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Oral versus intubated feeding and the effect on glycaemic and insulinaemic responses, gastric emptying and satiety.

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Abstract

Cephalic phase responses (CPR) are important in early initiation of digestion and maximal absorption of nutrients prior to ingestion. Bypassing CPR has been shown to have consequences on metabolic responses that may influence satiety. The aim of this study was to investigate if using gastric intubation to bypass oro-pharyngeal and oesophageal exposure would reduce CPR including insulin and blood glucose and whether these impact on gastric emptying and satiety.

Ten male subjects were tested on 2 occasions, 3-7 days apart after an overnight fast, in randomized order. Subjects were cannulated and intubated with a gastric tube for both tests. For test one, subjects ate 400ml soup with a spoon and for test two the soup was infused into the stomach at an equivalent rate. Subsequently measurements of glycaemic (GR) and insulinaemic responses (IR) from cannula samples, breath samples for measurement of gastric emptying using the \(^{13}\)C sodium acetate breath test and visual analogue scales (VAS) for satiety were taken over 180 minutes. There were differences in IR over the first 15 minutes (Oral: 169.0 ± 22.1; Gastric 124.1 ± 18.8; t(9)=2.67; p= 0.028) but no difference in GR. There were differences in gastric emptying half time (Oral: 85.0 ± 2.7 ; Gastric 79.4 ± 3.3; t(9)= 2.40; p=0.04) and ascension time (Oral: 68.2 ± 2.2; Gastric 64.0 ± 2.2 ; t(9)=2.57; p=0.03) with food taking longer to empty from the stomach on the Oral test day than on the Gastric test day. There was no significant difference in the satiety ratings. This study demonstrated that bypassing oro-pharyngeal and oesophageal exposure decreases the normal physiological CPR with detriment to IR and gastric emptying.

Keywords: glycaemic response, insulin, gastric emptying, cephalic, satiety
Oral ingestion of food and beverages provides a sensory experience including anticipation, sight, smell, chewing and taste. Bypassing this route removes much of this sensory stimulation and therefore reduces the normal physiological cephalic phase responses (CPR). These responses assist in early initiation of digestion and maximal absorption of nutrients prior to ingestion [1-3]. One response of particular interest is the CPR secretion of insulin (CPIR) and its role within glycaemic control [4-8]. Oral stimulation by food initiates fast release of insulin; that peaks between 1-4 minutes returning to baseline within ten minutes, the consequence of which avoids both peak levels of glucose release and subsequent gluconeogenesis and lipolysis [1, 3, 9].

Work by Teff [10] identified that CPIR caused a 30% reduction in plasma glucose post ingestion of food and Ahren and Holst [6] found that blocking neural pathways for CPR caused a reduction of 73% in CPIR, causing higher plasma glucose levels for longer following food ingestion. Western diets currently contain more energy dense foods with less fibre [11]. These foods may reduce oroosensory stimulation as they need less chewing and have a faster oral transit time [8]. This can result in a reduction in both CPRs and satiety [8, 12]. With the loss of oral sensory stimulation and associated CPIR an individual’s risk of hyperglycaemia and hyperinsulinaemia is believed to be increased, and if this becomes a consistent metabolic profile there is a greater risk of subsequent metabolic and cardio-vascular disease [12, 13]. To date, many of the studies have focused on looking at the effect on glycaemic and insulinaemic responses directly following sham feeding or oral stimulation feeding [14-16] for up 30 min but have not examined the
impact of the CPIR on the entire postprandial period to demonstrate if they would present greater metabolic risk.

Smeets et al. [8] believes that a loss of adequate oral sensory signalling from dietary choices that are more readily available in western society today are responsible for a reduction in satiety. Earlier work by Cecil et al. [14] identified that it is a combination of early oro-sensory stimulation with gastro-intestinal influences such as motility and distension that provides the greatest sensation of satiety. Furthermore utilising techniques that bypass oral CPR was found to increase rates of gastric emptying and decrease satiety [14]. Increasing rates of gastric emptying is likely to impact on satiety as food will remain in the stomach for a shorter time, decreasing the time that the stomach remains distended which could result in increased food consumption [14, 17].

Although there is much evidence that the loss of CPIR impacts on the metabolic profile of an individual there is some contradiction within the evidence [3-6, 8, 13]. Only recently have studies combining sensory signals and the implications on food consumption been undertaken [16]. Smeets et al. [8] identifies a need for further work to examine the impact of sensory signals on both short term metabolic pathways and satiety. Previous work has primarily focused on the effect of CPR on satiety and gastric emptying [14, 15] or on the role of CPR on immediate insulinaemic responses (IR) and glycaemic responses (GR) [16] but has not looked at the responses of both over the entire postprandial period where it is more likely to have a metabolic implication. This study therefore aimed to examine two components of CPR in combination, which is lacking from the extant literature. The first component that was measured was the effect
of oral stimulation on IR and GR. The second component measured was changes in gastric emptying and satiety.

Materials and Methods

Subjects

Twelve healthy males not suffering from diabetes or pre-diabetes were recruited for the study by means of advertisements and personal communications. Volunteers were given full details of the study protocol prior to giving their written informed consent. Ethical approval for this study was provided by the Research Officer for Faculty of Health and Life Sciences, Oxford Brookes University, UK, in accordance with the Declaration of Helsinki. All subject’s fasting blood glucose was <6.1mmol/l and their BMI was between 18.5 - 30kg/m². None of the subjects were taking any medication that would interfere with glucose metabolism or insulin signalling. None of the participants were smokers. Eating behaviour was determined using the Three Factor Eating Questionnaire [18]. Only those who did not consciously restrain their food intake due to psychological reasons, weight concerns and external stimuli were included in the study. All subjects were asked to rate their liking of the soup on a scale of 1-10 with 1 being strongly disliking it. All volunteers reported liking the soup and rated it as 7 or greater and hence were included in the study.

Study Design

The study required volunteers to attend the lab on three separate occasions. The first was for initial preliminary assessment and if volunteers were suitable to proceed with the study they were
required to attend for two subsequent test days; one consisting of oral ingestion of soup (Oral) and one consisting of gastric infusion of the soup into the stomach via a feeding tube (Gastric). The two tests days were carried out in random order, with a minimum of three, maximum seven days between tests.

Subjects were requested to record their food intake in a weighed food diary the night before attending for their first test and repeat this prior to their second test. They were requested to fast from 22.00 the night before although were able to drink water. Subjects were also requested to abstain from strenuous exercise and alcohol consumption the day before testing.

Preliminary assessment

Volunteers were requested to attend the lab after an overnight fast so a fasting blood glucose measurement could be taken via a fingerprick blood sample (HemoCue 201+ glucose analyzer, Angelholm, Sweden). A health questionnaire pertaining to food allergies and intolerances and any known metabolic conditions or medication was requested. Baseline anthropometric measurements of height, weight, body mass index (BMI) and blood pressure were undertaken from each individual subject. These aimed to screen for any medical conditions or medication that may interfere with glucose metabolism or insulin signalling; in which case the volunteer would be declined from participating further within the study.

The preliminary test required volunteers to attempt insertion of an oral gastric feeding tube (Vygon, 14 French Levine, length 125, Gastro-duodenal feeding tube, Ecouca, France). This ensured volunteers could satisfactorily undertake the procedure and familiarise themselves with
the technique. Self-insertion of the tube makes the process less stressful for the volunteer as it gives them control over the rate of insertion [19]. Tube insertion was required to a length of 50-55 cm and subjects needed to retain the tube placement comfortably. For subjects having difficulty, repeated attempts were not encouraged as this can impact on the gastric response.

Accurate placement of the tube was confirmed by inserting 100ml of water and using a 100ml syringe to aspirate the gastric contents. Once 80% of this can be aspirated then the tube was deemed to be in the stomach [20]. The gastric tube was then removed. Following preliminary testing, two volunteers were unable to pass the oral gastric tube (gastric intubation) and withdrew, leaving a subject group of 10 male participants (37.8±3.4 years; 1.77±0.03m; 75.4±4.2kg).

Subjects who were able to proceed with the study were then timed whilst ingesting 400ml of the test soup orally in order to measure the rate of normal feeding. This allowed determination of an individual flow rate in ml/min for gastric tube infusion of the soup using a syringe during the Gastric test session.

Experimental Test Protocol.

Subjects attended the lab in the morning between 7-8am after an overnight fasting. On arrival, cannulation of a superficial vein of the upper limb was undertaken to provide collection of blood samples for glucose and insulin measurement throughout the test protocol. Samples were taken at a baseline of – 5 minutes, following the onset of soup ingestion / infusion at 3 minute intervals for first 15 minutes and then subsequently at 15 minute intervals for a total of 180 minutes.
Baseline assessment of satiety using 100mm visual analogue scale (VAS) and breath samples for measurement of gastric emptying were also undertaken at -5 minutes.

Subjects inserted the oral gastric tube for both the Oral and the Gastric test in order to ensure there was no physiological difference between circumstances of each test that may influence findings. The oral gastric tube was removed by the subjects after completion of the first 15 minutes of the trial.

The 400ml of test soup was ingested orally by the subject or infused via the oral gastric tube at the rate of normal eating as determined from the pre-test trial. The test meal and quantity were based on previous similar studies [14, 15]. Timing of each test trial began at the point of initiating food eating / infusion. The test soup (Campbell’s Cup Soup, Cream of tomato, Leeds, UK) contained 25g of available carbohydrate and had 100mg of \(^{13}\text{C}\) labelled sodium acetate added. This is a naturally stable carbon isotope which is rapidly absorbed and oxidised within the liver to form labelled CO\(_2\) which subjects then exhale. The soup contained 170 kcal, 2.5g protein, 28.3g total carbohydrate, 4.9 g fat and 0.7g sodium. The soup was prepared by adding the soup powder to 300 ml of boiling water, 100 ml of water at room temperature and serving or intubating immediately.

**Gastric emptying**

Collection of breath via a straw tube into a glass vial (10ml Exetainer, Labco, Bucks, UK) allows analysis at a later stage as an indicator of the rate of gastric emptying. Work by Braden et al. [21] identified that this non-invasive method is reliable, safe and cost-effective for measuring rates of
gastric emptying. Subject’s breath samples were taken at baseline of -5 minutes, postprandial at 3,6,9,12,15 minutes and then every 15 minutes until 180 minutes. Samples were then analysed using isotope ratio mass spectrometry (ABCA, SerCon Limited, Crewe, UK) and results were expressed relative to V-PDB, an international standard for known $^{13}$C composition. For breath $^{13}$CO$_2$ levels using 130 known standard samples, the coefficient of variation across these samples has been shown to be 0.0044% [22]. $^{13}$CO$_2$ values were expressed as the excess amount in the breath above baseline and converted into moles. Data are then displayed as percentage of $^{13}$CO$_2$ dose recovered per hour and cumulative percentage $^{13}$CO$_2$ recovered over time. CO$_2$ production was assumed to be 300 mmol/m$^2$ body surface area per hour. Body surface area was calculated using a validated weight-height formula [23]. This was then fitted to a gastric emptying model developed by Ghoos et al., [24]. For all the data, $r^2$ coefficient between the modelled and raw data was calculated and $r^2>0.95$. From this model several parameters were measured. Lag phase and half time were calculated using the formulae derived by Ghoos et al., [24]. Lag phase is the time taken to maximal rate of $^{13}$CO$_2$ excretion [25] and is equivalent to the time of the inflection point [26]. Half time is the time it takes 50% of the $^{13}$C dose to be excreted [25]. Latency phase [26] is the point of intersection of the tangent at the inflection point of the $^{13}$CO$_2$ excretion curve representing an initial delay in the excretion curve. Ascension time [26] is the time course between the latency phase and the half time representing a period of high $^{13}$CO$_2$-excretion rates.

**Blood glucose**

Blood samples were used to test for blood glucose and insulin at each time point. Blood glucose was measured using the HemoCue® 201+ Glucose analyzer (HemoCue Ltd, Dronfield, UK). The HemoCue® is a reliable method of blood glucose analysis [27]. The laboratory's CV for 20 or
more duplicate measurements of fasting glucose (i.e. minute-to-minute variation in human subjects) was <5%. The inter-assay CV (i.e. analytical variation) on standard solutions was <3.6%.

**Insulin**

At each time point, 6 mL was collected into blood collection tubes treated with di Potassium EDTA (BD vacutainer, Oxford, UK) and immediately stored in crushed ice. Samples were then centrifuged 4000rpm, 4 ºC, for 10 minutes. Plasma was removed and stored at -40 ºC until analysis. Insulin concentrations in the plasma samples were determined by electrochemiluminescence immunoassay using an automated analyzer (Cobas® E411; Roche diagnostics, Burgess Hill, UK). The Cobas® system is a reliable method of blood insulin determination [28]. The unit of measurement was μU/ml.

On completion of the 180 minutes testing, the subject’s intra–venous cannula was removed.

**Visual analogue scales**

Throughout the test trials 100mm visual analogue scale (VAS) were utilised by each subject; at baseline, 6, and 15 minutes and then every subsequent 15 minutes for a total of 180 minutes in order to gain some comparison between oral ingestion and gastric infusion on their desire to eat and level of satiety. Each time point required subjects to make a vertical mark across the horizontal VAS line with anchor points of ‘not at all’ to ‘extremely’ for specific questions to rate their level of hunger, fullness and desire to eat and anchor points of ‘nothing at all’ to ‘large
amount’ for how much food they thought they could eat. Use of VAS as a reliable measure of subjective appetite and predictability of feeding behaviour is validated by Sorensen et al. [29].

Statistical analysis
Results of blood glucose, insulin and VAS data were converted to reflect the change in GR, IR and VAS respectively by subtracting the baseline value from those taken at set time points. It was this change response value that was then used within all subsequent analysis. Incremental area under the curve (IAUC) using the trapezoidal rule [30] was calculated for all GR, IR and the four parameters of the VAS. GR and IR IAUC were calculated for the first 15 min of the test, the first 60 min of the test and the entire 180 in of the test. Statistical analysis was undertaken using Statistical Package for Social Sciences (SPSS, version 19.0, USA). Mean differences between Oral and Gastric IAUC for total GR, IR and the four parameters of the VAS were analyzed using paired sample t-test and the effect size as calculated using Cohen’s d. Paired sample t-test was also used for comparison of gastric emptying times. Results are expressed as means ± standard error (SE) unless otherwise stated and significance was defined as p<0.05.

Results
Glycaemic Response
During the 180 minute test the GR peaked at 30 minutes in both Oral (2.35±0.25 mmol/L) and Gastric (2.76±0.35 mmol/L) tests (Figure 1). In both tests, this peak was followed by a rapid decline in glucose concentration with the nadir occurring at 75 minutes in the Oral test (-
1.25±0.19 mmol/L) and in the Gastric test (-1.41±0.29 mmol/L). There was no significant difference in the peak GR between the tests (t(9)=1.13; p=0.29; d=0.50).

There were no significant differences in GR IAUC following either 180 min (Oral: 71.3±9.5 mmol/L·min; Gastric 79.7±12.7 mmol/L·min; t(9)=0.68; p=0.51; d=0.24), 60 min (Oral: 64.9±9.5 mmol/L·min; Gastric 74.7±10.4 mmol/L·min; t(9)=0.78; p=0.45; d=0.04) or 15 min (Oral: 6.0±1.2 mmol/L·min; Gastric 6.1±1.7 mmol/L·min; t(9)=0.11; p=0.91; d=0.31).

**Insulinaemic response**

Over 180 minutes the IR (Figure 2) peaked at 30 minutes in both Oral (51.8±8.1 uU/ml) and Gastric (62.9±8.1 uU/ml) tests with a nadir at 165 minutes for Oral (-0.5±0.5 uU/ml) and at 135 minutes for Gastric (-1.2±0.3 uU/ml). There was no significant difference in the peak IR between the tests (t(9)=1.23; p=0.25; d=0.38).

There were no significant differences in IR AUC following 180 min (Oral: 1897.7±309.2 uU/ml·min; Gastric 2037.5±205.9 uU/ml·min; t(9)=0.61; p=0.56; d=0.19) or 60 min (Oral: 1638.7±262.0 uU/ml·min; Gastric 1870.5±196.8 uU/ml·min; t(9)=1.10; p=0.30; d=0.36) but there was a difference after 15 min, with the Oral test causing the greater IR (Oral: 169.0±22.1 uU/ml·min; Gastric 124.1±18.8 uU/ml·min; t(9)=2.67; p=0.028; d=0.63).

**Gastric emptying**

There were significant differences in gastric emptying times between the meals for half time (t(9)= 2.40; p=0.04) and ascension time (t(9)=2.57; p=0.03) but not for latency or lag phase.
(p>0.05). The food took ~4-5 min longer to empty from the stomach on the Oral test day than on the Gastric test day (Table 1).

Satiety

There were no significant differences in satiety ratings following the two different feeding methods for any of the parameters hunger (t(9)=0.38; p=0.71), fullness (t(9)=0.96; p=0.36), desire to eat (t(9)=1.60; p=0.15) and prospective consumption (t(9)=0.68; p=0.52) (Table 2; Figure 3).

Discussion

This study was the first to examine the entire IR and GR postprandial profile in combination with GR and satiety following Oral and Gastric feeding. The study demonstrated no significant differences between oral or intubated feeding on GR however the Oral method of feeding resulted in a greater IR over the first 15 minutes. There were also no significant differences found between Oral or Gastric feeding on satiety but gastric emptying was significantly accelerated by 4-5min on the Gastric test in comparison to the Oral test.

In comparing oral ingestion with intubated feeding it was hypothesised within the present study that bypassing oro-pharyngeal and oesophageal exposure would decrease the CPIR [31]. Findings from this present study based on the first 15 min of IAUC insulin data appear to replicate the characteristic early CPIR profile reported in previous work from oral ingestion of food [10]. However there were no differences in GR between the oral ingestion compared with
intubated feeding. Early CPIR occurs to a peak within the initial 1-4 minutes after gustatory stimulation returning to baseline within ten minutes [1-3, 9, 32]. Although overall it is a minimal rise in insulin concentration levels compared to those secreted postprandially (5uU/ml [5] for cephalic response compared to a postprandial response that could be ~60 uU/ml (current study)), it is believed to increase digestive secretions, decrease gut motility and decrease food intake [1-3].

The effects of CPIR on blood glucose appear to differ. Findings in a study by Teff et al. [32] identified that in normal weight healthy males, 4 minutes post ingestion of food there was a significant increase in insulin and also a significant drop in plasma glucose as a result of early CPIR. However as in the current study, this change in GR has not been replicated in all studies perhaps due to difficulty in measuring such small variations in blood samples [5, 8]. Ranawana et al. [33] also identified high variability in glucose absorption between individuals even after eating the same food. This presents some evidence that within-individual variance is also a possibility even in a controlled methodology which may account for the lack of differences seen here. A further consideration is that simultaneous release of glucagon during CPR may prevent a reduction in blood glucose levels caused by CPIR [5] but without measuring glucagon levels this is an unknown factor in the present study.

Other reasons for disparity within the results of studies on CPR maybe palatability and the duration of oral transit time [8]. To date there is mixed findings as to whether palatability directly impacts vagally activated pathways to increase concentrations of CPIR; which may influence study findings if there is inconsistency within the subject group [9, 29, 34]. However
within the present study an initial questionnaire undertaken identified that none of the subjects
had a dislike for the tomato soup, utilised. Expert opinion is also divided in relation to the effect
the texture or form of food choice may have on oral exposure time. Teff [34] believes there is a
lack of CPIR to liquid stimuli; suggesting that chewing is required for adequate vagal stimulation
for insulin secretion. However, Cecil et al. [14, 15, 35] validate the use of liquid soup for
initiating CPR where they found the influence of sight, smell, and taste played an important part
in stimulating both pancreatic and gastric secretions as well as influencing appetite regulatory
centres. Cassady et al. [36] and deGraaf [12] also identify that liquid such as soup when eaten
with a spoon extends oro-sensory transit time to increase both CPR and satiety. A final
explanation for the differences in results seen between studies may come from work by Cecil et
al. [15], who found that the macronutrient content of the soup plays an important role as high fat
soup suppressed hunger, induced fullness, and slowed gastric emptying more than the high-
carbohydrate soup when ingested orally but there was no differences between the soups when
they were given intragastically.

One of the main aims of the current research was to combine satiety and metabolic responses
within the one study. Oro-sensory stimulation has been shown to increase the secretion of gastro-
intestinal peptides, these peptides slow gastric emptying [5, 34]. The delay in gastric emptying
increases satiety by prolonging stomach distention [8, 14, 31]. The present study hypothesised
that bypassing oro-pharyngeal and oesophageal exposure would reduce levels of satiety by
reducing the insulinaemic response and accelerating gastric emptying. Bypassing oro-pharyngeal
and oesophageal exposure did result in a slight acceleration in gastric emptying and increased
insulinaemic response however it was not possible to detect any differences from this in satiety.
A recent study [16] was able to confirm that gastric infusion of nutrients induced greater appetite ratings than ingestion, alongside increases in satiety hormones however they were unable to detect changes in food intake. Cecil et al. [14, 15, 35] also utilised gastric intubation in a series of studies assessing the impact of bypassing oro-pharyngeal stimulation on satiety and gastric emptying. They identified that loss of oro-sensory stimulation impacted negatively on both satiety and gastric emptying, with subjects feeling fuller earlier with greater suppression of hunger when food was eaten orally. The present study failed to find significant differences between the tests for satiety; this may be due to the gastric emptying changes of only 4-5 min, which although significant may not be sufficient to decrease satiety. It may also be due to the large variability on the VAS data. However it should be noted that VAS assessments are only a measure of perceived hunger not actual food intake and an ad libitum test meal would have provided objective assessment of subsequent food intake [36, 37]. Although other studies have been able to identify changes in VAS with oral stimulation using a similar sample size they have not been able to detect changes in actual food intake [16]. An increased sample size however is hindered by the invasive nature of the intubation test procedure.

Conclusion

In conclusion this study was able to demonstrate that utilising an oral gastric tube for infusion of food to bypass oro-pharyngeal and oesophagaeal exposure decreases the normal physiological CPR with detriment to IR and marginal accelerations in gastric emptying but was unable to demonstrate any impact on satiety and GR. Potential future research could use a solid test meal and include an ad libitum test meal.
**Conflict of Interest Statement:** There are no conflicts of interest associated with this manuscript.

**Acknowledgements:** We are gratefully acknowledge Liz Kerrigan for her dedication, effort and expertise in Isotope Ratio Mass Spectrometry analysis.


List of figures:

Figure 1. Change in blood glucose response (mean ± standard error) following Oral and Gastric tests over 180 minutes (a) and over 15 minutes (b).

a) [Graph showing blood glucose response over time for Oral and Gastric tests with error bars]

b) [Graph showing blood glucose response over time for Oral and Gastric tests with error bars]
Figure 2. Change in insulinaemic response (mean ± standard error) following Oral and Gastric tests over 180 minutes (a) and over 15 minutes (b).

a)

b)
Figure 3. Change in satiety ratings from visual analogue scales (mean ± standard error) following Oral and Gastric tests for hunger (a), fullness (b), desire to eat (c) and prospective consumption (d).

(a)

(b)
List of Tables

Table 1: Gastric emptying times (mean ± standard error) following Oral and Gastric infusion of soups. *=p<0.05

<table>
<thead>
<tr>
<th>Time</th>
<th>Oral</th>
<th>Gastric</th>
<th>$d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency Phase (min)</td>
<td>16.8 ± 0.7</td>
<td>15.4 ± 1.3</td>
<td>0.44</td>
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<tr>
<td>Lag phase (min)</td>
<td>52.4 ± 1.8</td>
<td>48.4 ± 2.8</td>
<td>0.55</td>
</tr>
<tr>
<td>Half time (min)</td>
<td>85.0 ± 2.7</td>
<td>79.4 ± 3.3*</td>
<td>0.59</td>
</tr>
<tr>
<td>Ascension time (min)</td>
<td>68.2 ± 2.2</td>
<td>64.0 ± 2.2*</td>
<td>0.60</td>
</tr>
</tbody>
</table>
Table 2: Satiety rating, hunger, fullness, desire to eat and prospective consumption (mean ± standard error) following Oral and Gastric infusion test.

<table>
<thead>
<tr>
<th></th>
<th>Oral</th>
<th>Gastric</th>
<th>$d$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hunger (mm.min)</strong></td>
<td>1914 ± 489</td>
<td>2298 ± 731</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Fullness (mm.min)</strong></td>
<td>3964 ± 711</td>
<td>3330 ± 808</td>
<td>0.26</td>
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<tr>
<td><strong>Desire to eat (mm.min)</strong></td>
<td>1149 ± 712</td>
<td>2050 ± 802</td>
<td>0.38</td>
</tr>
<tr>
<td><strong>Prospective consumption (mm.min)</strong></td>
<td>1680 ± 621</td>
<td>2233 ± 848</td>
<td>0.24</td>
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