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

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24 **Abstract**

25

26 Cephalic phase responses (CPR) are important in early initiation of digestion and maximal

27 absorption of nutrients prior to ingestion. Bypassing CPR has been shown to have consequences

28 on metabolic responses that may influence satiety. The aim of this study was to investigate if

29 using gastric intubation to bypass oro-pharyngeal and oesophageal exposure would reduce CPR

30 including insulin and blood glucose and whether these impact on gastric emptying and satiety.

31 Ten male subjects were tested on 2 occasions, 3-7 days apart after an overnight fast, in

32 randomized order. Subjects were cannulated and intubated with a gastric tube for both tests. For

33 test one, subjects ate 400ml soup with a spoon and for test two the soup was infused into the

34 stomach at an equivalent rate. Subsequently measurements of glycaemic (GR) and insulinaemic

35 responses (IR) from cannula samples, breath samples for measurement of gastric emptying using

36 the $[^{13}C]$ sodium acetate breath test and visual analogue scales (VAS) for satiety were taken over

37 180 minutes. There were differences in IR over the first 15 minutes (Oral: 169.0 ± 22.1; Gastric

38 124.1 ± 18.8; $t(9)=2.67$; $p= 0.028$) but no difference in GR. There were differences in gastric

39 emptying half time (Oral: 85.0 ± 2.7 ; Gastric 79.4 ± 3.3; $t(9)= 2.40$; $p=0.04$) and ascension

40 time (Oral: 68.2 ± 2.2; Gastric 64.0 ± 2.2 ; $t(9)=2.57$; $p=0.03$) with food taking longer to empty

41 from the stomach on the Oral test day than on the Gastric test day. There was no significant

42 difference in the satiety ratings. This study demonstrated that bypassing oro-pharyngeal and

43 oesophageal exposure decreases the normal physiological CPR with detriment to IR and gastric

44 emptying.

45

46 **Keywords:** glycaemic response, insulin, gastric emptying, cephalic, satiety

Introduction

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

69   impact of the CPIR on the entire postprandial period to demonstrate if they would present greater

70   metabolic risk.

71

72   Smeets et al. [8] believes that a loss of adequate oral sensory signalling from dietary choices that

73   are more readily available in western society today are responsible for a reduction in satiety.

74   Earlier work by Cecil et al. [14] identified that it is a combination of early oro-sensory

75   stimulation with gastro-intestinal influences such as motility and distension that provides the

76   greatest sensation of satiety. Furthermore utilising techniques that bypass oral CPR was found to

77   increase rates of gastric emptying and decrease satiety [14]. Increasing rates of gastric emptying

78   is likely to impact on satiety as food will remain in the stomach for a shorter time, decreasing the

79   time that the stomach remains distended which could result in increased food consumption [14,

80   17].

81

82   Although there is much evidence that the loss of CPIR impacts on the metabolic profile of an

83   individual there is some contradiction within the evidence [3-6, 8, 13]. Only recently have

84   studies combining sensory signals and the implications on food consumption been undertaken

85   [16]. Smeets et al. [8] identifies a need for further work to examine the impact of sensory signals

86   on both short term metabolic pathways and satiety. Previous work has primarily focused on the

87   effect of CPR on satiety and gastric emptying [14, 15] or on the role of CPR on immediate

88   insulinaemic responses (IR) and glycaemic responses (GR) [16] but has not looked at the

89   responses of both over the entire postprandial period where it is more likely to have a metabolic

90   implication. This study therefore aimed to examine two components of CPR in combination,

91   which is lacking from the extant literature. The first component that was measured was the effect

92   of oral stimulation on IR and GR. The second component measured was changes in gastric

93   emptying and satiety.

94

95   **Materials and Methods**

96

97   *Subjects*

98   Twelve healthy males not suffering from diabetes or pre-diabetes were recruited for the study by

99   means of advertisements and personal communications. Volunteers were given full details of the

100   study protocol prior to giving their written informed consent. Ethical approval for this study was

101   provided by the Research Officer for Faculty of Health and Life Sciences, Oxford Brookes

102   University, UK, in accordance with the Declaration of Helsinki. All subject's fasting blood

103   glucose was <6.1mmol/l and their BMI was between 18.5 - 30kg/m^2. None of the subjects were

104   taking any medication that would interfere with glucose metabolism or insulin signalling. None

105   of the participants were smokers. Eating behaviour was determined using the Three Factor

106   Eating Questionnaire [18]. Only those who did not consciously restrain their food intake due to

107   psychological reasons, weight concerns and external stimuli were included in the study. All

108   subjects were asked to rate their liking of the soup on a scale of 1-10 with 1 being strongly

109   disliking it. All volunteers reported liking the soup and rated it as 7 or greater and hence were

110   included in the study.

111

112   *Study Design*

113   The study required volunteers to attend the lab on three separate occasions. The first was for

114   initial preliminary assessment and if volunteers were suitable to proceed with the study they were

115   required to attend for two subsequent test days; one consisting of oral ingestion of soup (Oral)

116   and one consisting of gastric infusion of the soup into the stomach via a feeding tube (Gastric).

117   The two tests days were carried out in random order, with a minimum of three, maximum seven

118   days between tests.

119

120   Subjects were requested to record their food intake in a weighed food diary the night before

121   attending for their first test and repeat this prior to their second test. They were requested to fast

122   from 22.00 the night before although were able to drink water. Subjects were also requested to

123   abstain from strenuous exercise and alcohol consumption the day before testing.

124

125   *Preliminary assessment*

126   Volunteers were requested to attend the lab after an overnight fast so a fasting blood glucose

127   measurement could be taken via a fingerprick blood sample (HemoCue 201+ glucose analyzer,

128   Angelholm, Sweden). A health questionnaire pertaining to food allergies and intolerances and

129   any known metabolic conditions or medication was requested. Baseline anthropometric

130   measurements of height, weight, body mass index (BMI) and blood pressure were undertaken

131   from each individual subject. These aimed to screen for any medical conditions or medication

132   that may interfere with glucose metabolism or insulin signalling; in which case the volunteer

133   would be declined from participating further within the study.

134

135   The preliminary test required volunteers to attempt insertion of an oral gastric feeding tube

136   (Vygon, 14 French Levine, length 125, Gastro-duodenal feeding tube, Ecouca, France). This

137   ensured volunteers could satisfactorily undertake the procedure and familiarise themselves with

138   the technique. Self-insertion of the tube makes the process less stressful for the volunteer as it

139   gives them control over the rate of insertion [19]. Tube insertion was required to a length of 50-

140   55 cm and subjects needed to retain the tube placement comfortably. For subjects having

141   difficulty, repeated attempts were not encouraged as this can impact on the gastric response.

142   Accurate placement of the tube was confirmed by inserting 100ml of water and using a 100ml

143   syringe to aspirate the gastric contents. Once 80% of this can be aspirated then the tube was

144   deemed to be in the stomach [20]. The gastric tube was then removed. Following preliminary

145   testing, two volunteers were unable to pass the oral gastric tube (gastric intubation) and

146   withdrew, leaving a subject group of 10 male participants (37.8±3.4 years; 1.77±0.03m;

147   75.4±4.2kg).

148

149   Subjects who were able to proceed with the study were then timed whilst ingesting 400ml of the

150   test soup orally in order to measure the rate of normal feeding. This allowed determination of an

151   individual flow rate in ml/min for gastric tube infusion of the soup using a syringe during the

152   Gastric test session.

153

154   *Experimental Test Protocol.*

155   Subjects attended the lab in the morning between 7-8am after an overnight fasting. On arrival,

156   cannulation of a superficial vein of the upper limb was undertaken to provide collection of blood

157   samples for glucose and insulin measurement throughout the test protocol. Samples were taken at

158   a baseline of – 5 minutes, following the onset of soup ingestion / infusion at 3 minute intervals

159   for first 15 minutes and then subsequently at 15 minute intervals for a total of 180 minutes.

160   Baseline assessment of satiety using 100mm visual analogue scale (VAS) and breath samples for

161   measurement of gastric emptying were also undertaken at -5 minutes.

162

163   Subjects inserted the oral gastric tube for both the Oral and the Gastric test in order to ensure

164   there was no physiological difference between circumstances of each test that may influence

165   findings. The oral gastric tube was removed by the subjects after completion of the first 15

166   minutes of the trial.

167

168   The 400ml of test soup was ingested orally by the subject or infused via the oral gastric tube at

169   the rate of normal eating as determined from the pre-test trial. The test meal and quantity were

170   based on previous similar studies [14, 15]. Timing of each test trial began at the point of

171   initiating food eating / infusion. The test soup (Campbell's Cup Soup, Cream of tomato, Leeds,

172   UK) contained 25g of available carbohydrate and had 100mg of [^{13}C] labelled sodium acetate

173   added. This is a naturally stable carbon isotope which is rapidly absorbed and oxidised within the

174   liver to form labelled CO_2 which subjects then exhale. The soup contained 170 kcal, 2.5g

175   protein, 28.3g total carbohydrate, 4.9 g fat and 0.7g sodium. The soup was prepared by adding

176   the soup powder to 300 ml of boiling water, 100 ml of water at room temperature and serving or

177   intubating immediately.

178

179   *Gastric emptying*

180   Collection of breath via a straw tube into a glass vial (10ml Exetainer, Labco, Bucks, UK) allows

181   analysis at a later stage as an indicator of the rate of gastric emptying. Work by Braden et al. [21]

182   identified that this non-invasive method is reliable, safe and cost-effective for measuring rates of

183   gastric emptying. Subject's breath samples were taken at baseline of -5 minutes, postprandial at

184   3,6,9,12,15 minutes and then every 15 minutes until 180 minutes. Samples were then analysed

185   using isotope ratio mass spectrometry (ABCA, SerCon Limited, Crewe, UK) and results were

186   expressed relative to V-PDB, an international standard for known ^{13}C composition. For breath

187   [13]CO_2 levels using 130 known standard samples, the coefficient of variation across these samples

188   has been shown to be 0.0044% [22]. [13]CO_2 values were expressed as the excess amount in the

189   breath above baseline and converted into moles. Data are then displayed as percentage of [13]CO_2

190   dose recovered per hour and cumulative percentage [13]CO_2 recovered over time. CO_2 production

191   was assumed to be 300 mmol/m^2 body surface area per hour. Body surface area was calculated

192   using a validated weight-height formula [23]. This was then fitted to a gastric emptying model

193   developed by Ghoos et al., [24]. For all the data, r^2 coefficient between the modelled and raw

194   data was calculated and r^2>0.95. From this model several parameters were measured. Lag phase

195   and half time were calculated using the formulae derived by Ghoos et al., [24]. Lag phase is the

196   time taken to maximal rate of [13]CO_2 excretion [25] and is equivalent to the time of the inflection

197   point [26]. Half time is the time it takes 50% of the ^{13}C dose to be excreted [25]. Latency phase

198   [26] is the point of intersection of the tangent at the inflection point of the [13]CO_2 excretion curve

199   representing an initial delay in the excretion curve. Ascension time [26] is the time course

200   between the latency phase and the half time representing a period of high [13]CO_2-excretion rates.

201

202   *Blood glucose*

203   Blood samples were used to test for blood glucose and insulin at each time point. Blood glucose

204   was measured using the HemoCue® 201+ Glucose analyzer (HemoCue Ltd, Dronfield, UK). The

205   HemoCue® is a reliable method of blood glucose analysis [27]. The laboratory's CV for 20 or

206 more duplicate measurements of fasting glucose (i.e. minute-to-minute variation in human

207 subjects) was <5%. The inter-assay CV (i.e. analytical variation) on standard solutions was

208 <3.6%.

209

210 *Insulin*

211 At each time point, 6 mL was collected into blood collection tubes treated with di Potassium

212 EDTA (BD vacutainer, Oxford, UK) and immediately stored in crushed ice. Samples were then

213 centrifuged 4000rpm, 4 ºC, for 10 minutes. Plasma was removed and stored at -40 ºC until

214 analysis. Insulin concentrations in the plasma samples were determined by

215 electrochemiluminescence immunoassay using an automated analyzer (Cobas® E411; Roche

216 diagnostics, Burgess Hill, UK). The Cobas® system is a reliable method of blood insulin

217 determination [28]. The unit of measurement was µU/ml.

218

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

220

221 *Visual analogue scales*

222 Throughout the test trials 100mm visual analogue scale (VAS) were utilised by each subject; at

223 baseline, 6, and 15 minutes and then every subsequent 15 minutes for a total of 180 minutes in

224 order to gain some comparison between oral ingestion and gastric infusion on their desire to eat

225 and level of satiety. Each time point required subjects to make a vertical mark across the

226 horizontal VAS line with anchor points of 'not at all to 'extremely' for specific questions to rate

227 their level of hunger, fullness and desire to eat and anchor points of 'nothing at all' to 'large

228   amount' for how much food they thought they could eat. Use of VAS as a reliable measure of

229   subjective appetite and predictability of feeding behaviour is validated by Sorensen et al. [29].

230

231   *Statistical analysis*

232   Results of blood glucose, insulin and VAS data were converted to reflect the change in GR, IR

233   and VAS respectively by subtracting the baseline value from those taken at set time points. It

234   was this change response value that was then used within all subsequent analysis. Incremental

235   area under the curve (IAUC) using the trapezoidal rule [30] was calculated for all GR, IR and

236   the four parameters of the VAS. GR and IR IAUC were calculated for the first 15 min of the test,

237   the first 60 min of the test and the entire 180 in of the test. Statistical analysis was undertaken

238   using Statistical Package for Social Sciences (SPSS, version 19.0, USA). Mean differences

239   between Oral and Gastric IAUC for total GR, IR and the four parameters of the VAS were

240   analyzed using paired sample t-test and the effect size as calculated using Cohen's *d*. Paired

241   sample t-test was also used for comparison of gastric emptying times. Results are expressed as

242   means ± standard error (SE) unless otherwise stated and significance was defined as $p<0.05$.

243

244   **Results**

245

246   *Glycaemic Response*

247   During the 180 minute test the GR peaked at 30 minutes in both Oral (2.35±0.25 mmol/L) and

248   Gastric (2.76±0.35 mmol/L) tests (Figure 1). In both tests, this peak was followed by a rapid

249   decline in glucose concentration with the nadir occurring at 75 minutes in the Oral test (-

250   1.25±0.19 mmol/L) and in the Gastric test (-1.41±0.29 mmol/L). There was no significant

251   difference in the peak GR between the tests (t(9)=1.13; p=0.29; d=0.50).

252

253   There were no significant differences in GR IAUC following either 180 min (Oral: 71.3±9.5

254   mmol/L·min; Gastric 79.7±12.7 mmol/L·min; t(9)=0.68; p=0.51; d=0.24), 60 min (Oral:

255   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

256   (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).

257

258   *Insulinaemic response*

259   Over 180 minutes the IR (Figure 2) peaked at 30 minutes in both Oral (51.8±8.1 uU/ml) and

260   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

261   minutes for Gastric (-1.2±0.3 uU/ml). There was no significant difference in the peak IR

262   between the tests (t(9)=1.23; p=0.25; d=0.38).

263

264   There were no significant differences in IR AUC following 180 min (Oral: 1897.7±309.2

265   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:

266   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

267   there was a difference after 15 min, with the Oral test causing the greater IR (Oral: 169.0±22.1

268   uU/ml·min; Gastric 124.1±18.8 uU/ml·min; t(9)=2.67; p=0.028; d=0.63).

269

270   *Gastric emptying*

271   There were significant differences in gastric emptying times between the meals for half time

272   (t(9)= 2.40; p=0.04) and ascension time (t(9)=2.57; p=0.03) but not for latency or lag phase

273   (p>0.05). The food took ~4-5 min longer to empty from the stomach on the Oral test day than on

274   the Gastric test day (Table 1)

275

276   *Satiety*

277   There were no significant differences in satiety ratings following the two different feeding

278   methods for any of the parameters hunger (t(9)=0.38; p=0.71), fullness (t(9)=0.96; p=0.36),

279   desire to eat (t(9)=1.60; p=0.15) and prospective consumption (t(9)=0.68; p=0.52) (Table 2;

280   Figure 3).

281

282   **Discussion**

283

284   This study was the first to examine the entire IR and GR postprandial profile in combination with

285   GR and satiety following Oral and Gastric feeding. The study demonstrated no significant

286   differences between oral or intubated feeding on GR however the Oral method of feeding

287   resulted in a greater IR over the first 15 minutes. There were also no significant differences

288   found between Oral or Gastric feeding on satiety but gastric emptying was significantly

289   accelerated by 4-5min on the Gastric test in comparison to the Oral test.

290

291   In comparing oral ingestion with intubated feeding it was hypothesised within the present study

292   that bypassing oro-pharyngeal and oesophageal exposure would decrease the CPIR [31].

293   Findings from this present study based on the first 15 min of IAUC insulin data appear to

294   replicate the characteristic early CPIR profile reported in previous work from oral ingestion of

295   food [10]. However there were no differences in GR between the oral ingestion compared with

296   intubated feeding. Early CPIR occurs to a peak within the initial 1- 4 minutes after gustatory

297   stimulation returning to baseline within ten minutes [1-3, 9, 32]. Although overall it is a minimal

298   rise in insulin concentration levels compared to those secreted postprandially (5uU/ml [5] for

299   cephalic response compared to a postprandial response that could be ~60 uU/ml (current study)),

300   it is believed to increase digestive secretions, decrease gut motility and decrease food intake [1-

301   3].

302

303   The effects of CPIR on blood glucose appear to differ. Findings in a study by Teff et al. [32]

304   identified that in normal weight healthy males, 4 minutes post ingestion of food there was a

305   significant increase in insulin and also a significant drop in plasma glucose as a result of early

306   CPIR. However as in the current study, this change in GR has not been replicated in all studies

307   perhaps due to difficulty in measuring such small variations in blood samples [5, 8]. Ranawana

308   et al. [33] also identified high variability in glucose absorption between individuals even after

309   eating the same food. This presents some evidence that within-individual variance is also a

310   possibility even in a controlled methodology which may account for the lack of differences seen

311   here. A further consideration is that simultaneous release of glucagon during CPR may prevent a

312   reduction in blood glucose levels caused by CPIR [5] but without measuring glucagon levels this

313   is an unknown factor in the present study.

314

315   Other reasons for disparity within the results of studies on CPR maybe palatability and the

316   duration of oral transit time [8]. To date there is mixed findings as to whether palatability

317   directly impacts vagally activated pathways to increase concentrations of CPIR; which may

318   influence study findings if there is inconsistency within the subject group [9, 29, 34]. However

319   within the present study an initial questionnaire undertaken identified that none of the subjects

320   had a dislike for the tomato soup, utilised. Expert opinion is also divided in relation to the effect

321   the texture or form of food choice may have on oral exposure time. Teff [34] believes there is a

322   lack of CPIR to liquid stimuli; suggesting that chewing is required for adequate vagal stimulation

323   for insulin secretion. However, Cecil et al. [14, 15, 35] validate the use of liquid soup for

324   initiating CPR where they found the influence of sight, smell, and taste played an important part

325   in stimulating both pancreatic and gastric secretions as well as influencing appetite regulatory

326   centres. Cassady et al. [36] and deGraaf [12] also identify that liquid such as soup when eaten

327   with a spoon extends oro-sensory transit time to increase both CPR and satiety. A final

328   explanation for the differences in results seen between studies may come from work by Cecil et

329   al. [15], who found that the macronutrient content of the soup plays an important role as high fat

330   soup suppressed hunger, induced fullness, and slowed gastric emptying more than the high-

331   carbohydrate soup when ingested orally but there was no differences between the soups when

332   they were given intragastically.

333

334   One of the main aims of the current research was to combine satiety and metabolic responses

335   within the one study. Oro-sensory stimulation has been shown to increase the secretion of gastro-

336   intestinal peptides, these peptides slow gastric emptying [5, 34]. The delay in gastric emptying

337   increases satiety by prolonging stomach distention [8, 14, 31]. The present study hypothesised

338   that bypassing oro-pharyngeal and oesophageal exposure would reduce levels of satiety by

339   reducing the insulinaemic response and accelerating gastric emptying. Bypassing oro-pharyngeal

340   and oesophageal exposure did result in a slight acceleration in gastric emptying and increased

341   insulinaemic response however it was not possible to detect any differences from this in satiety.

342   A recent study [16] was able to confirm that gastric infusion of nutrients induced greater appetite

343   ratings than ingestion, alongside increases in satiety hormones however they were unable to

344   detect changes in food intake. Cecil et al. [14, 15, 35] also utilised gastric intubation in a series of

345   studies assessing the impact of bypassing oro-pharyngeal stimulation on satiety and gastric

346   emptying. They identified that loss of oro-sensory stimulation impacted negatively on both

347   satiety and gastric emptying, with subjects feeling fuller earlier with greater suppression of

348   hunger when food was eaten orally. The present study failed to find significant differences

349   between the tests for satiety; this may be due to the gastric emptying changes of only 4-5 min,

350   which although significant may not be sufficient to decrease satiety. It may also be due to the

351   large variability on the VAS data. However it should be noted that VAS assessments are only a

352   measure of perceived hunger not actual food intake and an ad libitum test meal would have

353   provided objective assessment of subsequent food intake [36, 37]. Although other studies have

354   been able to identify changes in VAS with oral stimulation using a similar sample size they have

355   not been able to detect changes in actual food intake [16]. An increased sample size however is

356   hindered by the invasive nature of the intubation test procedure.

357

358   **Conclusion**

359

360   In conclusion this study was able to demonstrate that utilising an oral gastric tube for infusion of

361   food to bypass oro-pharyngeal and oesophageal exposure decreases the normal physiological

362   CPR with detriment to IR and marginal accelerations in gastric emptying but was unable to

363   demonstrate any impact on satiety and GR. Potential future research could use a solid test meal

364   and include an ad libitum test meal.
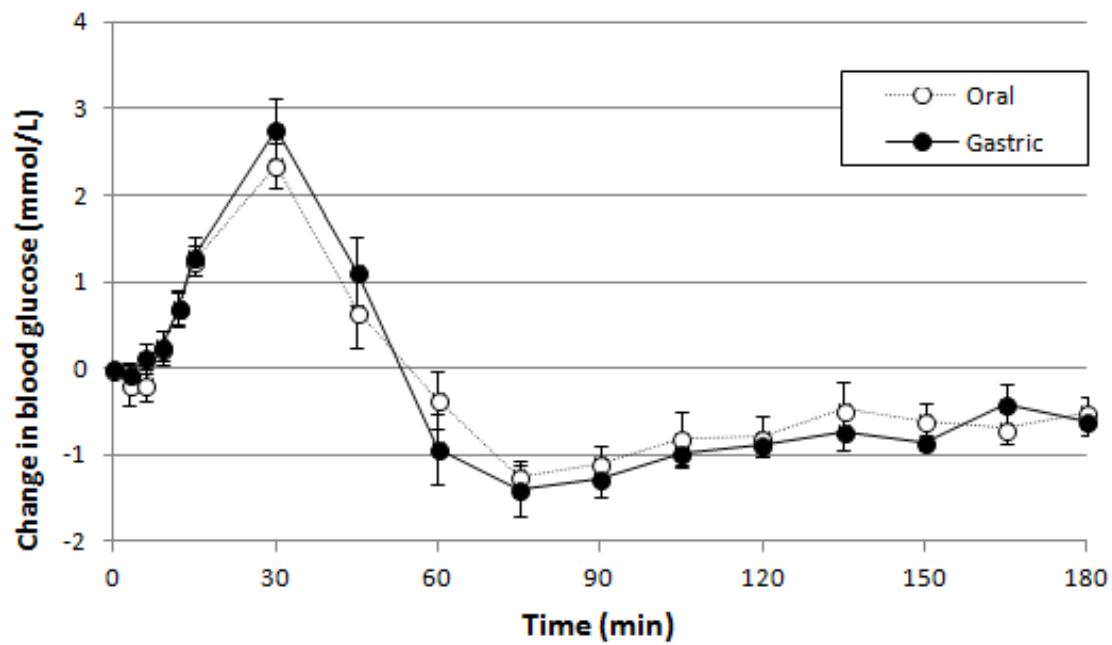
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481 **List of figures:**

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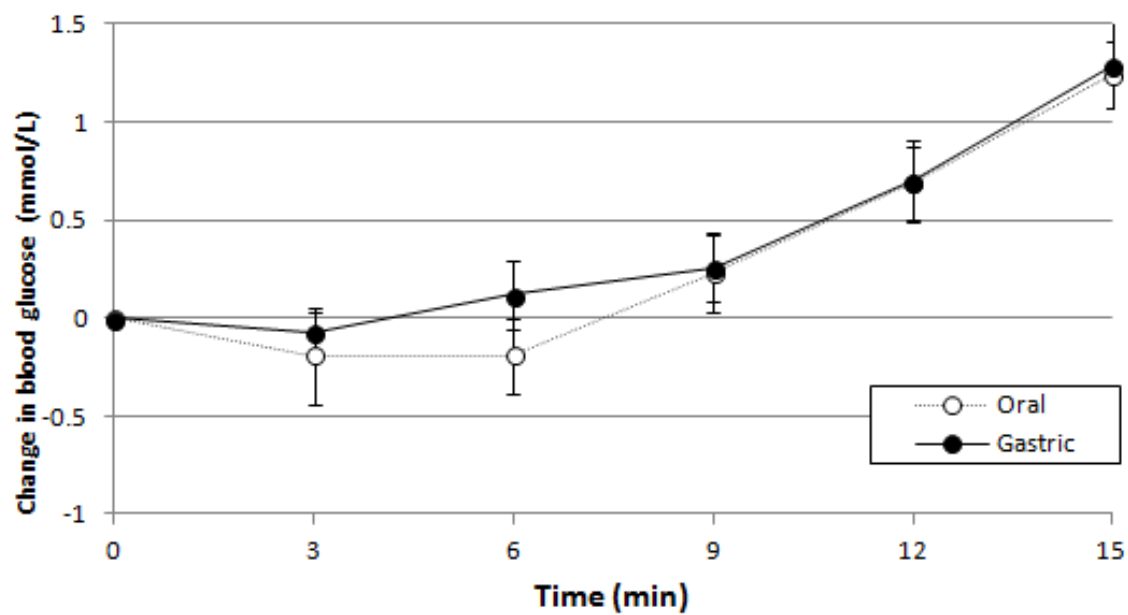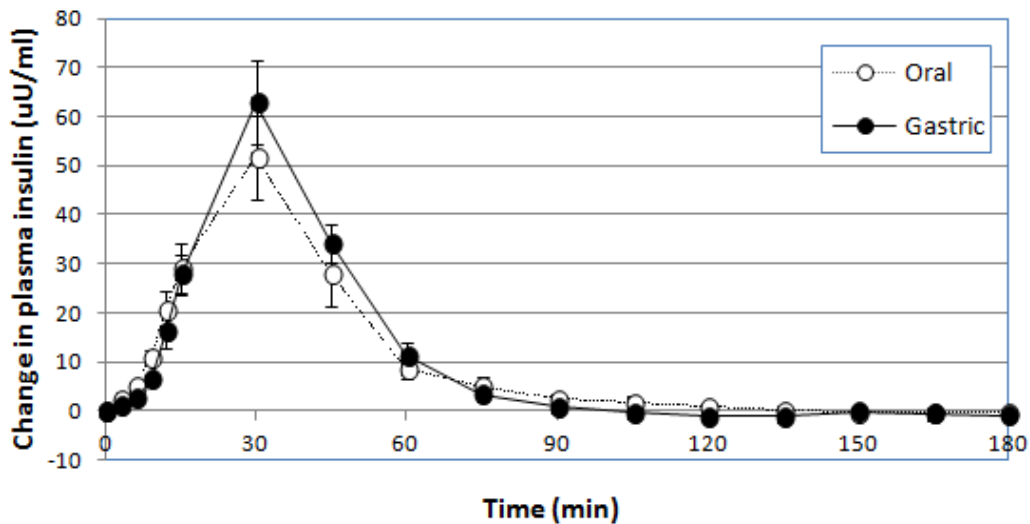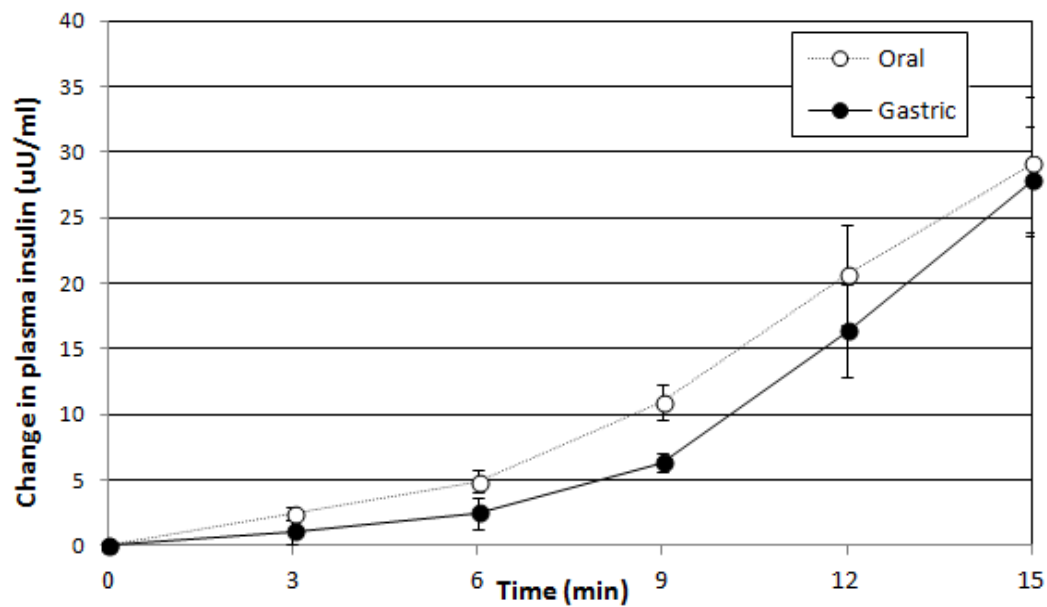
484 tests over 180 minutes (a) and over 15 minutes (b).

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487 b)

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509　　Figure 2. Change in insulinaemic response (mean ± standard error) following Oral and Gastric

510　　tests over 180 minutes (a) and over 15 minutes (b).

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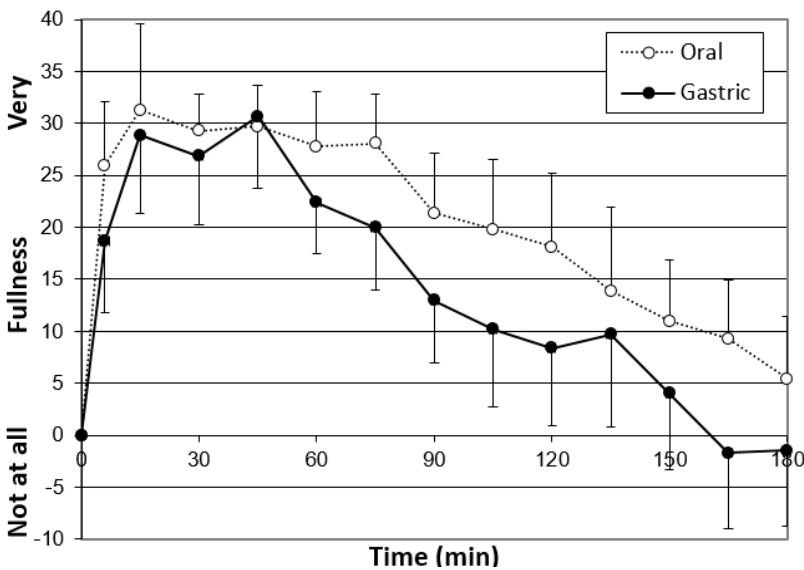
514　　b)
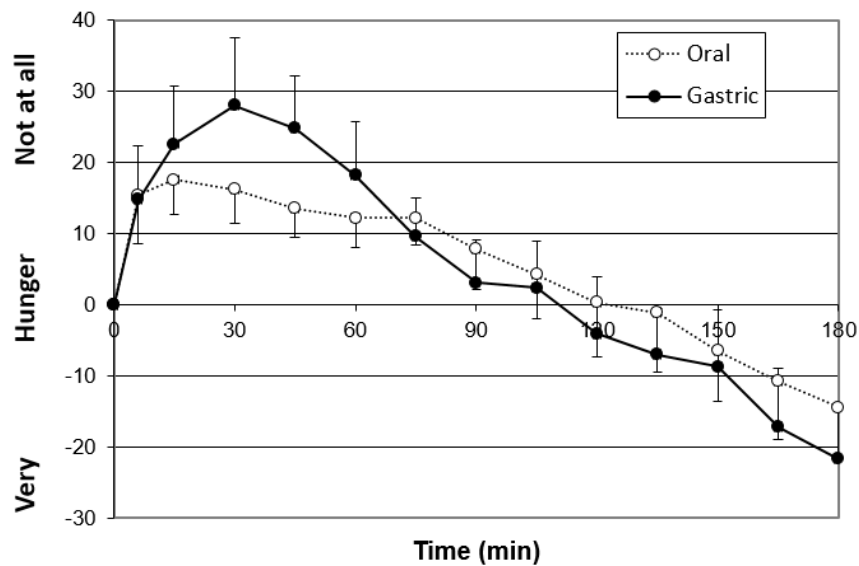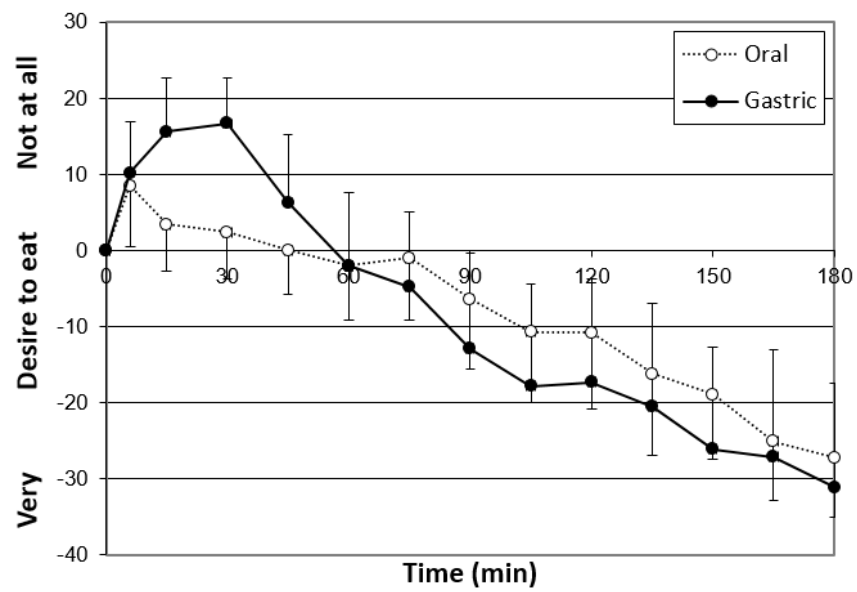
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518   Figure 3. Change in satiety ratings from visual analogue scales (mean ± standard error) following

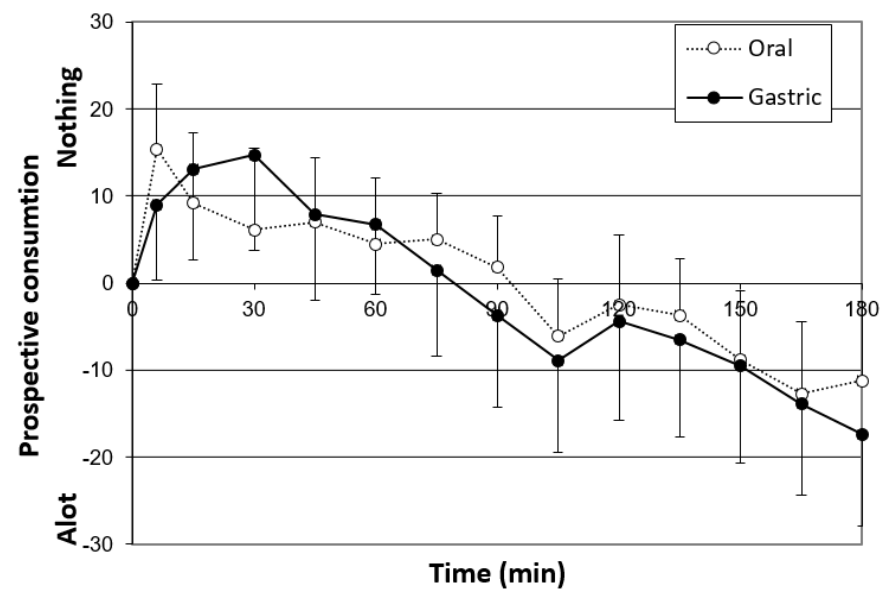519   Oral and Gastric tests for hunger (a), fullness (b), desire to eat (c) and prospective consumption

520   (d).

521   a)

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523   b)

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526   c)

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534 **List of Tables**

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536 Table 1: Gastric emptying times (mean ± standard error) following Oral and Gastric infusion of

537 soups. *=p<0.05

Time	Oral	Gastric	*d*
Latency Phase (min)	16.8 ± 0.7	15.4 ± 1.3	0.44
Lag phase (min)	52.4 ± 1.8	48.4 ± 2.8	0.55
Half time (min)	85.0 ± 2.7	79.4 ± 3.3*	0.59
Ascension time (min)	68.2 ± 2.2	64.0 ± 2.2*	0.60

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554   Table 2: Satiety rating, hunger, fullness, desire to eat and prospective consumption (mean ±

555   standard error) following Oral and Gastric infusion test.

	Oral	Gastric	*d*
Hunger (mm.min)	1914 ± 489	2298 ± 731	0.20
Fullness (mm.min)	3964 ± 711	3330 ± 808	0.26
Desire to eat (mm.min)	1149 ± 712	2050 ± 802	0.38
Prospective consumption (mm.min)	1680 ± 621	2233 ± 848	0.24

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