Effect of plain versus sugar-sweetened breakfast on energy balance and metabolic health: A secondary data analysis stratified by participant-defined sweet preference

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Abstract

Background: Variability in sweet preference between people is well established, with those who have a high preference colloquially identified as having a sweet tooth. Although characteristics have been described demonstrating key differences between those with and without a sweet tooth (such as differences in body mass index), it is less clear whether sweet preference moderates appetite and health responses to stimuli of different sweetness levels.

Objective: To explore appetite and health responses to a sugar-sweetened (SWEET) and unsweetened (PLAIN) porridge-based breakfast, according to whether participants identified as having a sweet tooth or not.

Methods: Secondary data analysis of a previously published randomised crossover trial in which $n = 29$ participants consumed an isocaloric PLAIN (~8 g sugar) and SWEET (~32 g sugar) porridge-based breakfast for three weeks each. Fasted pre- and post-intervention measures included blood biomarkers of health and appetite hormones, anthropometrics and metabolic rate, and a series of questionnaires assessing psychological appetite/approach to food. During each three week intervention, four days of lifestyle monitoring were conducted on days 1-4 and days 15-18, involving weighed food diaries, physical activity measurements (ActiHeart™), and visual analogue scales of appetite across the day. After study completion, participants were asked whether they believed they had a sweet tooth or not; $n = 27$ responded and were included in these analyses. Analyses were exploratory with no significance testing or *a priori* hypothesis.

Results: 16 participants reported not having a sweet tooth. Average body mass index was higher in those without a sweet tooth ($25.9 \pm 6.0 \text{ kg/m}^2$ versus $24.4 \pm 4.3 \text{ kg/m}^2$ for those with a sweet tooth), but waist-to-hip ratio was lower. Having a sweet tooth was associated with a higher desire for sweet across the day during both interventions compared to those without a sweet tooth, but also lower sugar intake. Sweet sensory-specific satiety was achieved in both groups post-breakfast during SWEET, whilst savoury sensory-specific satiety was achieved post-breakfast after both PLAIN and SWEET. Fasting plasma fibroblast growth factor 21 was higher in those with a sweet tooth, whilst fasting glucagon-like peptide-1 increased pre- to post-PLAIN ($\Delta 6.2$, 95 % CI 1.1, 11.4 pmol·L⁻¹), but was otherwise similar across interventions and between groups. Those without a sweet tooth reduced their energy intake from week 1 to week 3 of PLAIN ($\Delta -152$, 95 % CI -349, 45 kcal/d), whereas those with a sweet tooth (less reliably) increased their energy intake ($\Delta 131$, 95 % CI -131, 395 kcal/d). No changes in energy intake were noted during SWEET. Physical activity energy expenditure largely remained consistent between groups and across interventions, though those without a sweet tooth increased their physical activity energy expenditure from week 1 to week 3 of SWEET ($\Delta 166$, 95 % CI -8, 241 kcal/d).

Conclusion: Having a sweet tooth was associated with distinct characteristics, such as lower body mass index and higher fasted plasma fibroblast growth factor 21 concentrations. Sweet preference may moderate biopsychological metabolic and appetitive responses to savoury or sweet primes. Due to the small sample size and other methodological features of these analyses, future work should establish the causality of these findings, and may need to consider sweet preference *a priori* when designing health and appetite research relating to sweetness.

1 Introduction

2 Research has identified high variability in sweet taste preferences; colloquially, those who
3 have a distinct preference towards sweet flavours identify as having a “sweet tooth” (Connor
4 *et al.*, 1988; Drewnowski *et al.*, 2012). Whilst intuitively having an affinity for sweetness may
5 not appear to be much more than a personal preference, there is a genetic basis for sweet
6 preference (Reed & McDaniel, 2006); thus having a sweet tooth may be implicated in
7 appetite and metabolic health. For example, people with obesity and type 2 diabetes appear
8 typically have a lower preference for sweetness, despite having hypo- or ageusia (Bartoshuk
9 *et al.*, 2006; Stolbová *et al.*, 1999). Some have posited that the reduction in sweet taste
10 intensity may be implicated in polyphagia as more sweetness has to be experienced in order
11 to get the same hedonic reward (Herrera Moro Chao *et al.*, 2018). However, this runs
12 counter to the reduction in sweet preference also experienced (Yu *et al.*, 2014).

13
14 Currently, however, the impact of sweet preference in healthy adults under free-living
15 conditions is not well studied. Understanding this may proffer clues towards the role of sweet
16 preference in disease progression, and may offer ideas towards tailoring diets or guidelines
17 in order to increase adherence.

18
19 We recently conducted a randomised crossover study investigating the role of a plain
20 porridge breakfast *versus* an equicaloric high-sugar breakfast over three weeks in healthy
21 adults who were body mass index (BMI)-defined as being lean or having overweight/obesity
22 (Carroll *et al.*, 2020a). Overall, this study found no differential effect of the breakfasts in
23 nearly every health and appetite marker measured. The two key findings were that:
24 immediately after the sweet breakfast, desire for sweetness reduced acutely; and after
25 breakfast there was no difference between the two trial arms in the amount of sugar
26 consumed (as such, total daily sugar was higher after the sweet breakfast in both groups
27 due to the sugar given at breakfast). A speculative finding based on within-arm analyses
28 additionally suggested that the sweet breakfast may have mitigated the cholesterol-lowering
29 effects of oat β -glucan (as total cholesterol concentrations reduced pre- to post-plain but not
30 sweet breakfast). The present study is a hypothesis-generating exploratory secondary
31 analysis of the aforementioned breakfast study, but split by participant-identified sweet
32 preference (“sweet tooth”); as such, no *a priori* hypotheses are proposed.

Methods

Full details of the original study have previously been described (Carroll *et al.*, 2020a); as such, only a brief description is provided below.

Participants

Twenty-nine participants ($n = 22$ women) completed the study, with an average ($\pm$ standard deviation; *SD*) age of 33 ± 10 y, and BMI of 25.0 ± 5.2 kg/m². Of the 29 participants, $n = 11$ had a BMI ≥ 25 kg/m². All participants were identified as suitable for participation in the study according to the following (self-reported) exclusion criteria: < 18 or ≥ 70 y; known metabolic disease; weight loss > 5 kg in previous 3 mo; drug dependency (except caffeine and/or nicotine), pregnant or breastfeeding; on medication that has any potential contraindications relating to the study. Participants were all living in South West England at the time of the study, and data were collected between May 2017 and October 2018.

Ethical approval for the original study was obtained from the Research Ethics Approval Committee for Health at the University of Bath (reference: EP 16/17 166), and the study was conducted in accordance with the Declaration of Helsinki. No ethical approval was sought for the current data analysis as the data are available publicly in fully anonymised form (doi: 10.15125/BATH-00720); details on sweet preference (sweet tooth yes/no) are available in the Appendix and were used in conjunction with the published dataset.

Study design and protocol

This was a three week participant-blinded randomised crossover study (mode 6 d washout, range 4-60 d), whereby participants were provided with a breakfast consisting of just oats (PLAIN) or equicaloric oats + sugar (30 % by weight sugar with fewer oats) (SWEET). Participants chose how much milk to add according to their preference and this remained consistent across the study. Participants were told the study was investigating the health and appetitive effects of altering a flavour, nutrient, or combination of the two.

Pre- and post-intervention, participants came to the laboratory in an overnight fasted state after three days within-person standardised physical activity and one day within-person standardised diet. A fasted blood sample was drawn and resting metabolic rate and respiratory exchange ratio was measured, as well as anthropometrics, blood pressure, and a range of appetite questionnaires.

During each 21 d intervention period, participants underwent 8 d lifestyle monitoring consisting of weighed food diaries, appetite visual analogue scales (before and after breakfast, before lunch, and before dinner), and physical activity monitoring (Actiheart™). Lifestyle monitoring was conducted on days 1-4 and days 15-18 of each 21 d intervention period, so as to capture the beginning and end of the study, whilst reducing confounding from day-of-the-week differences in diet and activity.

Data analysis

Data were split according to whether participants identified as having a sweet tooth or not (see Appendix for these data). Identifying participant sweet preference was a *post hoc* idea deriving from the debrief with participants whereby trends were noticed in subjective experience of the study, such as appetite responses to the sweet breakfast. Once the study

was completed, participants were contacted asking whether they identified as having a sweet tooth or not prior to starting the study. To aid in them identifying whether they had a sweet tooth, the following scenario was presented: "if you had a two course meal, would you typically choose (savoury) starter and main, or (savoury) main and (sweet) dessert?". Twenty-seven participants responded and were therefore included in these analyses.

The original study was powered to detect a ~0.6 kg difference in body mass change between the two trial arms (PLAIN *versus* SWEET). Considering the need to split the data further such that there were four group comparisons (i.e. PLAIN with sweet tooth, PLAIN no sweet tooth, SWEET with sweet tooth, SWEET no sweet tooth), formally analysing the data statistically seemed error prone due to the drop in sample size and the doubling of comparisons. As such, data comparing the four group comparisons were analysed descriptively and visually with a view for hypothesis generation, rather than causal inference.

Data are presented as mean $\pm$ SD, or mean change (Δ) (95 % confidence interval; CI). Mean change pre- to post-intervention was calculated by post-intervention measure minus pre-intervention measure. Difference in change between PLAIN and SWEET was calculated by mean (pre- to post-intervention) change SWEET minus mean (pre- to post-intervention) change PLAIN. Trends in nutrient intake and physical activity compared change from the first (days 1-4) to the last (days 15-18) week of each intervention; difference in change scores are the average nutrient intake/energy expenditure in each three week intervention. Difference in change was estimated between PLAIN and SWEET comparing those with and without a sweet tooth (Δ no sweet tooth minus Δ sweet tooth), and difference in change between no sweet tooth and sweet tooth was estimated (Δ SWEET minus Δ PLAIN).

Finally, as the above analyses only investigated differences in change scores, data were visually inspected to understand whether mean scores were qualitatively different between all comparisons (no sweet tooth PLAIN, sweet tooth PLAIN, no sweet tooth SWEET, and sweet tooth SWEET).

Results

Out of 29 participants in the original study, a total of 27 gave information as to whether they felt they had a sweet tooth or not. Of these, 16 said they did not have a sweet tooth. There were no remarkable differences between those with and without a sweet tooth, though perhaps those with a sweet tooth were slightly older, and had a slightly lower BMI (particularly those with BMI ≥ 25 kg/m²) but higher waist-to-hip ratio compared to those without a sweet tooth (**Table 1**).

Table 1. Participant characteristics according to self-identified sweet tooth

	No sweet tooth (n = 16)	Sweet tooth (n = 11)
Sex (women)	12 (75 %)	8 (73 %)
Age	32 $\pm$ 10	36 $\pm$ 11
Waist-to-hip ratio	0.77 $\pm$ 0.06	0.82 $\pm$ 0.09
Body mass (kg)	73.5 $\pm$ 16.3	74.5 $\pm$ 12.4
BMI (kg/m ²)	25.9 $\pm$ 6.0	24.4 $\pm$ 4.3
BMI-lean	9 (56 %)	7 (64 %)
BMI-lean (kg/m ²)	22.0 $\pm$ 1.5	22.0 $\pm$ 1.0
BMI-overweight	7 (44 %)	4 (36 %)
BMI-overweight (kg/m ²)	31.0 $\pm$ 5.9	28.5 $\pm$ 4.7
PLAIN first	11 (69 %)	5 (45 %)

Data are n (%), or mean $\pm$ standard deviation

Abbreviations: BMI, body mass index; PLAIN, randomised to plain breakfast first

Participant flavour ratings of the two breakfasts are in **Table 2**. Ratings were broadly the same between participants regardless of sweet preferences. Small differences may be inferred regarding higher saltiness ratings for both breakfasts for those with a sweet tooth compared to those without a sweet tooth. Those with a sweet tooth additionally rated the SWEET breakfast as slightly less sweet, and more savoury, compared to those without a sweet tooth (**Table 2**). Liking of breakfasts was similar for PLAIN and SWEET regardless of sweet preference (**Table 2**). There was no obvious trend that liking of either of the breakfasts changed over the three week interventions in either group (data not shown).

Table 2. Participant flavour ratings of the PLAIN and SWEET breakfasts

	No sweet tooth (n = 16)	Sweet tooth (n = 11)
	PLAIN breakfast	
Liking (mm)	42 $\pm$ 27	47 $\pm$ 21
Sweetness (mm)	16 $\pm$ 21	13 $\pm$ 15
Saltiness (mm)	6 $\pm$ 6	13 $\pm$ 16
Savouriness (mm)	46 $\pm$ 37	48 $\pm$ 32
Fattiness (mm)	11 $\pm$ 16	11 $\pm$ 12
	SWEET breakfast	
Liking (mm)	46 $\pm$ 27	50 $\pm$ 29
Sweetness (mm)	87 $\pm$ 10	81 $\pm$ 22
Saltiness (mm)	4 $\pm$ 2	10 $\pm$ 14
Savouriness (mm)	21 $\pm$ 30	31 $\pm$ 29
Fattiness (mm)	10 $\pm$ 14	11 $\pm$ 10

Data are mean $\pm$ standard deviation of a 100 mm visual analogue scale rating, taken during days 1-4 and days 15-18 of each intervention

Table 3 shows anthropometric and other (non-invasive) health markers pre- and post- each breakfast intervention, split by whether participants identified as having a sweet tooth or not. Most markers did not differentially change remarkably. Those without a sweet tooth had a consistent but small increase in fasted carbohydrate oxidation after both the PLAIN (Δ 0.02, 95 % CI 0.00, 0.04) and SWEET (Δ 0.02, 95 % CI 0.00, 0.03) interventions (**Figure 1d**), as well as an increase of 3 (95 % CI 1, 6) mmHg in diastolic blood pressure after the SWEET intervention only (**Figure 1b**). Those with a sweet tooth appeared to have a consistently lower systolic blood pressure compared to those without (**Figure 1a**). No such differences in change were found as consistently (determined by 95 % CI) in those without a sweet tooth. There appeared to be no differences in the way those with and without a sweet tooth responded to either intervention with regards to anthropometrics and other markers of health measured in **Table 3**.

Table 4 and **Figure 2** shows fasted plasma/serum biomarkers of health and appetite. In those with a sweet tooth, there was a small increase pre- to post-intervention in fasted glucagon-like peptide-1 concentration after the PLAIN intervention (Δ 6.2, 95 % CI 1.1, 11.4 pmol·L⁻¹; **Table 4** and **Figure 2d**), and an increase in fasted triacylglycerol concentrations after the SWEET intervention (Δ 0.17, 95 % CI 0.02, 0.32 mmol·L⁻¹; **Table 4** and **Figure 2b**). More weakly, both those with and without a sweet tooth had similar reductions (Δ ~0.18 mmol·L⁻¹) in fasted plasma total cholesterol concentrations after PLAIN; however, after SWEET, those without a sweet tooth had a small increase in total cholesterol (Δ 0.11, 95 % CI -0.17, 0.29 mmol·L⁻¹) whereas those with a sweet tooth had no change (Δ -0.01, 95 % CI -0.17, 0.15 mmol·L⁻¹; **Table 4** and **Figure 2a**).

Whilst responses to interventions did not seem to differ between PLAIN and SWEET, those with a sweet tooth had an approximately double fasted plasma fibroblast growth factor 21 concentrations (**Figure 2e**). There appeared to be no differences in the fibroblast growth factor 21 response in those with and without a sweet tooth. Those with a sweet tooth appeared to have a small reduction in fasted plasma triacylglycerol concentrations after SWEET (Δ -0.38, 95 % CI -0.76, 0.00 mmol·L⁻¹; **Table 4**), though this may have been the result of an outlier skewing the mean (data not shown).

Table 5 shows fasted pre- and post-intervention appetite visual analogue scales. After the PLAIN intervention, those without a sweet tooth rated their hunger slightly higher (Δ 9, 95 % CI 1, 17 mm), and those with a sweet tooth rated their desire for salt slightly lower (Δ -13, 95 % CI -24, -1 mm). After the SWEET intervention, those without a sweet tooth rated their desire for sweet (Δ -17, 95 % CI -30, -5 mm), salt (Δ -16, 95 % CI -26, -7 mm), savoury (Δ -12, 95 % CI -19, -4 mm), and fatty (Δ -5, 95 % CI -10, 0 mm) lower, and those with a sweet tooth rated their hunger slightly higher (Δ 15, 95 % CI 1, 28 mm). Pre- to post-PLAIN, thirst had a reduction in those with a sweet tooth (Δ -14, 95 % CI -29, 1 mm) (**Table 5**).

Those without a sweet tooth appeared to have a slightly higher savoury desire overall than those with a sweet tooth (~10 mm higher rating). Additionally, those with a sweet tooth appeared to have generally lower ratings for desire for sweet (~5 mm; **Table 5**). During PLAIN, there were no remarkable differences in change comparing those with *versus* without a sweet tooth. However, during SWEET, average change was different between those with and without a sweet tooth, showing those without a sweet tooth to have a reduction in pre- to post-SWEET sweet desire which was not found in those with a sweet tooth (Δ -20, 95 % CI -36, -4 mm; **Table 5**). Additionally, those with a sweet tooth, had a greater reduction in savoury desire after SWEET compared to PLAIN (Δ 11, 95 % CI -1, 23 mm).

Table 3. Fasting anthropometric and other non-invasive markers of health pre- to post-intervention

	No sweet tooth (n = 16)			Sweet tooth (n = 11)			Difference in Δ no sweet tooth vs. sweet tooth	Difference in Δ PLAIN vs. SWEET
	PLAIN breakfast							
	Pre	Post	Δ	Pre	Post	Δ	PLAIN vs. PLAIN	No sweet tooth
Body mass (kg)	73.6 ± 16.2	73.5 ± 16.4	-0.1 (-0.6, 0.5)	74.4 ± 12.3	74.7 ± 12.0	0.2 (-0.2, 0.7)	-0.3 (-1.1, 0.5)	0.3 (-0.5, 1.0)
Body mass index (kg/m²)	26.0 ± 6.0	25.9 ± 6.0	0.0 (-0.2, 0.2)	24.3 ± 4.2	24.3 ± 4.1	0.1 (-0.1, 0.2)	-0.1 (-0.4, 0.1)	0.1 (-0.2, 0.4)
Waist-to-hip ratio	0.77 ± 0.06	0.77 ± 0.05	0.00 (-0.02, 0.01)	0.82 ± 0.10	0.82 ± 0.09	0.00 (-0.02, 0.01)	0.00 (-0.24, 0.02)	-0.01 (-0.03, 0.01)
SBP (mmHg)	118 ± 9	117 ± 9	-1 (-3, 1)	115 ± 10	116 ± 11	1 (-3, 5)	-2 (-7, 3)	3 (-1, 7)
DBP (mmHg)	76 ± 6	77 ± 6	1 (-2, 3)	76 ± 6	77 ± 6	1 (-2, 4)	-1 (-5, 4)	2 (-1, 6)
Urine specific gravity	1.014 ± 0.009	1.014 ± 0.009	0.000 (-0.004, 0.0003)	1.012 ± 0.006	1.015 ± 0.007	0.003 (-0.002, 0.007)	-0.003 (-0.009, 0.003)	-0.001 (-0.004, 0.003)
RMR (kcal/d)	1518 ± 221	1486 ± 247	-31 (-90, 27)	1525 ± 311	1558 ± 330	33 (-56, 123)	-65 (-182, 52)	60 (-29, 149)
RER	0.83 ± 0.03	0.85 ± 0.03	0.02 (0.00, 0.04)	0.85 ± 0.05	0.83 ± 0.06	-0.01 (-0.04, 0.02)	0.03 (-0.01, 0.07)	0.00 (-0.02, 0.02)
	SWEET breakfast						SWEET vs. SWEET	Sweet tooth
Body mass (kg)	73.0 ± 16.2	73.2 ± 16.1	0.2 (-0.4, 0.7)	74.3 ± 12.7	74.4 ± 12.5	0.2 (-0.3, 0.6)	0.0 (-0.7, 0.8)	-0.4 (-1.0, 0.2)
Body mass index (kg/m²)	25.8 ± 6.0	25.8 ± 5.9	0.01 (-0.1, 0.3)	24.2 ± 4.3	24.3 ± 4.3	0.1 (-0.1, 0.2)	0.0 (-0.1, 0.3)	-0.1 (-0.3, 0.1)
Waist-to-hip ratio	0.77 ± 0.05	0.76 ± 0.05	-0.01 (-0.03, 0.00)	0.82 ± 0.09	0.83 ± 0.10	0.01 (-0.01, 0.03)	-0.02 (-0.05, 0.00)	-0.01 (-0.03, 0.02)
SBP (mmHg)	116 ± 9	118 ± 10	2 (-1, 5)	113 ± 9	116 ± 10	3 (-1, 6)	-1 (-5, 4)	4 (-8, 1)
DBP (mmHg)	76 ± 5	79 ± 8	3 (1, 6)	75 ± 7	76 ± 7	2 (-2, 5)	2 (-3, 6)	-3 (-6, 1)
Urine specific gravity	1.013 ± 0.008	1.012 ± 0.009	-0.001 (-0.003, 0.001)	1.018 ± 0.009	1.014 ± 0.007	0.004 (-0.010, 0.002)	0.003 (-0.004, 0.010)	0.001 (-0.007, 0.009)
RMR (kcal/d)	1487 ± 238	1515 ± 266	28 (-36, 93)	1529 ± 265	1577 ± 312	47 (-24, 119)	-19 (-122, 84)	-66 (-156, 23)
RER	0.83 ± 0.03	0.85 ± 0.05	0.02 (0.00, 0.03)	0.86 ± 0.11	0.84 ± 0.05	-0.02 (-0.09, 0.04)	0.04 (-0.03, 0.12)	0.04 (-0.03, 0.10)

Data are mean $\pm$ standard deviation, or Δ (95 % confidence interval)

Abbreviations: DBP, diastolic blood pressure; RER, respiratory exchange ratio; RMR, resting metabolic rate; SBP, systolic blood pressure

Figure 1. Pre- to post-intervention fasting health markers according to sweet preference: (a) systolic blood pressure; (b) diastolic blood pressure; (c) resting metabolic rate; (d) respiratory exchange ratio. Error bars are 95 % confidence intervals. Abbreviations: PLAIN, plain breakfast intervention; SWEET, sweet breakfast intervention

Table 4. Fasting plasma/serum concentrations of health biomarkers and appetite hormones pre- to post-intervention

	No sweet tooth (n = 13)			Sweet tooth (n = 9)			Difference in Δ sweet tooth vs. no sweet tooth	Difference in Δ PLAIN vs. SWEET
	PLAIN breakfast							
	Pre	Post	Δ	Pre	Post	Δ	PLAIN vs. PLAIN	No sweet tooth
Glucose (mmol·L ⁻¹)	5.4 ± 0.4	5.4 ± 0.4	0.0 (-0.2, 0.1)	5.4 ± 0.5	5.5 ± 0.4	0.1 (-0.1, 0.2)	-0.1 (-0.34, 0.14)	0.1 (-0.1, 0.3)
Total cholesterol (mmol·L ⁻¹)	4.47 ± 0.83	4.30 ± 0.68	-0.18 (-0.39, 0.04)	4.32 ± 0.91	4.13 ± 0.62	-0.18 (-0.52, 0.15)	0.01 (-0.43, 0.44)	0.3 (-0.1, 0.7)
Triacylglycerol (mmol·L ⁻¹)	0.79 ± 0.35	0.82 ± 0.40	0.04 (-0.02, 0.10)	0.99 ± 0.66	1.20 ± 0.75	0.21 (-0.13, 0.56)	-0.18 (-0.58, 0.23)	-0.06 (-0.14, 0.02)
Insulin (pmol·L ⁻¹)	31.6 ± 22.0	33.1 ± 20.7	1.5 (-8.6, 11.6)	39.5 ± 34.0	40.3 ± 29.6	0.8 (-10.4, 12.0)	0.65 (-15.5, 16.8)	3.80 (-14.2, 21.7)
GLP-1 (pmol·L ⁻¹)	15.5 ± 10.2	16.7 ± 8.3	1.2 (-5.5, 7.9)	17.4 ± 9.7	23.6 ± 11.0	6.2 (1.1, 11.4)	-5.0 (-14.0, 3.9)	1.0 (-6.8, 8.7)
FGF21 (pg·mL ⁻¹)*	531 ± 489	664 ± 525	133 (-133, 400)	1178 ± 813	1262 ± 1048	84 (-253, 420)	50 (-434, 533)	-61 (-291, 169)
Osmolality (mOsm·kg ⁻¹)**	295 ± 5	297 ± 4	2 (-1, 5)	298 ± 7	296 ± 8	-2 (-6, 1)	4 (-1, 9)	0 (-4, 4)
SWEET breakfast							SWEET vs. SWEET	Sweet tooth
Glucose (mmol·L ⁻¹)	5.4 ± 0.4	5.5 ± 0.4	0.05 (-0.08, 0.17)	5.5 ± 0.5	5.5 ± 0.3	0.03 (-0.24, 0.29)	0.02 (-0.31, 0.35)	-0.1 (-0.5, 0.2)
Total cholesterol (mmol·L ⁻¹)	4.23 ± 0.92	4.34 ± 0.75	0.11 (-0.17, 0.39)	4.20 ± 0.73	4.19 ± 0.69	-0.01 (-0.17, 0.15)	0.12 (-0.22, 0.47)	0.2 (-0.1, 0.5)
Triacylglycerol (mmol·L ⁻¹)	0.84 ± 0.34	0.81 ± 0.28	-0.03 (-0.08, 0.03)	0.93 ± 0.41	1.10 ± 0.54	0.17 (0.02, 0.32)	-0.20 (-0.38, - 0.02)	-0.38 (-0.76, 0.00)
Insulin (pmol·L ⁻¹)	37.9 ± 20.7	43.5 ± 20.4	5.6 (-9.6, 20.8)	33.8 ± 19.7	40.9 ± 26.0	7.1 (-2.3, 16.4)	-1.48 (-20.5, 17.6)	-7.9 (-18.6, 2.7)
GLP-1 (pmol·L ⁻¹)	14.3 ± 5.5	16.5 ± 4.8	2.2 (-1.0, 5.4)	18.1 ± 11.6	18.1 ± 10.3	0.0 (-5.9, 5.8)	2.2 (-5.1, 9.6)	-6.2 (-14.4 2.1)
FGF21 (pg·mL ⁻¹)*	591 ± 523	664 ± 575	73 (-163, 308)	1024 ± 927	976 ± 781	-48 (-267, 170)	121 (-241, 482)	-35 (-296, 226)
Osmolality (mOsm·kg ⁻¹)**	294 ± 5	297 ± 5	2 (-1, 5)	295 ± 6	295 ± 3	1 (-3, 4)	1 (-4, 6)	3 (-2, 8)

Data are mean ± standard deviation, or mean Δ (95 % confidence interval)

*n = 6 for those with no sweet tooth, n = 7 for those with a sweet tooth

**n = 12 for those with no sweet tooth, n = 10 for those with a sweet tooth

Abbreviations: FGF21, fibroblast growth factor 21; GLP-1, glucagon-like peptide-1

Figure 2. Pre- to post-intervention fasting health markers according to sweet preference: (a) plasma total cholesterol concentration; (b) plasma triacylglycerol concentration; (c) serum insulin concentration; (d) serum glucagon-like peptide-1 concentration; (e) plasma fibroblast growth factor 21 concentration. Error bars are 95 % confidence intervals. Abbreviations: PLAIN, plain breakfast intervention; SWEET, sweet breakfast intervention

Table 5. Fasting subjective appetite visual analogue scale ratings pre- to post-intervention

	No sweet tooth (n = 16)			Sweet tooth (n = 11)			Difference in Δ sweet tooth vs. no sweet tooth	Difference in Δ PLAIN vs. SWEET
	PLAIN breakfast							
	Pre	Post	Δ	Pre	Post	Δ	PLAIN vs. PLAIN	No sweet tooth
Hunger	54 $\pm$ 24	63 $\pm$ 23	9 (1, 17)	57 $\pm$ 27	55 $\pm$ 23	-2 (-19, 15)	11 (-10, 31)	-3 (-17, 11)
Fullness	23 $\pm$ 20	23 $\pm$ 21	1 (-9, 11)	30 $\pm$ 25	28 $\pm$ 21	-3 (-13, 7)	3 (-11, 18)	-4 (-14, 7)
Quantity*	65 $\pm$ 20	66 $\pm$ 21	1 (-7, 9)	57 $\pm$ 11	58 $\pm$ 19	1 (-12, 14)	0 (-16, 16)	-1 (-11, 9)
Thirst	53 $\pm$ 22	49 $\pm$ 25	-3 (-17, 10)	56 $\pm$ 28	42 $\pm$ 29	-14 (-29, 1)	11 (-10, 32)	1 (-18, 19)
Desire for sweet	43 $\pm$ 25	38 $\pm$ 25	-5 (-18, 8)	35 $\pm$ 26	35 $\pm$ 28	0 (-5, 6)	-6 (-21, 9)	-12 (-24, 1)
Desire for salt	30 $\pm$ 25	26 $\pm$ 23	-3 (-19, 13)	39 $\pm$ 14	26 $\pm$ 23	-13 (-24, -1)	9 (-11, 30)	-13 (-32, 6)
Desire for savoury	52 $\pm$ 28	51 $\pm$ 31	-1 (-12, 10)	44 $\pm$ 20	42 $\pm$ 23	-2 (-13,8)	1 (-15, 18)	-11 (-21, 1)
Desire for fatty	22 $\pm$ 21	21 $\pm$ 26	-1 (-11, 9)	26 $\pm$ 25	25 $\pm$ 24	-1 (-8, 5)	0 (-12, 13)	-4 (-16, 8)
	SWEET breakfast						SWEET vs. SWEET	Sweet tooth
Hunger	53 $\pm$ 24	60 $\pm$ 25	6 (-7, 19)	41 $\pm$ 25	56 $\pm$ 22	15 (1, 28)	-8 (-28, 12)	-13 (-34, 8)
Fullness	25 $\pm$ 17	22 $\pm$ 19	-3 (-9, 4)	29 $\pm$ 30	27 $\pm$ 16	-2 (-12, 8)	-1 (-13, 12)	5 (-11, 21)
Quantity*	67 $\pm$ 19	67 $\pm$ 20	0 (-10, 10)	45 $\pm$ 18	55 $\pm$ 16	9 (-2, 21)	-9 (-25, 7)	-10 (-28, 7)
Thirst	55 $\pm$ 22	53 $\pm$ 25	-3 (-15, 9)	51 $\pm$ 22	56 $\pm$ 27	5 (-4, 14)	-8 (-23, 8)	10 (-6, 25)
Desire for sweet	47 $\pm$ 23	30 $\pm$ 25	-17 (-30, -5)	33 $\pm$ 21	36 $\pm$ 24	3 (-6, 11)	-20 (-36, -4)	-3 (-10, 4)
Desire for salt	44 $\pm$ 27	27 $\pm$ 23	-16 (-26, -7)	35 $\pm$ 22	31 $\pm$ 26	-4 (-22, 14)	-12 (-34, 10)	17 (-5, 39)
Desire for savoury	60 $\pm$ 25	48 $\pm$ 28	-12 (-19, -4)	48 $\pm$ 24	40 $\pm$ 25	-9 (-21, 4)	-3 (-19, 13)	11 (-1, 23)
Desire for fatty	27 $\pm$ 27	22 $\pm$ 27	-5 (-10, 0)	21 $\pm$ 20	29 $\pm$ 27	9 (-9, 26)	-14 (-34, 7)	-7 (-23, 8)

Data are mean millimetres on a 100 mm scale $\pm$ standard deviation, or Δ (95 % confidence interval)

*This scale asked "how much do you think you can eat?"

Table 6 shows pre- to post-intervention changes in appetite inventories. All changes had small effect sizes, even when confidence intervals suggest a reliable effect size. After PLAIN in those without a sweet tooth, restraint appeared to be slightly lower ($\Delta -1$, 95 % CI -2, 0), as did chronotype ($\Delta -2$, 95 % CI -5, 0, indicating a small shift towards a more evening chronotype). After PLAIN in those with a sweet tooth, Food Craving Inventory scores suggested a reduction in desire for fat ($\Delta -2$, 95 % CI -4, 0), carbohydrates/starch ($\Delta -2$, 95 % CI -3, 0), and fast food fatty ($\Delta -1$, 95 % CI -2, 0) components; equally Three Factor Eating Questionnaire hunger increased slightly ($\Delta 1$, 95 % CI 0, 2). After SWEET, those without a sweet tooth also reported a small reduction in Food Craving Inventory scores for fat ($\Delta -1$, 95 % CI -2, 0) and fast food fat ($\Delta -1$, 95 % CI -1, 0) components, and slightly lower Three Factor Eating Questionnaire disinhibition ($\Delta -1$, 95 % CI -2, 0) (**Table 6**).

Table 7 shows the macronutrient breakdown during the interventions. Weighed diet diaries were completed on the first four days of each intervention week (days 1-4) and the same four days of the last week (days 15-18) in order to reduce any day-of-the-week effects. In terms of energy intake, those without a sweet tooth seemed to have a reduction during PLAIN ($\Delta -152$, 95 % CI -349, 45 kcal/d), whilst those with a sweet tooth appeared to have an increased during PLAIN ($\Delta 131$, 95 % CI -131, 395 kcal/d). The changes during SWEET were minimal, but if anything, followed the opposite trend (a small increase for those without a sweet tooth and a small decrease for those with a sweet tooth) (**Figure 3a**). During SWEET, those with a sweet tooth appeared to have a reduction in fibre intake compared to PLAIN ($\Delta -5$, 95 % CI -10, 0 g/d; **Table 3**).

During PLAIN, those with a sweet tooth appeared to increased their carbohydrate intake ($\Delta 35$, 95 % CI -4, 75 g/d) (**Figure 3b**), though this was not driven by an increase in sugar intake ($\Delta 3$, 95 % CI -15, 21 g/d). It is interesting to note that this increase in carbohydrate (35 g/d, ~140 kcal) is roughly in line with the increase in energy intake (131 kcal/d). Sugar intake was consistently lower in those with a sweet tooth across both interventions (**Figure 3c**). Those without a sweet tooth appeared to increase their carbohydrate intake more during SWEET compared to PLAIN ($\Delta 40$, 95 % CI 13, 68 g/d), and this was largely but not exclusively driven by an increase in sugar intake ($\Delta 27$, 95 % CI 15, 39; **Table 7**). Sugar also increased during SWEET relative to PLAIN for those with a sweet tooth ($\Delta 20$, 95 % CI -5, 45 g/d; **Table 7**), but without the concomitant increase in carbohydrates ($\Delta 4$, 95 % CI -41, 49 g/d).

Table 6. Fasting appetite inventory scores pre- to post-intervention

	No sweet tooth (n = 16)			Sweet tooth (n = 11)			Difference in Δ sweet tooth vs. no sweet tooth	Difference in Δ PLAIN vs. SWEET
	PLAIN breakfast							
	Pre	Post	Δ	Pre	Post	Δ	PLAIN vs. PLAIN	No sweet tooth
Trait food cravings	116 ± 24	115 ± 27	-1 (-8, 5)	118 ± 40	117 ± 39	-1 (-7, 5)	0 (-10, 9)	-11 (-30, 8)
State food craving	44 ± 10	43 ± 12	-1 (-5, 4)	41 ± 13	41 ± 14	0 (-6, 6)	-1 (-9, 7)	1 (-4, 6)
FCI-fat	12 ± 4	12 ± 3	0 (-1, 2)	12 ± 5	10 ± 2	-2 (-4, 0)	2 (0, 5)	-1 (-3, 1)
FCI-sweet	15 ± 5	16 ± 6	1 (-1, 3)	16 ± 3	15 ± 4	-1 (-3, 1)	2 (-1, 5)	-2 (-5, 1)
FCI-CHO/starch	16 ± 5	15 ± 5	-1 (-3, 2)	13 ± 3	12 ± 3	-2 (-3, 0)	1 (-2, 4)	0 (-3, 3)
FCI-fast food fatty	8 ± 3	9 ± 4	1 (-1, 3)	9 ± 3	8 ± 3	-1 (-2, 0)	2 (-1, 5)	-2 (-4, 1)
TFEQ-restraint	10 ± 5	9 ± 6	-1 (-2, 0)	11 ± 6	10 ± 6	-1 (-3, 1)	0 (-2, 2)	0 (-1, 2)
TFEQ-disinhibition	7 ± 3	7 ± 3	0 (-1, 1)	8 ± 4	7 ± 4	-1 (-2, 1)	1 (-1, 2)	-1 (-2, 0)
TFEQ-hunger	6 ± 4	7 ± 4	0 (0, 1)	6 ± 4	7 ± 4	1 (0, 2)	0 (-2, 1)	-1 (-2, 0)
Chronotype*	55 ± 8	52 ± 9	-2 (-5, 0)	50 ± 9	50 ± 11	0 (-2, 3)	-3 (-6, 1)	2 (-1, 5)
	SWEET breakfast						SWEET vs. SWEET	Sweet tooth
Trait food cravings	121 ± 30	116 ± 28	-12 (-29, 4)	114 ± 43	113 ± 41	-1 (-8, 5)	-11 (-30, 8)	2 (-7, 12)
State food craving	44 ± 11	44 ± 10	0 (-4, 4)	39 ± 10	42 ± 14	3 (-2, 7)	-3 (-9, 4)	-3 (-12, 6)
FCI-fat	13 ± 4	12 ± 4	-1 (-2, 0)	12 ± 5	12 ± 6	0 (-2, 1)	-1 (-3, 2)	2 (1, 4)
FCI-sweet	16 ± 6	15 ± 5	-1 (-3, 1)	16 ± 6	16 ± 5	0 (-3, 4)	-2 (-6, 2)	0 (-3, 4)
FCI-CHO/starch	17 ± 4	16 ± 4	-1 (-3, 1)	13 ± 5	14 ± 4	0 (-1, 2)	-1 (-4, 1)	1 (-1, 4)
FCI-fast food fatty	9 ± 3	9 ± 3	-1 (-1, 0)	8 ± 3	7 ± 3	0 (-2, 1)	0 (-2, 1)	2 (0, 3)
TFEQ-restraint	9 ± 5	9 ± 6	-1 (-2, 1)	10 ± 5	10 ± 6	0 (-1, 1)	-1 (-3, 1)	1 (-2, 3)
TFEQ-disinhibition	8 ± 3	7 ± 3	-1 (-2, 0)	7 ± 4	8 ± 4	0 (0, 1)	-1 (-2, 0)	0 (-1, 1)
TFEQ-hunger	8 ± 3	7 ± 3	0 (-1, 1)	6 ± 4	6 ± 4	0 (-1, 0)	0 (-1, 1)	-1 (-2, 0)
Chronotype*	54 ± 7	53 ± 8	0 (-2, 1)	50 ± 10	51 ± 10	1 (-1, 2)	-1 (-3, 1)	-1 (-4, 2)

Data are mean $\pm$ standard deviation, or Δ (95 % confidence interval)

*Chronotype measured using the Morningness-Eveningness Questionnaire

Abbreviations: CHO, carbohydrates; FCI, Food Cravings Inventory; NNS, non-nutritive sweetener; TFEQ, Three Factor Eating Questionnaire

Table 8 shows the breakdown of energy expenditure during the intervention periods, with recordings taken the same days as the food diaries. No notable changes or differences in change were found pre- to post-intervention, except an increase in energy expenditure for those with no sweet tooth during SWEET (Δ 166, 95 % CI -8, 241 kcal/d). The increase in activity seems to be from slightly higher vigorous activity energy expenditure (Δ 37, 95 % CI -27, 101 kcal/d), though this did also coincide with less sedentary energy expenditure (Δ -55, 95 % CI -176, 65).

Overall, those with a sweet tooth appeared to expend less energy overall from physical activity (**Figure 4a**). Those with a sweet tooth on average expended less energy during PLAIN than those without a sweet tooth (Δ -103, 95 % CI -325, 118 kcal/d), driven primarily by lower light activity expenditure (Δ -32, 95 % CI -129, 66; **Table 8**). Physical activity energy expenditure at the beginning of PLAIN in those without a sweet tooth was ~92 kcal/d more than at the beginning of SWEET. This was driven primarily by a consistently higher light physical activity energy expenditure than during SWEET (no sweet tooth: PLAIN 256 ± 100 kcal/d *versus* SWEET 208 ± 71 kcal/d) as well as slightly higher moderate and vigorous activity energy expenditure (**Table 8** and **Figure 4**).

At the beginning of PLAIN, those without a sweet tooth also expended ~86 kcal/d more than those with a sweet tooth during PLAIN; similar to above, this was driven by higher light (PLAIN: no sweet tooth 256 ± 100 kcal/d *versus* sweet tooth 209 ± 90 kcal/d) and vigorous (PLAIN: no sweet tooth 105 ± 113 kcal/d *versus* 69 ± 66 kcal/d) activity energy expenditure (**Table 8**). By the end of PLAIN, those with and without a sweet tooth had similar physical activity energy expenditure. Those with a sweet tooth appeared to do more vigorous physical activity at the beginning of SWEET compared to the beginning of PLAIN (sweet tooth: PLAIN 69 ± 66 kcal/d *versus* SWEET 90 ± 101 kcal/d), but this difference dissipated by the end of the intervention periods (**Figure 4e**).

Table 7. Nutrient breakdown during the first (days 1-4) and last (days 15-18) of the intervention periods

	No sweet tooth (n = 16)			Sweet tooth (n = 11)			Difference in Δ sweet tooth vs. no sweet tooth	Difference between Δ PLAIN vs. SWEET
	PLAIN breakfast							
	Days 1-4	Days 15-18	Δ	Days 1-4	Days 15-18	Δ		
El (kcal/d)	2281 $\pm$ 715	2129 $\pm$ 621	-152 (-349, 45)	2273 $\pm$ 658	2404 $\pm$ 607	131 (-131, 395)	-284 (-623, 56)	184 (-16, 383)
CHO (g/d)	255 $\pm$ 79	242 $\pm$ 67	-13 (-32, 6)	253 $\pm$ 79	288 $\pm$ 97	35 (-4, 75)	-48 (-96, 0)	40 (13, 68)
Fibre (g/d)	25 $\pm$ 11	26 $\pm$ 11	2 (-1, 5)	29 $\pm$ 10	27 $\pm$ 9	-2 (-5, 2)	3 (-2, 9)	-1 (-3, 2)
Sugar (g/d)	95 $\pm$ 44	89 $\pm$ 45	-6 (-19, 6)	84 $\pm$ 38	87 $\pm$ 37	3 (-15, 21)	-9 (-33, 14)	27 (15, 39)
Fat (g/d)	86 $\pm$ 35	81 $\pm$ 29	-4 (-17, 9)	91 $\pm$ 27	84 $\pm$ 26	-7 (-21, 7)	3 (-17, 23)	4 (-5, 12)
Saturates (g/d)	29 $\pm$ 15	28 $\pm$ 13	-1 (-5, 3)	32 $\pm$ 12	28 $\pm$ 11	-4 (-11, 2)	3 (-5, 11)	1 (-4, 5)
Protein (g/d)	100 $\pm$ 44	94 $\pm$ 40	-5 (-17, 7)	89 $\pm$ 34	101 $\pm$ 38	12 (-5, 28)	-17 (-39, 5)	2 (-7, 11)
Total water (g/d)	2901 $\pm$ 1201	2827 $\pm$ 1194	-74 (-319, 172)	3058 $\pm$ 2365	2885 $\pm$ 1458	-174 (-991, 644)	100 (-850, 1050)	2 (-178, 182)
	SWEET breakfast						SWEET vs. SWEET	Sweet tooth
El (kcal/d)	2376 $\pm$ 765	2404 $\pm$ 869	28 (-194, 250)	2324 $\pm$ 626	2277 $\pm$ 592	-47 (-446, 351)	75 (-418, 567)	-49 (-415, 318)
CHO (g/d)	290 $\pm$ 107	285 $\pm$ 85	-5 (-35, 26)	273 $\pm$ 89	279 $\pm$ 83	7 (-49, 62)	-11 (-79, 57)	4 (-41, 49)
Fibre (g/d)	25 $\pm$ 11	25 $\pm$ 12	0 (-2, 2)	28 $\pm$ 12	23 $\pm$ 7	-5 (-10, 0)	5 (-1, 11)	-3 (-6, 0)
Sugar (g/d)	121 $\pm$ 55	117 $\pm$ 49	-4 (-18, 10)	105 $\pm$ 42	110 $\pm$ 44	5 (-15, 25)	-8 (-35, 18)	20 (-5, 45)
Fat (g/d)	84 $\pm$ 26	90 $\pm$ 42	7 (-8, 21)	83 $\pm$ 30	79 $\pm$ 23	4 (-23, 15)	11 (-15, 36)	-7 (-25, 11)
Saturates (g/d)	28 $\pm$ 14	30 $\pm$ 17	2 (-1, 5)	30 $\pm$ 12	27 $\pm$ 8	-3 (-12, 5)	5 (-5, 16)	-2 (-9, 5)
Protein (g/d)	99 $\pm$ 39	99 $\pm$ 42	0 (-8, 9)	100 $\pm$ 37	93 $\pm$ 35	-7 (-24, 10)	7 (-13, 28)	1 (-16, 19)
Total water (g/d)	2866 $\pm$ 1291	2781 $\pm$ 1510	177 (-294, 647)	3013 $\pm$ 1866	3187 $\pm$ 1845	175 (-257, 606)	2 (-670, 673)	135 (-315, 585)

Data are mean $\pm$ standard deviation, or Δ (95 % confidence interval)

Abbreviations: CHO, carbohydrate; EI, energy intake

Figure 3. Macronutrient intake from the first *versus* the last week of each intervention according to sweet preference: (a) energy intake; (b) carbohydrate intake; (c) sugar intake; (d) fat intake. Error bars are 95 % confidence intervals. Abbreviations: PLAIN, plain breakfast intervention; SWEET, sweet breakfast intervention

Table 8. Physical activity (kcal/d) breakdown during the first (days 1-4) and last (days 15-18) of the intervention periods

	No sweet tooth*			Sweet tooth*			Difference between Δ no sweet tooth vs. sweet tooth:	Difference between Δ PLAIN vs. SWEET:
	PLAIN breakfast							
	Days 1-4	Days 15-18	Δ	Days 1-4	Days 15-18	Δ	PLAIN vs. PLAIN	No sweet tooth**
PAEE	827 ± 475	774 ± 362	-54 (-200, 92)	741 ± 333	791 ± 277	50 (-99, 198)	-103 (-325, 118)	26 (-89, 140)
Sedentary	120 ± 52	120 ± 51	0 (-5, 5)	130 ± 47	135 ± 42	5 (-13, 22)	-5 (-25, 16)	49 (-12, 110)
Light	256 ± 100	262 ± 143	6 (-72, 84)	209 ± 90	247 ± 64	37 (-10, 84)	-32 (-129, 66)	-42 (-102, 18)
Moderate	280 ± 223	270 ± 199	-11 (-63, 41)	275 ± 184	267 ± 130	-8 (-87, 70)	-3 (-105, 99)	31 (-10, 73)
Vigorous	105 ± 113	90 ± 66	-15 (-60, 30)	69 ± 66	68 ± 69	-1 (-39, 38)	-14 (-77, 49)	20 (-35, 75)
	SWEET breakfast						SWEET vs. SWEET	Sweet tooth***
PAEE	735 ± 392	852 ± 434	166 (-8, 241)	721 ± 325	704 ± 360	-17 (-152, 118)	133 (-64, 330)	-59 (-139, 22)
Sedentary	182 ± 235	127 ± 57	-55 (-176, 65)	136 ± 59	126 ± 40	-10 (-30, 9)	-45 (-183, 93)	1 (-14, 16)
Light	208 ± 71	232 ± 80	24 (-25, 72)	187 ± 71	207 ± 63	19 (-25, 63)	4 (-66, 75)	-28 (-55, -1)
Moderate	260 ± 236	259 ± 207	-1 (-50, 48)	264 ± 178	243 ± 179	-21 (-59, 17)	20 (-46, 87)	-14 (-53, 24)
Vigorous	90 ± 79	126 ± 120	37 (-27, 101)	90 ± 101	72 ± 58	-18 (-71, 34)	55 (-34, 144)	1 (-29, 32)

Data are mean $\pm$ standard deviation, or Δ (95 % confidence interval). All data are kcal/d.

*Due to missing data, the sample size within each group dropped as follows: PLAIN no sweet tooth n = 13; PLAIN sweet tooth n = 10; SWEET no sweet tooth n = 11; SWEET sweet tooth n = 9

**n = 10

***n = 9

Abbreviations: PAEE, physical activity energy expenditure

Figure 4. Physical activity energy expenditure breakdown from the first *versus* the last week of each intervention according to sweet preference: (a) physical activity energy expenditure; (b) sedentary energy expenditure; (c) light activity energy expenditure; (d) moderate activity energy expenditure; (e) vigorous activity energy expenditure. Error bars are 95 % confidence intervals. Abbreviations: PLAIN, plain breakfast intervention; SWEET, sweet breakfast intervention

Figure 5 shows appetite across the day according to each intervention, split by whether participants identified as having a sweet tooth or not. Broadly it does not appear that interventions affected these appetites. It may be that after breakfast, before lunch, and before dinner those with a sweet tooth felt fuller, particularly during PLAIN, and those with no sweet tooth felt least full during SWEET (**Figure 5b**). Contrarily, those with a sweet tooth also appeared to feel they could eat more than those without a sweet tooth after eating breakfast (both PLAIN and SWEET) (**Figure 5c**). Across both PLAIN and SWEET, those with a sweet tooth also experienced higher thirst compared to those without a sweet tooth (**Figure 5d**).

Figure 6 shows hedonic appetites across the day according to each intervention, split by whether participants identified as having a sweet tooth or not. Perhaps unsurprisingly, those with a sweet tooth had a higher desire for sweet throughout the day compared to those without a sweet tooth; interestingly though, time trends in sweet desire across the day are similar between those with and without a sweet tooth (**Figure 6a**). Savoury desire across the day appeared to be higher in those with a sweet tooth during SWEET compared to any other group (**Figure 6b**). Trends across the day were similar for all comparisons in relation to fatty desire, though perhaps slightly higher for those with a sweet tooth during both PLAIN and SWEET, compared to those without a sweet tooth (**Figure 6c**). In terms of salt desire, this was highest in those with a sweet tooth during PLAIN, and lowest for those without a sweet tooth during PLAIN; during SWEET both those with and without a sweet tooth had very similar salt desire ratings (**Figure 6d**).

Figure 5. Appetite ratings across the day: (a) hunger; (b) fullness; (c) quantity ("how much can you eat?"); (d) thirst. Error bars are 95 % confidence intervals. Abbreviations: PLAIN, plain breakfast intervention; SWEET, sweet breakfast intervention; VAS, visual analogue scale

Figure 6. Hedonic appetite ratings across the day: (a) sweet; (b) savoury; (c) fat; (d) salt. Error bars are 95 % confidence intervals. Abbreviations: PLAIN, plain breakfast intervention; SWEET, sweet breakfast intervention; VAS, visual analogue scale

Discussion

This exploratory subanalysis examined whether the health and appetitive effects of a three week randomised crossover intervention comparing a plain porridge breakfast to an isocaloric sugar-sweetened breakfast were moderated by sweet preference (participant identification as having a sweet tooth or not). Overall, there were some key characteristic differences between those with and without a sweet tooth and evidence that sweet preference may moderate some psychological, physiological, and behavioural responses to the interventions.

Liking of both PLAIN and SWEET breakfasts was similar between those with and without a sweet tooth, with no change in liking across the 3 week intervention periods (data not shown). Previous research has shown that despite changes in sweet intensity, pleasantness does not appear to change when simple sugars were manipulated (Wise *et al.*, 2015). Our findings, however, may indicate that neither breakfast was particularly pleasant, regardless of sweet preference. It should therefore be acknowledged that outcomes in this subanalysis may have differed if breakfasts were optimised to individual preference, as pleasantness (liking) has been implicated in moderating satiety (Vickers, 1988).

The PLAIN and SWEET breakfasts were rated similarly in terms of fattiness between those with and without a sweet tooth, potentially suggesting some interrater reliability as fattiness was not manipulated. During PLAIN, both those with and without a sweet tooth rated the savouriness similarly, but those with a sweet tooth rated the SWEET breakfast as ~33 % more savoury compared to those without a sweet tooth. Additionally, but to a much lesser extent, those with a sweet tooth rated both breakfasts as less sweet compared to those without a sweet tooth.

Such a finding might suggest that at least in this context, sweetness during SWEET was enhanced for those without a sweet tooth via a contrast effect; i.e. the lower perceived savouriness of the SWEET breakfast might make it taste sweeter than in those with a sweet tooth. There appeared to be no differences in breakfast taste ratings from the first to third weeks of the interventions (data not shown); previous research has shown a change in (sweet) taste ratings after three months (Wise *et al.*, 2015) and sweet thresholds and preferences after 12 months (Ebbeling *et al.*, 2020), suggesting a three week intervention was not long enough to influence taste perception.

It is unclear whether having a sweet tooth directly relates to how intensely sweetness is perceived and sweet liking and consumption (Mattes, 1985). This may explain why there was only small differences in the perception of sweetness of the SWEET breakfast between those with and without a sweet tooth. Rather, greater bitter sensitivity appears to drive higher sweet preferences (Drewnowski *et al.*, 2012; Duffy *et al.* 2003); thus it is a limitation within the study that bitterness was not measured.

A similar proportion of men and women identified as having a sweet tooth or not, though more participants overall identified as not having a sweet tooth. Previous research has found men may have a higher preference for sweet than women (Connor & Booth, 1988; Hayes & Duffy, 2008; Monneuse & Louis-Sylvestre, 1991). Our findings may differ due to unbalanced sampling, as most participants ($n = 20$ out of 27) were women, making inferences regarding (a lack of) sex differences unreliable.

Those with a sweet tooth typically had a lower BMI and this group had a greater proportion of participants with BMI < 25 kg/m² compared to those without a sweet tooth. Whilst the

difference in change pre- to post-interventions was similar between those with and without a sweet tooth, those with a sweet tooth appeared to have a higher waist:hip ratio overall (0.77 without a sweet tooth versus 0.82 with a sweet tooth). Therefore, whilst a sweet tooth may relate to a lower BMI, it may also be implicated in a less metabolically healthy fat deposition phenotype. In terms of BMI, our finding accords with previous research showing that body mass is not an accurate predictor of sweet preference (Salbe *et al.*, 2004), and those with obesity prefer lower sugar (but higher fat) stimuli (Drewnowski *et al.*, 1985). Such a difference may be due to the overall higher fasted plasma fibroblast growth factor 21 concentrations in those with a sweet tooth compared to those without a sweet tooth (regardless of the intervention) with research typically showing lower BMI and mixed findings on waist:hip ratio (Frayling *et al.*, 2018; Søberg *et al.*, 2017). Inferences on fibroblast growth factor 21 should be made with added caution as these were only taken in a subgroup of the original study sample (though sweet preference was included as a randomisation strata when selecting these samples; Carroll *et al.*, 2020a).

Fibroblast growth factor 21 has been implicated in glucoregulatory health, and sweet preference and intake (Søberg *et al.*, 2017; Weng *et al.*, 2015). Intravenous infusion of fibroblast growth factor 21 suppresses carbohydrate and sweet intake in rodents (Talukdar *et al.*, 2016); accordingly, in our analyses, those with a sweet tooth (and higher fibroblast growth factor 21) consumed less sugar than those without a sweet tooth, with particularly prominent differences during SWEET. Finally, fibroblast growth factor 21 reduces dopaminergic activity in the nucleus accumbens (Talukdar *et al.*, 2016). This could offer a speculative explanation the incongruent findings between lower sugar intake and higher desire for sugar in those with compared to without a sweet tooth, in that there is lower motivation to seek desired foods.

Fasted plasma glucagon-like peptide-1 was also higher in those with a sweet tooth and may further contribute to the lower BMI status of this group due to its effects on increasing satiety and lowering hedonic reward. Interestingly, concentrations increased most obviously for those with a sweet tooth after PLAIN, but no obvious corresponding changes in fasted appetite or desires. Whilst glucagon-like peptide-1 analogues seem to reduce sweet desire (Kadouh *et al.*, 2019), it is unclear whether either sweet ingestion or sweet preference can influence glucagon-like peptide-1 concentrations, particularly in the fasted state, or the metabolic and/or appetitive implications of this.

Nonetheless, lower circulating glucagon-like peptide-1 may be a risk factor for type 2 diabetes (Lastya *et al.*, 2014), thus if our data are showing a causal relationship, it could mean that those with a sweet tooth have lower type 2 diabetes risk, and this speculatively may be further enhanced by consuming a low sugar (non-sweet) breakfast. The magnitude of change was ~1.4 time higher, which is approximately half of what would be expected in the fasted to postprandial state (Chen *et al.*, 2020). Despite the elevated glucagon-like peptide-1 concentration in those with a sweet tooth after PLAIN, insulin did not increase pre- to post-intervention. An elevation in insulin might be expected due to the incretin effect of glucagon-like peptide-1 (Holst, 2007); thus perhaps the change was not large enough to induce insulin secretion, and as such may not have been sufficient to induce change in other outcomes (such as diet).

Whilst gluco-regulatory markers remained fairly consistent (despite higher fibroblast growth factor and glucagon-like peptide-1 in those with a sweet tooth), fasted plasma lipid concentrations showed some interesting trends. Triacylglycerol was higher at baseline and increased consistently after both PLAIN and SWEET interventions for those who had a

sweet tooth, but remained stable for those without a sweet tooth. Due to the hepatic metabolism of fructose, sugar (fructose) intake can increase lipogenesis resulting in higher circulating triacylglycerol concentrations. However, in these analyses, those with a sweet tooth had lower sugar intake, and for both groups, fructose intake (estimated as half total sugar intake) remained below a range associated with elevated fasting triacylglycerol concentration (≥ 100 g/d) (Livesey & Taylor, 2008). Thus, it may be that those with a sweet tooth have a predisposition to slightly elevated fasting triacylglycerol concentrations, another factor perhaps relating to the genetics of sweet preference, or a chance finding (considering effect sizes were quite small).

On the other hand, during PLAIN, fasted plasma total cholesterol concentrations were lower in those with a sweet tooth, and in both groups has a similar reduction pre- to post-PLAIN. The decrease of ~ 0.2 mmol·L⁻¹ is what would be expected after regular oat beta glucan consumption (Whitehead *et al.*, 2014). However, during SWEET, pre-intervention total cholesterol was similar between those with and without a sweet tooth, but only elevated (slightly) for those without a sweet tooth and remained stable for those with a sweet tooth. Having a sweet tooth has previously been associated with higher total cholesterol concentrations (Shin *et al.*, 2018), though these participants also had higher intakes of sugar, contrary to the current analyses.

Our finding that sweet preference may moderate the blood lipid response to sugar ingestion is worthy of future investigation on two counts. Firstly, as posited in the original paper (in the supplementary file) it may be that sugar mitigates the cholesterol lowering effect of oat beta glucan (Carroll *et al.*, 2020a). This has implications for cholesterol-lowering health claims on high-fibre but also high-sugar breakfast cereals. Secondly, this finding may offer insight into individual responses to sugar; in this case, those without a sweet tooth should perhaps consume sugar more cautiously. Whether these differences (if causal) are due to the genetic basis of sweet preference, or the behavioural consequence of this genetic basis is unclear and also warrants investigation (Reed & McDaniel, 2006).

Additionally, previous research has shown sucrose to reduce high density lipoprotein cholesterol concentrations, potentially suggesting the increase in total cholesterol after SWEET in those without a sweet tooth may be driven primarily by low density lipoprotein cholesterol (Archer *et al.*, 1998; Yudkin *et al.*, 1986). Considering differential blood lipid responses to sucrose intake have been found according to apolipoprotein E genotypes (Erkkilä *et al.*, 2001), future research should perhaps explore whether this relationship has any relation to sweet preference (such as taste receptor 1 or fibroblast growth factor 21 genes).

Further, those without a sweet tooth had a small increase in fasted carbohydrate oxidation pre- to post-both interventions whilst those with a sweet tooth had an increase in fat oxidation. This seems counterintuitive considering the increase in carbohydrate intake in those with a sweet tooth pre- to post-PLAIN. These findings, if true, may suggest there are differential effects of a high carbohydrate breakfast on fasted substrate oxidation according to sweet preference. This may have implications in terms of metabolic flexibility, yet to our knowledge has not been investigated yet.

Additionally, diastolic blood pressure increased pre- to post-SWEET in those without a sweet tooth, by ~ 3 mmHg. For comparison, a salt reduction diet can lead to a reduction of diastolic blood pressure of 1-2 mmHg (Whelton *et al.*, 2002); thus an increase after just three weeks on a high sugar intervention could be a clinically meaningful finding. As with the sugar-

cholesterol interaction described above, there may also be a sugar-blood pressure interaction, for those without a sweet tooth.

For those without a sweet tooth, there was a modest reduction in desire for sweet, savoury, and fatty pre- to post-SWEET, not seen in those with a sweet tooth. This broadly accords with visual analogue scales across the day during the intervention. Such a finding may suggest that those without a sweet tooth achieve a greater hedonic satiety to flavours when faced with a consistent non-preferable stimulus (sugar). If this is the case, it would still be unclear as to why this satiety affected all flavour desires and not just sweet, as sensory-specific satiety would predict (Rolls, 1986).

Two particularly interesting trends were found from visual analogue ratings across the day. Firstly, during SWEET, there was a distinct sensory-specific satiety after breakfast, regardless of sweet preference. The magnitude of this effect is similar between those with and without a sweet tooth. Equally, sweet desire across the day during PLAIN had no such sensory-specific satiety response (as expected), but by pre-dinner, sweet desire had reduced slightly in those with a sweet tooth, and increased slightly for those without a sweet tooth, such that it was very similar between the two groups. Sweet taste perception has been shown to have a potential diurnal rhythm, syncing with leptin (Nakamura *et al.*, 2008); thus such a rhythm apply to sweet desire, and potentially be moderated by sweet preference.

Total daily sugar intake was consistently lower in those with a sweet tooth, particularly during SWEET. This finding appears contrary to previous research (Connor *et al.*, 1988; Duffy *et al.*, 2003; Jayasinghe *et al.*, 2017; Shin *et al.*, 2018). Intake of non-nutritive sweeteners was not measured, however; thus sweet desire may have been satiated via other means. If intake of non-nutritive sweetener did increase during this time, whilst it appeared successful at mitigating sugar intake, it did not mitigate sweet desire. Such a finding might be indicative of the different neural pathway activation from sucrose *versus* non-nutritive sweeteners, mitigating hedonic reward (Frank *et al.*, 2007; Green & Murphy, 2012), though with our current data this is pure speculation.

It is unclear whether the lower sugar intake caused the elevated desire for sweet in those with a sweet tooth, or whether factors determining sweet preference caused less sugar to be consumed. It is of interest that fibroblast growth factor 21 was consistently higher in those with a sweet tooth as this has been shown to reduce sugar intake (Talukdar *et al.*, 2016). This hormone seems a strong contender to explain these findings, although it does not explain the increase in non-sugar carbohydrate intake towards the end of the SWEET intervention in those with a sweet tooth as this would be expected to also decrease.

The second particularly interesting appetite finding is the desire for savoury trend across the day. After breakfast, a clear sensory-specific satiety response occurred, even after the SWEET breakfast. This may suggest that the savouriness of the porridge was still apparent even with a 30 % by weight substitution of oats for sugar. The magnitude was weakest in those with a sweet tooth during SWEET perhaps highlighting lower sensitivity to savouriness in the presence of sweetness. It is peculiar that savoury desire was also highest during SWEET for those with a sweet tooth, suggesting they additionally had a "savoury tooth". This increase in desire, nonetheless, did not translate to an increase in carbohydrate intake. It is therefore unclear as to why carbohydrate intake increased during PLAIN in those with a sweet tooth.

Considering nutrient intake did not alter substantively, it is unsurprising that psychological approach to food did not particularly change. However, with such small sample sizes, it is likely any real changes were undetectable. Alternatively, it may be that fat preference is a stronger predictor of constructs that were investigated, such as restraint (Elfhag & Erlanson-Albertson, 2006), meaning we were unable to detect meaningful effects using sweet preference.

The changes in physical activity were small; broadly speaking, in week 1 of PLAIN, those without a sweet tooth had greater physical activity energy expenditure, and this seemed mostly driven by higher light and vigorous energy expenditure. Those without a sweet tooth increased their activity notably from week 1 to week 3 SWEET, largely from greater vigorous energy expenditure. Considering the increase in physical activity in those without a sweet tooth during SWEET, it is surprising that triacylglycerol concomitantly increased. Minimal research has been conducted on sweet preference, responses to sweet primes, and physical activity. In 1898, a rat study was conducted showing greater activity when rats were fed bread compared to dog biscuits or beef and bread (Stewart, 1898). The inference from this study might be that higher glycaemic index food increases activity (in rodents). Thus, our present analyses do not support this position.

There were also some interesting findings relating sweet preference to several hydration-related factors. Those with a sweet tooth rated both the PLAIN and SWEET breakfasts approximately double the saltiness than those without a sweet tooth. Those without a sweet tooth also had a lower salt desire pre- to post-SWEET, and those with a sweet tooth had a lower salt desire pre- to post-PLAIN. The magnitude of difference (~13-16 mm) is about two thirds of that seen in a recent hydration study, whereby participants' fasting desire for salt was ~23 mm higher when rehydrated than when ~2 % hypohydrated (by body mass) (Carroll *et al.*, 2019).

Throughout the interventions, those with a sweet tooth had a consistently higher desire for salt during PLAIN, of a similar magnitude as pre- to post-PLAIN fasted desire. Pre- and post-breakfast salt desire was relatively similar across all comparisons, and the largest difference was salt desire pre-dinner. This is contrary to the aforementioned hydration study, whereby salt desire differences dissipated postprandially (Carroll *et al.*, 2019). Whilst the exact trend here is unclear and may be an artefact of small sample sizes or between-group comparisons, these findings may indicate that salt desire is moderated by sweet preference and may be more pronounced in those with a sweet tooth given a PLAIN prime. Unfortunately salt was not analysed as part of the dietary assessment, but perhaps should be considered in the future.

During the interventions, those with a sweet tooth consistently had a higher thirst rating (~10 mm) than those without a sweet tooth, regardless of the intervention. Fasted pre- to post-intervention thirst ratings were similar between groups, but those with a sweet tooth had a reduction in thirst rating of ~14 mm pre- to post-PLAIN. This is approximately half the magnitude of difference between those who are hypohydrated compared to those who are euhydrated (Carroll *et al.*, 2019), potentially representing a moderate to strong effect for a non-hydration related intervention, and considering hydration markers (urine specific gravity and serum osmolality) were not different enough to explain this difference. It is noteworthy that the difference in thirst ratings is similar to the difference in salt desire ratings, though trends to not appear to accord with trends seen during a hydration intervention suggesting alternative mechanisms may be dominating.

During the intervention, the increased thirst appears to coincide with a small ~100 mL higher intake of total water in those with a sweet tooth compared to those without. It is of course unclear whether this small increase was due to higher thirst, or why the higher fluid intake did not appear to satiate the thirst. As described above, fibroblast growth factor 21 is implicated in sweet preference and was higher in those with a sweet tooth. This hormone is also implicated in thirst and increases drinking in animal models (Turner *et al.* 2018), and thus may proffer an explanation towards the higher water intake in those with a sweet tooth. However, evidence in humans is inconclusive as hydration status has not been shown to alter fasting plasma fibroblast growth factor 21 concentrations, though drinking behaviours have not been measured (Carroll *et al.*, 2020b). Further research might investigate interactions between thirst, sweet preference, and fibroblast growth factor 21.

Whilst this exploratory analysis offers some interesting insights into the potential different ways those with and without a sweet tooth respond to a sugar prime, several critical limitations need to be acknowledged. Firstly, these analyses were severely underpowered. The original study was powered to detect a difference in change in body mass between PLAIN and SWEET; thus further splitting the data and increasing comparison groups severely limits inferences. For this reason, we opted to avoid null hypothesis significance testing, but did provide confidence to give a sense of the reliability. Confidence intervals in samples as small as ours can result in erroneous inferences and thus should be interpreted cautiously. Further, the small samples meant some mean scores may have been skewed by outliers. This problem is further exacerbated by the unequal number of participants who had or did not have a sweet tooth, and the fact that participants were not randomised by sweet preference upon enrolment to the original study. Moreover, whilst participants were randomised according to sex BMI status, considering the consistent differences in sweet preference, future work should perhaps investigate these groups separately. It was infeasible based on sample size to further split our data by sex or BMI status. Lastly in regards to sample size, some variables had missing data, such as physical activity energy expenditure, and all blood measures, but particularly fibroblast growth factor 21 which was only measured in a random subsample in the original study; randomisation was stratified by sweet preference for fibroblast growth factor 21, however (Carroll *et al.*, 2020a).

Secondly, as with any unplanned *post hoc* secondary subanalyses, causality cannot be inferred, particularly considering the lack of sweet preference randomisation strata. The method of obtaining data regarding sweet preference was crude and unvalidated, adding limitations to the strength of the inference that can be made. Thirdly, data were compared four ways: within-person pre- to post-intervention; within-person PLAIN to SWEET; between-person delta pre- to post-intervention; and between-person delta PLAIN to SWEET. The original study was design to test within-person delta PLAIN to SWEET. As such, the analyses we have presented have violated assumptions underlying a randomised crossover trial design, particularly by making between-person comparisons. Finally, as breakfast liking was similar regardless of sweet preference and breakfast type (PLAIN/SWEET), it may be that the interventions were not different enough to induce more robust effects according to participant preference. Thus future work should tailor breakfasts to participant preference and use a less savoury vehicle for sweet/plain administration.

Nonetheless, this study provides novel exploratory psychological, physiological, and behavioural insights regarding sweet preference and sugar priming. Due to the above methodological and statistical limitations, we claim no causality within our findings, but do offer several noteworthy associations warranting further investigation. Moreover,

associations accord with previous research adding strength to the likely validity of the novel associations presented herein.

Conclusion

Overall, this exploratory analysis provides evidence that having a sweet tooth may not only impact appetite, but may also moderate the cardiometabolic response to a sweet or plain prime. Such findings, if confirmed in future work, could have implication for public health recommendations regarding the health effects of sugar intake. Considering the study design, these results are non-causal and lack temporal direction in terms of the effects of sweet preference on the investigated outcomes. Future research should therefore investigate the causality of the relationships highlighted, whilst in the meantime consider *a priori* stratification by sweet preference.

References

- Archer, S., Liu, K., Dyer, A. R., Ruth, K., Jacobs, D. R., Van Horn, L., Hilner, J. E., & Savage, P. J., 1998. Relationship between changes in dietary sucrose and high density lipoprotein cholesterol: The CARDIA Study. *Annals of Epidemiology*, 8(7), 433-8, doi: 10.1016/S1047-2797(98)00007-6.
- Bartoshuk, L. M., Duffy, V. B., Hayes, J. E., Moskowitz, H. R., & Snyder, D. J., 2006. Psychophysics of sweet and fat perception in obesity: Problems, solutions and new perspectives. *Philosophical Transactions of the Royal Society B*, 361(1471), doi: 10.1098/rstb.2006.1853.
- Carroll, H. A., 2020. Redefining thirst: A conceptual four-compartment model characterising types of thirst, and their underlying mechanisms and interactions. *NutriXiv*, doi:10.31232/osf.io/q7gvd.
- Carroll, H. A., Chen, Y-C., Templeman, I. S., James, L. J., Betts, J. A., & Trim, W. V., 2020b. The effect of hydration status on plasma FGF21 concentrations in humans: A subanalysis of a randomised crossover trial. *PLoS ONE*, doi: 10.1371/journal.pone.0235557.
- Carroll, H. A., Chen, Y-C., Templeman, I. S., Wharton, P., Reeves, S., Trim, W. V., Chowdhury, E., Brunstrom, J., Rogers, P. J., Thompson, D., James, L. J., Johnson, L., & Betts, J. A., 2020a. Effect of plain versus sugar-sweetened breakfast on energy balance and metabolic health: A randomized crossover trial. *Obesity*, 28(4), 740-8, doi: 10.1002/oby.22757.
- Carroll, H. A., Templeman, I., Y-C., Chen, Edinburgh, R. M., Burch, E. K., Jewitt, J. T., Povey, G., Robinson, T. D., Dooley, W. L., Jones, R., Tsintzas, K., Gallo, W., Melander, O., Thompson, D., James, L. J., Johnson, L., Betts, J. A., 2019. Effect of acute hypohydration on glycemic regulation in health adults: A randomized crossover trial. *Journal of Applied Physiology*, 126(2), 422-30, doi: 10.1152/jappphysiol.00771.2018.
- Chen, Y-C., Smith, H. A., Hengist, A., Chrzanowski-Smith, O. J., Mikkelsen, U. R., Carroll, H. A., Betts, J. A., Thompson, D., Saunders, J., Gonzalez, J. T., 2020. Co-ingestion of whey protein hydrolysate with milk minerals rich in calcium potential stimulates glucagon-like peptide-1 secretion: An RCT in healthy adults. *European Journal of Nutrition*, 59, 2449-62, doi: 10.1007/s00394-019-02092-4.
- Connor, M. T., & Booth, 1988. Preferred sweetness of a lime drink and preference for sweet over non-sweet foods, related to sex and reported age and body weight. *Appetite*, 10, 25-35, doi: 10.1016/S0195-6663(88)80030-8.
- Connor, M. T., Haddon, A. H., Pickering, E. S., & Booth, D. A., 1988. Sweet tooth demonstrated: Individual differences in preference for both sweet foods and foods highly sweetened. *Journal of Applied Psychology*, 73(2), 275-80, doi: 10.1037/0021-9010.73.2.275.
- Drewnowski, A., Brunzell, J. D., Sande, K., Iverius, P. H., & Greenwood, M. R., 1985. Sweet tooth reconsidered: Taste responsiveness in human obesity. *Physiology & Behavior*, 35(4), 617-22, doi: 10.1016/0031-9384(85)90150-7.
- Drewnowski, A., Mennella, J. A., Johnson, S. L., & Bellisle, F., 2012. Sweetness and food preference. *Journal of Nutrition*, 142(6), S1142-8, doi: 10.3945/jn.111.149575.

Duffy, V., Peterson, J. M., Dinehart, M. E., & Bartoshuk, L. M., 2003. Genetic and environmental variation in taste: Associations with sweet intensity, preference, and intake. *Topics in Clinical Nutrition*, 18(4), 209-20.

Ebbeling, C. B., Feldman, H. A., Steltz, S. K., Quinn, N. L., Robinson, L. M., Ludwig, D. S., 2020. Effects of sugar-sweetened, artificially sweetened, and unsweetened beverages on cardiometabolic risk factors, body composition, and sweet taste preference: A randomized controlled trial. *Journal of the American Heart Association*, 9(15), doi: 10.1161/JAHA.119.015668.

Elfhag, K., & Erlanson-Albertson, C., Sweet and fat taste preference in obesity have different associations with personality and eating behavior. *Physiology & Behaviour*, 88(1-2), 61-6, doi: 10.1016/j.physbeh.2006.03.006.

Erkkilä, A. T., Sarkkinen, E. S., Lindi, V., Lehto, S., Laakso, M., & Uusitupa, M. I. J., 2001. APOE polymorphism and the hypertriglyceridemic effect of dietary sucrose. *American Journal of Clinical Nutrition*, 73(4), 746-52, doi: 10.1093/ajcn/73.4.746.

Hayes, J. E., & Duffy, V. B., 2008. Oral sensory phenotype identifies level of sugar and fat required for maximal liking. *Physiology & Behavior*, 95(1-2), 77-87, doi: 10.1016/j.physbeh.2008.04.023.

Frank, G. K. W., Oberndorfer, T. A., Simmons, A. N., Paulus, M. P., Fudge, J. L., Yang, T. T., & Kaye, W. H., 2007. Sucrose activates human taste pathways differently from artificial sweetener. *Neuroimage*, 39(4), 1559-69, doi: 10.1016/j.neuroimage.2007.10.061.

Frayling, T.M., Beaumont, R.N., Jones, S.E., Yaghootkar, H., Tuke, M.A., Ruth, K.S., Casanova, F., West, B., Locke, J., Sharp, S., Ji, Y., Thompson, W., Harrison, J., Etheridge,

A.S., Gallins, P.J., Jima, D., Wright, F., Zhou, Y., Innocenti, F., Lindgren, C.M., Grarup, N., Murray, A., Freathy, R.M., Weedon, M.N., Tyrrell, J., & Wood, A.R., 2018. A Common Allele in FGF21 Associated with Sugar Intake Is Associated with Body Shape, Lower Total Body-Fat Percentage, and Higher Blood Pressure. *Cell Reports*, 23(2), 327-336.

Green, E., & Murphy, C., 2012. Altered processing of sweet taste in the brain of diet soda drinkers. *Physiology & Behavior*, 107(4), 560-7, doi: 10.1016/j.physbeh.2012.05.006.

Herrera Moro Chao, D., Argmann, C., Van Eijk, M., Boot, R.G., Ottenhoff, R., Van Roomen, C., Foppen, E., Siljee, J. E., Unmehopa, U. A., Kalsbeek, A., & Aerts, J. M., 2016. Impact of obesity on taste receptor expression in extra-oral tissues: emphasis on hypothalamus and brainstem. *Scientific Reports*, 6, doi: 10.1038/srep29094.

Holst, J. J., 2007. The physiology of glucagon-like peptide 1. *Physiological Reviews*, 87(4), 1409-39, doi: 10.1152/physrev.00034.2006.

Jayasinghe, S. N., Kruger, R., Walsh, D. C. I., Cao, G., Rivers, S., Richter, M., & Breier, B. H., 2017. Is sweet taste perception associated with sweet food liking and intake? *Nutrients*, 9(7), doi: 10.3390/nu9070750.

Kadouh, H., Chedid, V., Halawi, H., Burton, D. D., Clark, M. M., Khemani, D., Vella, A., Acosta, A., & Camilleri, M., 2019. GLP-1 analog modulates appetite, taste preference, gut hormones, and regional body fat stores in adults with obesity. *Journal of Clinical Endocrinology & Metabolism*, 105(5), 1552-63, doi: 10.1210/clinem/dgz140.

Lastya, A., Saraswato, M. R., ^ Suastika, K., 2014. The low level of glucagon-like peptide-1 (GLP-1) is a risk factor of type 2 diabetes mellitus. *BMC Research Notes*, 7, doi: 10.1186/1756-0500-7-849.

Mattes, R. D., 1985. Gustation as a determinant of ingestion: Methodological issues. *American Journal of Clinical Nutrition*, 41(4), 672-83, doi: 10.1093/ajcn/41.4.672.

Livesey, G., & Taylor, G., 2008. Fructose consumption and consequences for glycation, plasma triacylglycerol, and body weight: meta-analyses and meta-regression models of intervention studies. *American Journal of Clinical Nutrition*, 88(5), 1419-37, doi: 10.3945/ajcn.2007.25700.

Monneuse, M. O., & Louis-Sylvestre, F. B. J., 1991. Impact of sex and age on sensory evaluation of sugar and fat in dairy products. *Physiology & Behavior*, 50(6), 1111-7, doi: 10.1016/0031-9384(91)90569-a.

Nakamura, Y., Sanematsu, K., Ohta, R., Shirosaki, S., Koyano, K., Nonaka, K., Shigemura, N., & Ninomiya, Y., 2008. Diurnal variation of human sweet taste recognition thresholds is correlated with plasma leptin levels. *Diabetes*, 57(10), 2661-5.

Reed, D. R., & McDaniel, A. H., 2006. The human sweet tooth. *BMC Oral Health*, 6, S17, doi: 10.1186/1472-6831-6-S1-S17.

Rolls, B. J., 1986. Sensory-specific satiety. *Nutrition Reviews*, 44(3), 93-101.

Salbe, A. D., DelParigi, A., Pratley, R. E., Drewnowski, A., & Tataranni, P. A., 2004. Taste preferences and body weight changes in an obesity-prone population. *American Journal of Clinical Nutrition*, 79(3), 372-8, doi: 10.1093/ajcn/79.3.372.

Shin, Y., Lee, S., & Kim, Y., 2018. Sweet preference associated with the risk of hypercholesterolemia among middle-aged women in Korea. *Journal of Atherosclerosis & Thrombosis*, 25(12), 1215-21, doi: 10.5551/jat.43000.

Søberg, S., Sandholt, C. H., Jespersen, N. Z., Toft, U., Madsen, A. J., von Holstein-Rathlou, S., Grevengoed, T. J., Christensen, K. B., Bredie, W. L. P., Potthoff, M. J., Solomon, T. P. J., Scheele, C., Linneberg, A., Jørgensen, T., Pedersen, O., Hansen, T., Gillum, M. P., & Grarup, N., 2017. FGF21 is a sugar-induced hormone associated with sweet intake and preference in humans. *Cell Metabolism*, 25(5), 1045-53, doi: 10.1016/j.cmet.2017.04.009.

Stewart, C. C., 1898. Variations in Daily Activity Produced by Alcohol and by Changes in Barometric Pressure and Diet, with a Description of Recording Methods. *American Journal of Physiology*, 1(1), 40-56.

Stolbová, K., Hahn, A., Beneš, B., Andel, M., & Trešlová, L., 1999. Gustometry of diabetes mellitus patients and obese patients. *International Tinnitus Journal*, 5(2), 135-40.

Talukdar, S., Owen, B. M., Song, P., Hernandez, G., Zhang, Y., Zhou, Y., Scott, W. T., Paratala, B., Turner, T., Smith, A., Bernardo, B., Müller, C. P., Tang, H., Mangelsdorf, D. J., Goodwin, B., Kliewer, S. A., 2016. FGF21 regulates sweet and alcohol preference. *Cell Metabolism*, 23(2), 344-9, doi: 10.1016/j.cmet.2015.12.008.

Turner, T., Chen, X., Zahner, M., Opsahl, A., DeMarco, G., Boucher, M., Goodwin, B., & Perreault, M., 2018. FGF21 increases water intake, urine output and blood pressure in rats. *PLoS ONE*, doi: 10.1371/journal.pone.0202182.

Vickers, Z., 1988. Sensory specific satiety in lemonade using a just right scale for sweetness. *Journal of Sensory Studies*, 3(1), 1-8.

Weng, Y., Chabot, J.R., Bernardo, B., Yan, Q., Zhu, Y., Brenner, M.B., Vage, C., Logan, A., Calle, R., & Talukdar, S., 2015. Pharmacokinetics (PK), pharmacodynamics (PD) and integrated PK/PD modeling of a novel long acting FGF21 clinical candidate PF-05231023 in diet-induced obese and leptin-deficient obese mice. *PLoS One*, 10(3), e0119104.

Whelton, P. K., He, J., Appel, L. J., Cutler, J. A., Havas, S., Kotchen, T. A., Roccella, E. J., Stout, R., Vallbona, C., Winston, M. C., Karimbakas, J., & the National High Blood Pressure Education Program Coordinating Committee, 2002. Primary prevention of hypertension: Clinical and public health advisory from The National High Blood Pressure Education Program. *Journal of the American Medical Association*, 288(15), 1882-8, doi: 10.1001/jama.288.15.1882.

Whitehead, A., Beck, E. J., Tosh, S., & Wolever, T.M., 2014. Cholesterol-lowering effects of oat beta-glucan: a meta-analysis of randomized controlled trials. *American Journal of Clinical Nutrition*, 100(6), 1413-21.

Wise, P. M., Nattress, L., Flammer, L. J., & Beauchamp, G. K., 2015. Reduced dietary intake of simple sugars alters perceived sweet taste intensity but not perceived pleasantness. *American Journal of Clinical Nutrition*, 103, 50-60, doi: 10.3945/ajcn.115.112300.

Yu, J. H., Shin, M-S., Lee, J. R., Choi, J. H., Koh, E. H., Lee, W. J., Park, J-Y., & Kim, M-S., 2014. Decreased sucrose preference in patients with type 2 diabetes mellitus. *Diabetes Research and Clinical Practice*, 104(2), 214-9, doi: 10.1016/j.diabres.2014.02.007.

Yudkin, J., Eisa, J., Kang, S. S., Meraji, S., & Bruckdorfer, K. R., 1986. Dietary sucrose affects plasma HDL cholesterol concentration in young men. *Annals of Nutrition & Metabolism*, 30, 261-6, doi: 10.1159/000177202.

Appendix

Participant sweet preference

The following data show the participant ID code and their reported sweet preference (sweet tooth yes/no). The rest of the data are publicly available from doi: 10.15125/BATH-00720.

PS01	yes
SP02	yes
SP05	yes
PS25	yes
PS26	yes
SP27	yes
PS31	yes
SP34	yes
PS37	yes
SP38	yes
SP39	yes
PS03	no
PS04	no
PS06	no
PS07	no
SP09	no
PS11	no
SP13	no
PS14	no
PS16	no
PS18	no
SP32	no
PS33	no
SP35	no
PS36	no
SP40	no
PS41	no

Note: participants 22 and 29 did not provide their sweet preference