neurogastroenterol Motil* 12: 415–419, 2000. doi:10.1046/j.1365-2982.2000.00218.x.
35. **Stubbs RJ, Hughes DA, Johnstone AM, Rowley E, Reid C, Elia M, Stratton R, Delargy H, King N, Blundell JE.** 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, 2000. doi:10.1017/S0007114500001719.
36. **Tosh SM, Chu Y.** Systematic review of the effect of processing of whole-grain oat cereals on glycaemic response. *Br J Nutr* 114: 1256–1262, 2015. doi:10.1017/S0007114515002895.
37. **Trahair LG, Marathe CS, Standfield S, Rayner CK, Feinle-Bisset C, Horowitz M, Jones KL.** Effects of small intestinal glucose on glycaemia, insulinaemia and incretin hormone release are load-dependent in obese subjects. *Int J Obes* 41: 225–232, 2017. doi:10.1038/ijo.2016.202.