Compare the effects of beverages containing MDX and artificial sweeteners (AS) on hunger/satiety, post-prandial blood glucose levels and subsequent food (calorie) intake.

7MNT0005 Nutrition Research Skills

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Abstract:

This study aims to analyze the metabolic impact of artificial sweeteners (AS) and maltodextrin (MDX) on human health, considering the increasing global prevalence of diabetes and obesity. We conducted a study to compare the effects of meals supplemented with MDX (a polysaccharide used as a food additive) and Splenda (a popular artificial sweetener) on post-meal blood glucose levels, hunger, fullness, alertness, pleasantness, desire to eat and subsequent calories intake among 51 participants from the KCL MSc nutrition. Our methodology consisted of conducting a randomized controlled study where participants were allocated to consume a meal with MDX or Splenda. Visual analogue scale scores (VAS scores) and self-glucose testing were used to measure the results. The main findings indicated no differences between the two groups in post-meal appetite, feeling of fullness/hunger, alertness, and food intake. Although there were temporary differences in blood glucose levels at certain time intervals, the overall impact of MDX and Splenda on postprandial blood glucose did not differ significantly. These findings suggest that the metabolic effects of MDX and Splenda on short-term measures such as blood sugar levels and fullness are similar. This study provides evidence that artificial sweeteners (AS) have similar metabolic effects as other carbohydrates, challenging the belief that AS can be used as a substitute for dietary sugar in regulating blood sugar levels, which is crucial for individuals trying to manage their weight or blood sugar levels. Nevertheless, this study is constrained by the limited number of participants. Therefore, it is advisable to do additional research to explore the long-term effects in different populations and forms of AS.

Key word: Artificial Sweeteners, Glucose, Nutrition, Metabolic Health

Context

1. Introduction

Over the past few years, diabetes and obesity have been on the rise, resulting in heightened public concern regarding dietary components. Among them, artificial sweeteners (AS) have gained significant public and scientific community interest. [1][2] Extensive data and studies have demonstrated that AS may serve as an alternative to natural sugar in food processing. [3][4] This is not only due to its sweetness, which is 200-13,000 times than natural sugar [16], but also the fact that the body is unable to absorb and utilize AS. So, they are commonly used to limit sugar intake, manage weight, and regulate blood glucose. However, the research findings regarding their long-term health effects are inconclusive. [5][6] Hence, to ascertain the suitability of AS as a substitute, this study conducted a comparison of the impacts of a meal comprising Maltodextrin (MDX) and Splenda (AS) on postprandial blood glucose, hunger, fullness, alertness, and total calorie consumption on the following day. This study aims to provide a scientific foundation for understanding the impacts of AS on human health and offer dietary recommendations to the public.

2. Methods

2.1. *Subject*

The participants consisted of 51 students from KCL's MSc nutrition, including 41 women and 10 men. All participants were approximately the same age, and their BMI was healthy (BMI mean=22.90, SD=4.19). All participants maintained fasting throughout the night before the experiment and did not consume anything on the experimental day. Before participating in the experiment, all participants explicitly indicated their consent to consume the meals offered during the study.

2.2. *Test meals*

Two breakfasts consist of typical English breakfast items such as the same margarine (12g), skimmed milk (150 ml), white bread toast (37g, 1.5 slices), and rice krispies (30g), but they differ in the breakfast drinks (meal A: 250 ml water+4.5g MDX; meal B: 250 ml water+4.5g Splenda, equivalent to 6 teaspoons of Splenda). The preparation and serving techniques were standardized as well, and everything was prepared immediately before use.

2.3. *Ratings of subjective sensations*

Postprandial alertness, hunger/fullness, and pleasantness were evaluated using a 100 mm visual analogue scale score (VAS score) at a certain time (Appendix Table 1). The participants monitored their postprandial blood glucose levels as well. It is important to note that the timing of the subjects' breakfast intake should be controlled within 15 minutes. This helps minimize experiment variability and replicate everyday routines. Each measure is evaluated using an individual VAS score anchored at opposing ends of the emotion spectrum. For instance, one end is labelled "not at all hungry" (0) and the other is labelled "extremely hungry" (100). Following breakfast, participants were asked to score their level of pleasantness of the meal also using the VAS score, with endpoints labelled as "not at all pleasant" (0) and "very pleasant" (100)

2.4. *Protocol*

The experiment lasted 4 weeks. Initially, the participants were randomly allocated into four groups. After they fasted for one night, different groups arrived in the laboratory at 9 AM every Wednesday and randomly ate 2 types of breakfasts. Participants were provided

with a VAS score booklet and a timer after arriving. First, they need to assess the fasting VAS score. Then, they ate the test meal together in a comfortable and uninterrupted environment, at the same time starting timing. After their meal, the participants kept monitoring the time. At the specific time point (Appendix Table 1), they independently measured their blood glucose and VAS scores in another room. When they finished all the measurements, the participants departed from the laboratory and proceeded with their daily routines, including unrestricted eating and drinking. However, they need to record their dietary intake throughout the day. By the end of the day, the participants logged their dietary information into Nutritics, and moved all the results into a sharing document.

2.5.*Statistical analysis*

The Nutritics website automatically estimated the subjects' energy consumption throughout the day after breakfast. Investigating the relationship between each variable's VAS scores, drink intakes, and time points using SPSS statistical software, including independent sample t-tests and repeated ANOVA. Furthermore, the trapezoidal formula （AUC and iAUC） accurately estimated the area under the curve of physiological indicators such as alertness, hunger, fullness, and postprandial blood glucose.[14] Simultaneously, the line chart effectively describes the trend of diverse physiological indicators, offering powerful data to support this research.

3. Result

3.1.*Alertness*

The Sig. (2-tailed) values at all time were bigger than 0.05 (P>0.05). This indicates no statistically significant difference in alertness VAS scores between meals in 3h. Appendix Figure 1A displays that although there is little difference between the two groups at the beginning and finish, the overall trends of the two groups are similar. Additionally, the SEM for both groups largely overlapped, but after adjusting the baseline (Appendix Figure 1B), the level of alertness in meal B was much greater than in meal A. Appendix Table 2 displays, after adjusting the baseline, the total iAUC of meal B was considerably greater than that of meal A, suggesting that meal B significantly impacts alertness as time passes. Nevertheless, running ANOVA tests on the AUC and iAUC of all participants determined that the impact of the two meals was not statistically significant (P=0.826). The interaction effect between time and meal was also insignificant (P=0.695). However, the effect of time was shown to be significant ($p<0.001$). This indicates that 2 meals do not alter the pattern of alertness changes over time, which means the two meals did not significantly affect the increase or decrease in alertness.

3.2.*Hunger*

The data shows that the P-values>0.05 at most of the time. Therefore, there was no difference between the two breakfasts. Nevertheless, in 180 minutes, a two-sided P-value=0.068 and a one-sided P-value=0.034<0.05. The one-sided test showed a significant result. This implies that the distinct components of the two breakfasts might result in varying alertness in 180 minutes. Appendix Figure 2A demonstrates that the hunger scores of both groups were similar at the first (0 min). Following the time, between 15 - 30 minutes, there was a significant drop in hunger scores. The hunger scores then exhibited a progressive increase in both groups as time progressed. For most time points, the hunger score of Meal A was slightly higher than that of Meal B

(Appendix Figure 2B). Appendix Table 3 indicates no significant difference between the two groups in the AUC and iAUC. To summarize, whereas the hunger scores of different breakfasts varied at some time, there is no statistical evidence to suggest that the two groups caused different effects on hunger.

3.3.*Fullness*

The data indicates that the P-values > 0.05 most of the time. Like the hunger VAS score after the meal, P(one-sided) =0.043, P(two-sided) =0.086 at 180 minutes. Despite the two-sided P-value>0.05, the one-sided test yielded significant results. So, there could be a significant difference in the fullness of the two meals at 180 minutes. After analyzing the line graphs (Appendix Figure 3 A), it is evident that there is a declining pattern in fullness, which means the individuals experienced a gradual decrease in fullness over time. However, most data showed no notable differences between the 2 breakfasts (Appendix Figure 3B). Appendix Table 4 demonstrates that, following the modification of the baseline, there is also no noteworthy disparity between the two groups. The data from Group B exhibits a modest increase compared to Group A. This implies that Meal B may offer slightly more fullness over time, although the difference is not substantial.

3.4.*Desire to eat.*

The data in Appendix Figure 4A suggest that the two meals had similar effects at the initial time point (0 min), but at 15 minutes, it decreased significantly in both. At subsequent times (30min-180min), the desire to eat in both groups gradually increased. However, the data for meal A was always slightly higher than for meal B (Appendix Figure 4B). Combined with the SPSS results (P>0.05), there was no significant difference in changes in appetite between the two groups at any time. The AUC and iAUC data in Appendix Table 5 also shows that Group A's value is generally higher than Group B's at each time. However, after running ANOVA on the AUC and iAUC of all subjects, it showed that the interaction effect of time and meal was not significant (P=0.505), the effect of meal type was not significant (P=0.203), but the time effect was significant. (P<0.01). This means that different breakfasts did not change the pattern of appetite over time, and there were no substantial differences between the two breakfasts and the desire to eat.

3.5.*Pleasantness*

Following the analysis of the data, the p-value=0.282> 0.05. Thus, there is no statistically significant difference between the pleasure VAS scores and the two meals. Appendix Figure 5 illustrates that the mean VAS score of Group A is slightly greater than that of Group B. Nevertheless, the SEM bars intersect, indicating that the distinction between the two groups is not statistically significant. Consequently, there was no notable difference between the two meals in terms of their impact on breakfast pleasure.

3.6.*Subsequent food intake（Calories）*

The significance level (p-value) = 0.855>0.05. Therefore, there is insufficient evidence to reject the null hypothesis, which means there is no statistical difference in calorie consumption between the two Meals. The graph (Appendix Figure 6) illustrates that the mean energy consumption of Meal A is marginally lower than that of Meal B. However, the difference seems minimal. Therefore, the two breakfasts did not result in statistically significant differences in the total calories consumed throughout the day.

3.7.*The blood sugar level in 3h*

Initially, most of the time showed the P-value>0.05. Only three time points, 30, 45, and

60 minutes, P-values <0.05 (P30min=0.036, P45min=0.012, P60min=0.04). This indicates a significant disparity in blood glucose between the meals and 3 certain times, suggesting that group A might result in increasing blood glucose in 30-60 minutes. Appendix Figure 7A demonstrates the initial blood sugar levels of the two groups were comparable. Following the meals, blood sugar levels rose in both groups, with the highest point observed in group A at 45 minutes and 30 minutes in group B separately, and the maximum for group A was bigger (Appendix Figure 7B). Subsequently, both groups' glucose declined, showing a more rapid decline in group A. Appendix Table 6 indicates that the increase in blood sugar levels in group A was slightly greater than in group B. Nevertheless, multiple ANOVA tests on the AUC and iAUC of all participants revealed the meals had a non-significant effect (P=0.282), whereas the time had a highly significant effect (P<0.001). The interaction between time and meal was also insignificant (P=0.271). So, there were no significant interaction effects between them. In other words, the two breakfasts did not significantly impact blood sugar levels.

4. Discussion

The findings indicated that breakfasts containing MDX and AS did not exhibit any differences in postprandial hunger/fullness, alertness, pleasure, desire to eat, blood glucose levels, and food consumption. This is consistent with the earlier studies. While AS may not directly elevate blood sugar levels, it can indirectly impact glucose, leading to chain reactions. For example, studies have shown that mice have AS receptors. After AS binds to the receptor, it activates the G-protein and activates phospholipase Cβ2, resulting in an increase in intracellular calcium concentration. This signalling ultimately promotes the insertion of GLUT2 (a glucose transporter) into the intestinal cell membrane, increasing glucose absorption and indirectly increasing blood sugar. [5] Studies [6] have also shown that the sweet taste receptor subunit can recognize dietary sugar and AS, both of which can increase the gene expression of SGLT1 (sodium-dependent glucose transporter 1) in wild mice, leading to increasing glucose absorption capacity. What's more, it can also promote the secretion of intestinal hormones, promoting the expression of SGLT1 and forming potential positive feedback. Although AS has fewer calories, it can also activate a series of downstream reactions by binding to sweet taste receptors in the body, indirectly causing an increase in glucose. In addition, studies have also shown that certain types of AS may change the composition of the intestinal microbial community, which may affect glucose metabolism and insulin sensitivity, indirectly affecting blood sugar levels [7]. Research has also indicated that long-term exposure to sucralose can result in decreased insulin sensitivity, acute insulin response (AIR), and increased production of glucagon-like peptide-1 (GLP-1) [11], For example, sucralose and saccharin can lead to gut microbiota changes associated with glucose intolerance [8]. Glucose intolerance is an intermediate state between normal blood sugar levels and diabetes. In this state, the blood sugar levels are higher than normal but have not yet reached the diagnostic criteria for diabetes [9]. Study [10] has also supported the idea that when consumed at 300 mg/kg/day, Splenda can negatively impact the gastrointestinal system by disrupting gut flora and protein levels. However, it is important to acknowledge that the above research still requires validation in humans, and individual differences or the effects of different AS still

need to be further researched.

After consumption of dietary sugar, it is converted into simple sugars, such as glucose, then absorbed into the bloodstream, directly increasing blood sugar levels. Although their mechanisms for raising blood sugar are not the same, they ultimately have the same outcomes. Nevertheless, the alertness and calories consumed after meal A were much higher in Group B. Additionally, group B experienced a more rapid increase in blood sugar. The disparity in alertness may be attributed to the blood sugar instability caused by AS. However, less literature indicates that consuming Splenda leads to fluctuations in blood sugar. The increased food consumption in Group B may be attributed to the correlation between AS and high-calorie items. It has been proposed that AS may impact the brain's perception of sweetness and energy, potentially influencing overall energy consumption. [12] concluded that 3kcal aspartame would produce an obvious disappearance of negative feelings, and its effect is about half of the effect induced by 188kcal glucose. indicating that glucose reduced motivation to eat and increased satiety, while aspartame had the opposite effect. Additionally, there are ideas suggesting that individuals can acquire knowledge about food through taste reactions. If sweetness is commonly linked to high-calorie items, the sweet flavors of AS might elicit a desire for high-calorie foods [13].

In conclusion, though AS reduces sugar consumption, this study demonstrates that AS does not exhibit any notable differences compared to dietary sugar in regulating blood sugar levels, satiety, and daily energy intake. This is crucial for public health, particularly for those with diabetes and responsible for their weight.

However, there are still several limitations. Firstly, the sample size is insufficient, resulting in an imbalance of males and females, with all the samples being young and healthy college students. Furthermore, individuals did not complete the whole meal, resulting in the subject's blood sugar being influenced by other foods. So, next time, before the experiment, examine all the participants' dietary patterns and ask them to try their best to consume every food. Simultaneously, the utilization of VAS SCORE has the potential to induce errors. Thus, employing a more intuitive method to assess would be advantageous (Appendix Table 7). Additionally, long-term research is required to validate the results as well as investigate various demographics, including women, children, etc., [15] and the diverse impacts of different AS. Subsequent research should consider the physiological variations of individuals. It is also important to evaluate whether quantities of AS will result in distinct glucose and whether there is a threshold impact.

5. Reference

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6. Appendix

Table 1. Experimental schedule	
Time	Assessment
Before breakfast	Pre-meal VAS ratings
Start eating breakfast （0min）	Starting timing
Immediately after breakfast （15min）	Record time taken to eat meal and complete post-breakfast pleasantness and appetite ratings
30, 45, 60, 75, 90, 120, 150, 180min after starting breakfast	VAS ratings and blood sugar self-testing.
Lunch and dinner at the day, Before resting at night	Record the food eaten in the whole day in nutritics and move all results to a sharing document (including VAS score, blood sugar testing and nutritics' result)

Table 1. Experimental schedule

AUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	50.94	50.1285	49.6245	49.8435	49.875	47.7525	95.445	96.471	94.3755	584.4555
meal B	60.8925	53.739	51.08325	50.06925	48.12525	44.42775	81.045	81.579	87.1395	558.1005
iAUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	1.245	2.0565	2.5605	2.3415	2.31	4.4325	8.925	7.899	9.9945	41.7645
meal B	4.9425	12.096	14.75175	15.76575	17.70975	21.40725	50.625	50.091	44.5305	231.9195

Table 2. AUC and iAUC of alertness (AUC=(V1+V2)(T2-T1)/2;iAUC=(AUCx-AUC$_{0min}$))*

AUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	51	21.62775	26.844	31.50375	37.7535	44.841	102.435	124.1895	149.625	589.8195
meal B	41.28	13.443	18.95775	26.20725	31.902	35.9295	83.88	99.855	116.223	467.6775
iAUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	30.12	59.49225	54.276	49.61625	43.3665	36.279	59.805	38.0505	14.376	385.3815
meal B	30.06	57.897	52.38225	45.13275	39.438	35.4105	58.8	42.825	26.457	388.4025

Table 3. AUC and iAUC of hunger (AUC=(V1+V2)(T2-T1)/2;iAUC=(AUCx-AUC$_{0min}$))*

AUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	72.5925	110.75025	106.59525	99.111	93.42225	86.48475	154.032	136.1565	112.875	972.0195
meal B	77.9775	113.739	106.3215	98.655	94.278	92.16675	175.833	154.5555	137.682	1051.20825
AUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	38.4075	76.56525	72.41025	64.926	59.23725	52.29975	85.662	67.7865	44.505	561.7995
meal B	37.4175	73.179	65.7615	58.095	53.718	51.60675	94.713	73.4355	56.562	564.48825

Table 4. AUC and iAUC of fullness (AUC=(V1+V2)(T2-T1)/2;iAUC=(AUCx-AUC$_{0min}$))*

AUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	48.95325	18.6225	23.5575	28.845	32.70675	39.48675	100.317	120.093	146.187	558.76875
meal B	40.41675	16.56675	23.19	25.4175	29.0025	33.585	76.476	92.778	116.2215	453.654
iAUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
meal A	31.70325	62.034	57.099	51.8115	47.94975	41.16975	60.996	41.22	18.375	412.35825
meal B	27.83325	51.68325	45.06	42.8325	39.2475	34.665	60.024	43.722	20.2785	365.346

Table 5. AUC and iAUC of Desire (AUC=(V1+V2)(T2-T1)/2;iAUC=(AUCx-AUC$_{0min}$))*

AUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
Meal A	94.44	116.8125	128.37	125.7825	115.755	106.065	193.5625	175.0675	163.13	1218.985
Meal B	90.4725	109.56	116.895	112.6425	106.3875	100.83	190.331111	175.556111	159.445	1162.11972
iAUC	0–15min	15–30min	30–45min	45–60min	60–75min	75–90min	90–120min	120–150min	150–180min	Total
Meal A	12.255	34.6275	46.185	43.5975	33.57	23.88	29.1925	10.6975	4.63	238.635
Meal B	10.8075	29.895	37.23	32.9775	26.7225	21.165	31.0011111	16.2261111	7.445	213.469722

Table 6. AUC and iAUC of glucose (AUC=(V1+V2)(T2-T1)/2;iAUC=(AUCx-AUC$_{0min}$))*

Hunger VAS Score Instruction: How hunger do you feel after breakfast? **0=Not hungry at all; 10=Very hungry**, Choose **a score closest to how you feel now**.									
0min	*15min*	*30min*	*45min*	*60min*	*75min*	*90min*	*120min*	*150min*	*180min*
0	0	0	0	0	0	0	0	0	0
2	2	2	2	2	2	2	2	2	2
4	4	4	4	4	4	4	4	4	4
6	6	6	6	6	6	6	6	6	6
8	8	8	8	8	8	8	8	8	8
10	10	10	10	10	10	10	10	10	10

Table 7. An example of advisable VAS score

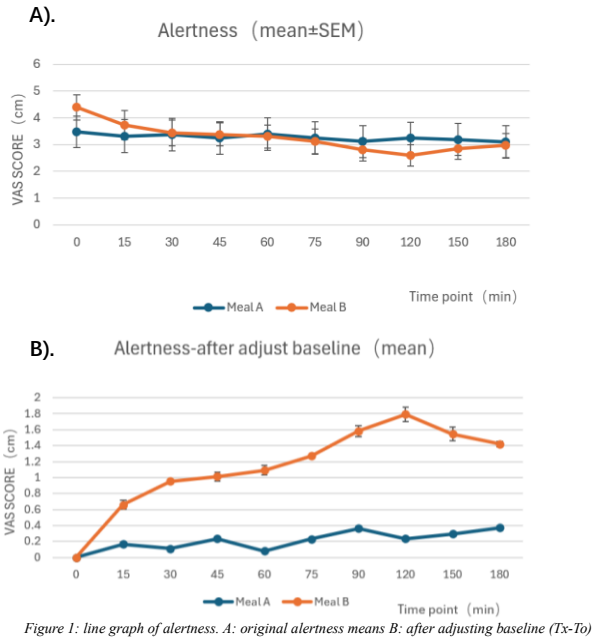

Figure 1: line graph of alertness. A: original alertness means B: after adjusting baseline (Tx-To)

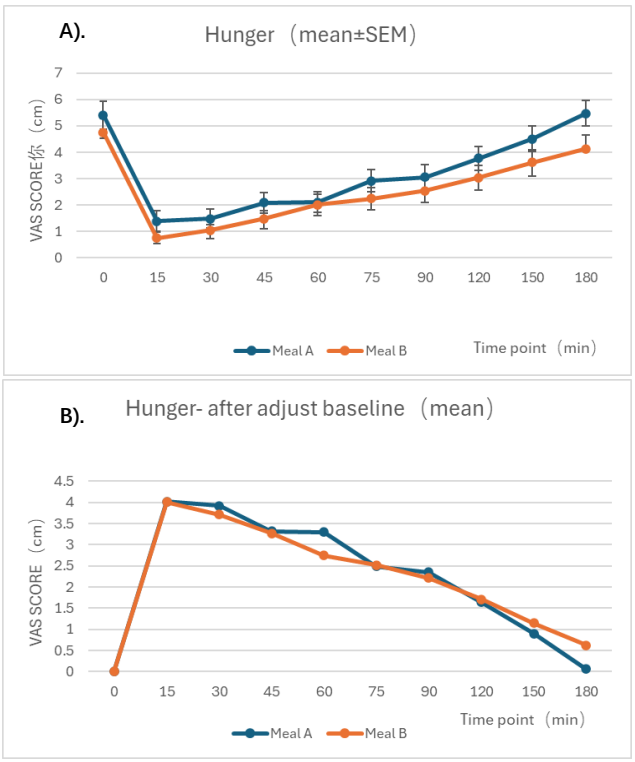

Figure 2: line graph of hunger. A: original huger means B: after adjusting baseline (Tx-To)

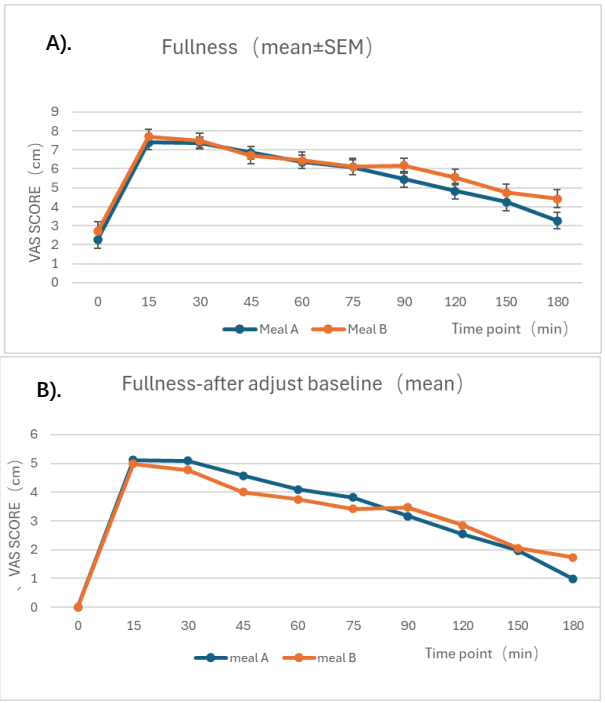

Figure 3: line graph of fullness. A: original fullness means B: after adjusting baseline (Tx-To)

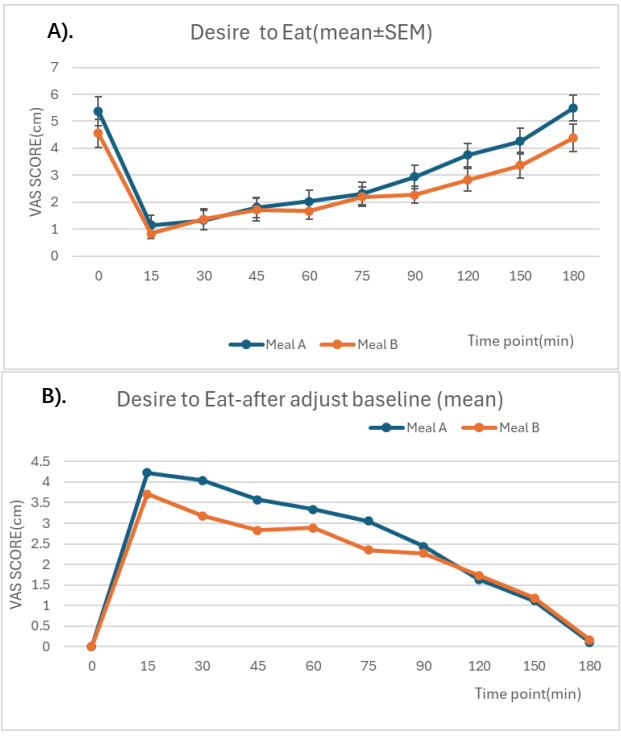

Figure 4: line graph of Desire. A: original Desire means. B: after adjusting baseline (Tx-To)

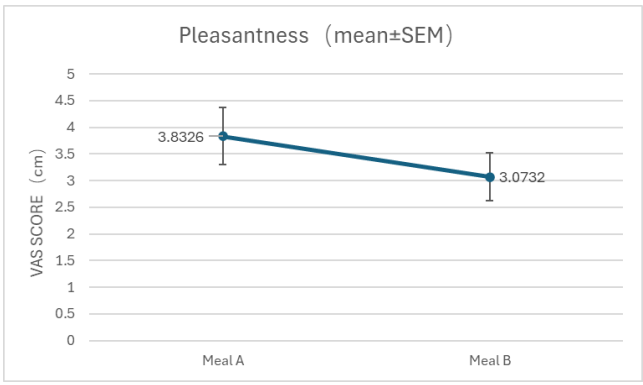

Figure 5: line graph of mean and SEM pleasantness after meals

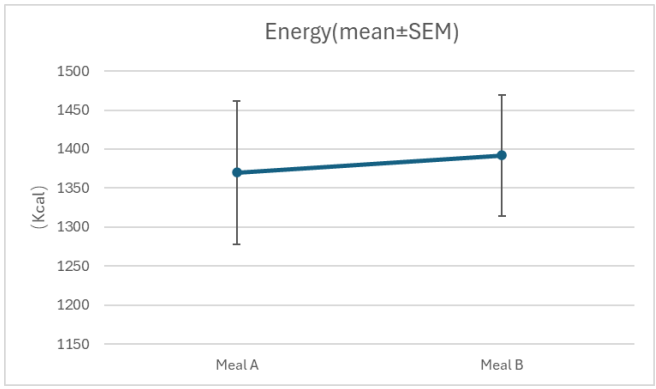

Figure 6: line graph of mean and SEM of calories after meals

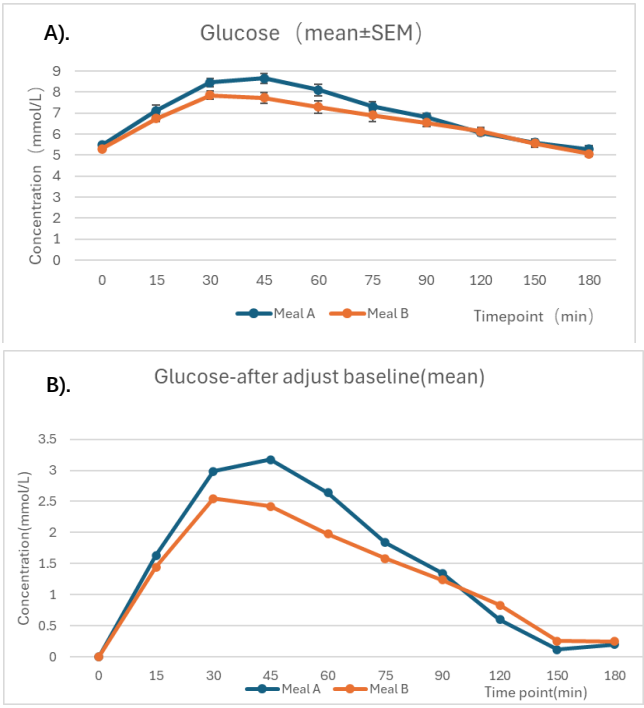

Figure 7: line graph of glucose. A: original glucose means B: after adjusting baseline (Tx-To)