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Examination of Gastrointestinal Symptoms, Stress, and Lifestyle Factors With the Consumption of Gluten and Inulin in Healthy Adults

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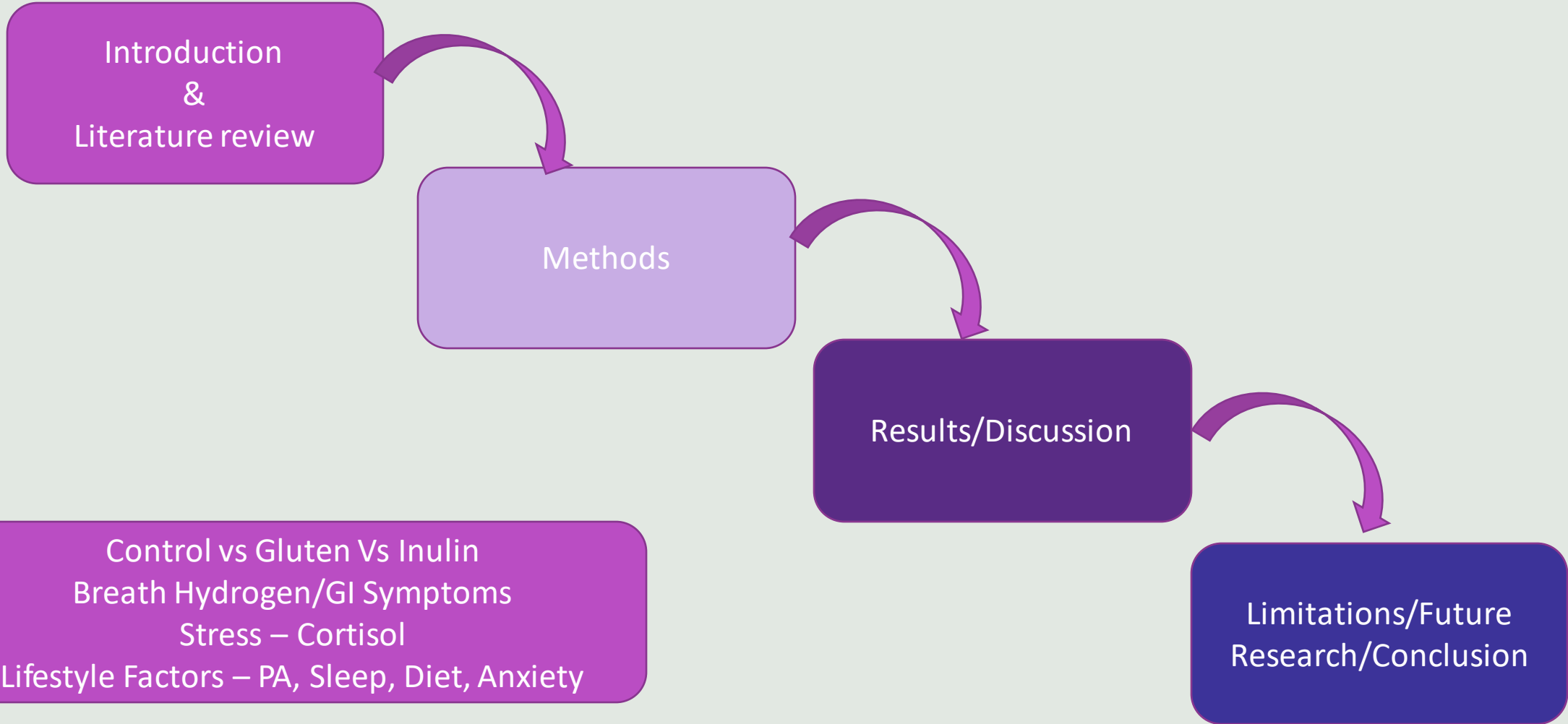
The background of the slide is a microscopic image of plant tissue, showing a cross-section of cells with distinct cell walls. The image is overlaid with a semi-transparent dark grey layer. Several decorative colored circles are scattered across the slide: a large purple circle in the top right, a medium purple circle in the middle left, a small blue circle in the bottom right, and a small orange circle in the top right corner.

Examination of Gastrointestinal Symptoms, Stress, and Lifestyle Factors With the Consumption of Gluten and Inulin in Healthy Adults

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Katie Brewer, Lydia Anderson, Elissa Rooney, and Dr. Alexa Evenson, RD, CFS

CSBSJU Scholarship and Creativity Day 2022

Overview of the Panel



The WHY?

AE

- GI symptoms are highly prevalent and affect approximately 40% of the population at any one point in time.
 - *2/3rds of these cases are chronic, with fluctuating symptoms*
- Many have no explanation for their symptoms
 - Pathophysiology is **COMPLEX**
- Frequently asked: Should I go gluten free?



Dietary Intake and GI symptoms

- GI symptoms related to high-fiber intake include:
 - Discomfort, bloating, and gas.
- Fruits and Veggies
 - 10% of American's are eating the recommended amount
 - Recommended amount:
 - Fruit: 2 cups per day
 - Vegetables: 2-3 cups per day
- Fruits/Veggies related to GI symptoms
 - IBS symptoms associated with higher intake of fruit and vegetables



FODMAPs and Gluten

FODMAPs (Inulin)

- Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
 - Inulin is a fructan (fructo-oligosaccharides)
 - Soluble non-viscous fiber
- Consuming a diet lower in FODMAPs may be beneficial in managing GI symptoms



Gluten

- Gluten is a protein
- Foods high in gluten: wheat, barley, rye
 - Gluten often found in high FODMAP foods
- Contradicting evidence on the effect on GI symptoms



Sensory Background

- Gluten
 - By itself, gluten has been described to have a "chalky" and "stringy" mouthfeel
 - Causes a thicker consistency
 - Decreases the sweetness of a product, whereas other studies have shown it not to have any affect
- Inulin
 - Forms gel-like texture; consistency and mouthfeel
 - Can work as a flavor-enhancer
 - Most studies have shown little impact on the sweetness
- Changing sensory factors can impact satiety



Satiety

INULIN

- Consuming inulin has been shown to:
 - DECREASE hunger
 - INCREASE fullness
- Soluble fiber
 - Delay gastric emptying rates
 - Fermentable fiber



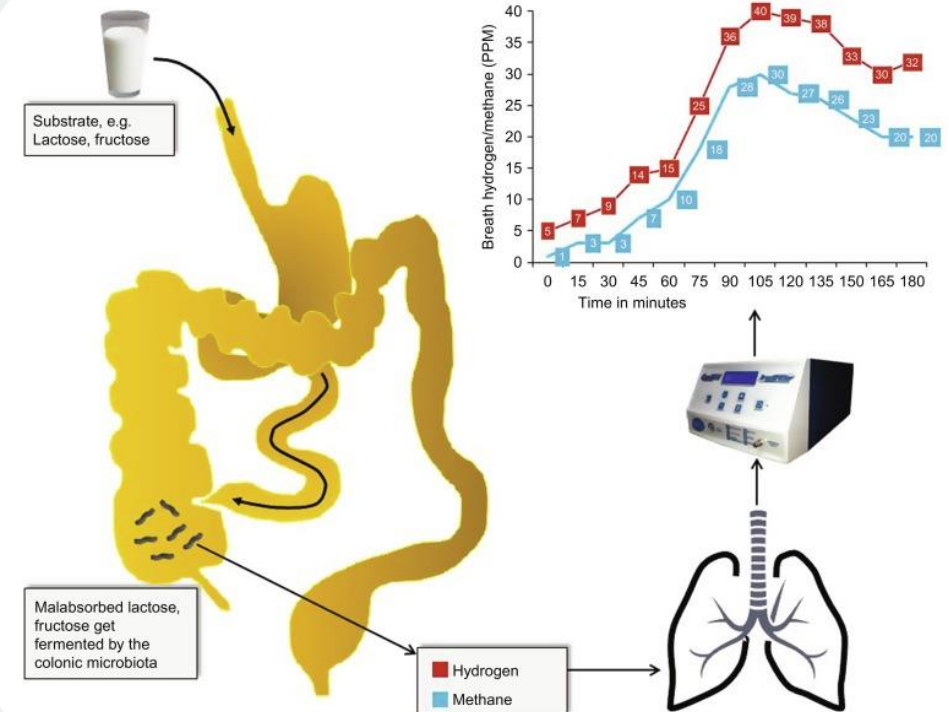
GLUTEN

- There is evidence on both sides of gluten and satiety as it has been shown to BOTH:
 - INCREASE and DECREASE fullness



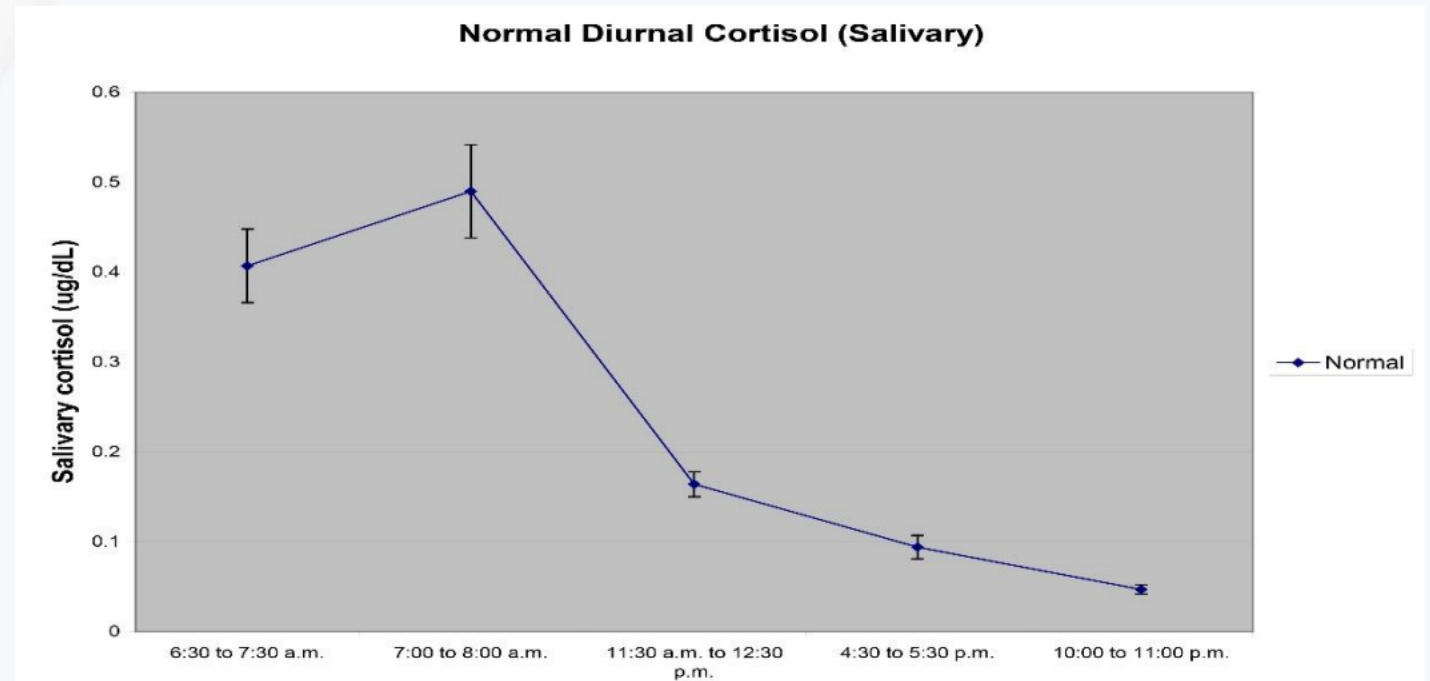
GI Symptoms + Breath Hydrogen

- H⁺ is produced when unabsorbed carbohydrates are fermented in the colon
- Analysis of hydrogen (H⁺) gas concentration in exhaled breath
- Increase of 20ppm = significant
- Individuals with IBS have increased breath H⁺ and GI symptoms following the consumption of FODMAPs



Cortisol/Stress + GI Symptoms

- No studies directly comparing H+ and cortisol concentration
- An increase in cortisol levels = increase in the physiological stress response/GI symptoms
- Moderate perceived stress due to occupation is associated with higher occurrences of GI symptoms



(Internal Salimetrics Data, n=26. Time of Cortisol peak will vary in individuals relative to their normal wake-up time.)

Anxiety and GI Symptoms

- Generalized Anxiety Disorder – 7 (GAD-7)
- Strong association between GI symptoms and anxiety.
 - When GI symptoms increase, anxiety increases too.
- Trait Anxiety:
 - Independently related to GI symptoms.
- Our Study Looked at:
 - State anxiety
 - Trait Anxiety



Physical Activity and GI Symptoms

- High-intensity activity decreased gastric blood flow to reduce diarrheal symptoms
- High-intensity activity reduces gastric emptying/motility
- High-intensity activity aggravates endothelial tight junctions causing systemic inflammation from leaking bacterial endotoxins
- Moderate-intensity activity significantly increases anti-inflammatory cytokines overall reducing abdominal pain
- Mod-Int PA – Butyrate (SCFA), promotes anti-inflammatory cytokines
- Yoga reduced GI symptoms equally to low-FODMAP diets and improved the quality of life



Sleep and GI Distress

- Fiber intake is related to more restorative deeper sleep
- There are a small number of studies that focus on diet and sleep latency, quality and quantity

• **Diet low in fiber** \longleftrightarrow **sleep**

- Sleep can also increase total energy consumption and is related to decreased consumption of high fiber foods
- Sleepiness and daytime fatigue are some of the top reported disturbances of IBS symptoms, and poor sleep has been shown to impact GI distress into the following day



Objectives/RQs

- 1. Was there a difference in Breath H+ and GI symptoms in healthy adults (non-IBS) after consumption of gluten and inulin?
- 2. Examine differences and relationships with cortisol and breath H+/GI symptoms
 - One of the first studies to look at this
- 3. Examine how Lifestyle Variables may play a role in breath H+/GI symptoms based on Gluten or Inulin Consumption
 - Diet, Physical Activity, Sleep, Anxiety

AE



Methods



Research Design

- Randomized, Blinded, Crossover Design
- Inclusion/Exclusion
 - 18 years of age
 - BMI 18.5-29.9 kg/m²
 - No identified GI disorders or chronic diseases
 - Non-Smokers
 - Not Pregnant
 - Not taken Antibiotics Recently
 - Did not take prescription medications that alter GI function



AE

Participants

- Mostly CSBSJU students/faculty
- n=24
- 12 females and 12 males
- Mean Age: 21.83 years
- Mean BMI: 23.11 kg/m²

Smoothie Recipe

Ingredients:

- 75 g frozen strawberries
- 38 g frozen raspberries
- 25 g frozen unripe banana
- 25 g soy protein powder
- 60 g Ocean Spray diet cranberry raspberry juice
- 75 g water
- 3 g liquid stevia
- 3 g liquid strawberry extract
- 5 g inulin or gluten powder (depending on treatment)

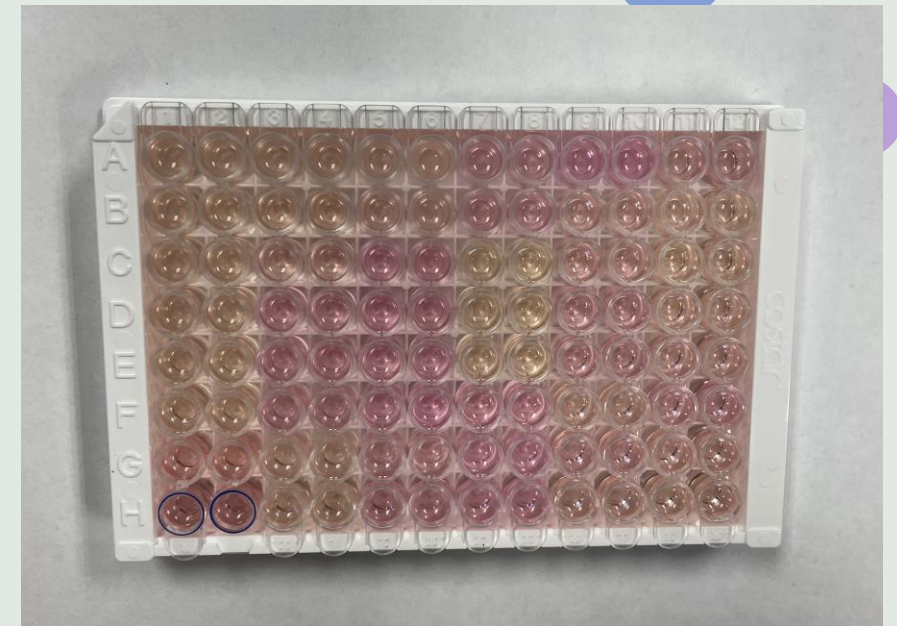


Table 1. Nutrient Profile between Smoothie Treatments

Smoothie Type	Total Kcal	Total Fat (g)	Carbohydrates (g)	Fiber (g)	Sugar (g)	Protein (g)
Control	172.04	1.72	23.94	4.92	14.74	20.16
Gluten	195.54	1.82	24.63	4.92	14.74	24.92
Inulin	172.04	1.72	28.94	9.92	14.74	20.16

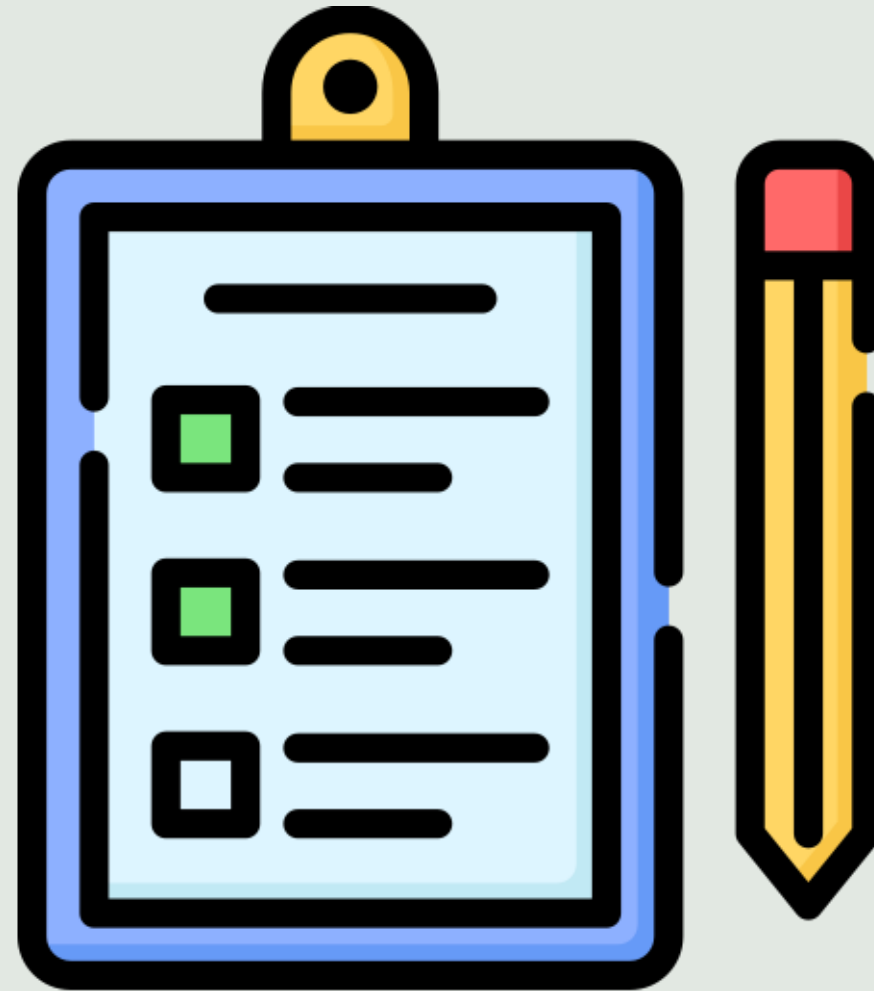
Cortisol Collection

- Saliva was Collected at 4 times points using a collection aid to fill a cryovial.
 - Samples were kept in a portable cooler and then stored in -80°C after session.
- Salimetrics Expanded Range High Sensitivity Salivary Cortisol Enzyme Immunoassay (ELISA).
- Samples were analyzed ELISA Kit with samples ran in duplicate.
- A special THANK YOU to Dr. McIntee in the Chemistry Department for his help in completing cortisol assays!



Questionnaires

- Demographics
- GI Symptoms Survey
- Dietary Intake
- VAS
- PSQI
- IPAQ-SF
- STICSA



VAS - Satiety

- Visual Analogue Scale
- Measures subjective appetite sensations
- Computerized scale- 100 mm lines
- 4 questions assessing:
 - Hunger
 - Satisfaction
 - Fullness
 - Volume



How hungry do you feel?

	I am not hungry at all 0	I have never been more hungry 100
How hungry do you feel?	<input type="range"/>	

How satisfied do you feel?

	I am completely empty 0	I cannot eat another bite 100
How satisfied do you feel?	<input type="range"/>	

Pittsburgh Sleep Quality Index

The PSQI measures 7 different categories of sleep

- Sleep quality
- Sleep latency
- Sleep duration
- Habitual sleep efficiency
- Sleep disturbances
- Use of sleeping medications
- Daytime dysfunction

A score of 5 or more is indicative of poor sleep quality

Name _____ Date _____

Sleep Quality Assessment (PSQI)

What is PSQI, and what is it measuring?

The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

During the past month,

- When have you usually gone to bed? _____
- How long (in minutes) has it taken you to fall asleep each night? _____
- What time have you usually gotten up in the morning? _____
- How many hours of actual sleep did you get at night? _____
 - How many hours were you in bed? _____

5. During the past month, how often have you had trouble sleeping because you	Not during the past month (0)	Less than once a week (1)	Once or twice a week (2)	Three or more times a week (3)
A. Cannot get to sleep within 30 minutes				
B. Wake up in the middle of the night or early morning				
C. Have to get up to use the bathroom				
D. Cannot breathe comfortably				
E. Cough or snore loudly				
F. Feel too cold				
G. Feel too hot				
H. Have bad dreams				
I. Have pain				
J. Other reason (s), please describe, including how often you have had trouble sleeping because of this reason (s):				
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				
9. During the past month, how would you rate your sleep quality overall?	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)

Scoring

Component 1	#9 Score	C1 _____
Component 2	#2 Score (<15min (0), 16-30min (1), 31-60 min (2), >60min (3)) + #5a Score (if sum is equal 0=0; 1-2=1; 3-4=2; 5-6=3)	C2 _____
Component 3	#4 Score (>7(0), 6-7 (1), 5-6 (2), <5 (3))	C3 _____
Component 4	(total # of hours asleep) / (total # of hours in bed) x 100 >85%=0, 75%-84%=1, 65%-74%=2, <65%=3	C4 _____
Component 5	# sum of scores 5b to 5j (0=0; 1-9=1; 10-18=2; 19-27=3)	C5 _____
Component 6	#6 Score	C6 _____
Component 7	#7 Score + #8 score (0=0; 1-2=1; 3-4=2; 5-6=3)	C7 _____

Add the seven component scores together _____ Global PSQI _____

A total score of "5" or greater is indicative of poor sleep quality.

If you scored "5" or more it is suggested that you discuss your sleep habits with a healthcare provider

IPAQ-SF Questionnaire

- International Physical Activity Questionnaire Short Form (IPAQ-SF)
- 7 item Questionnaire: vigorous, moderate, walking physical activity, and sedentary activity
 - Added yoga
 - 9 item total as it asks about frequency and duration

During the last 7 days, how many days did you participate in:

	0	1	2	3	4	5	6	7
VIGOROUS intensity physical activity that significantly increased your heart rate and breathing longer than 10 minutes? (e.g. heavy weight lifting, running, aerobics, or fast bicycling?)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
MODERATE intensity physical activity which somewhat increased your heart rate and breathing longer than 10 minutes (e.g. carrying light loads, bicycling at a regular pace, jogging).	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
WALKING longer than 10 minutes at a time.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
YOGA	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

How much time (in minutes) did you usually spend doing vigorous, moderate, walking, or yoga physical activities on one of those days, if applicable.

Vigorous intensity

Moderate intensity

Walking

Yoga

The last question is about the time you spent sitting on weekdays during the last 7 days. Include time spent at work, at home, while doing coursework and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

Thinking about the last week, how much time (in minutes) on an average weekday did you spend sitting?

Minutes a day

STICSA Questionnaire

- State-Trait Inventory of Cognitive & Somatic Anxiety
- 21 – item questionnaire that assessed State Anxiety
 - 11 items = Somatic
 - 10 items = Cognitive
- 21 – item questionnaire that assessed Trait anxiety
 - 11 items = Somatic
 - 10 items = Cognitive
- Measured on a scale of 1 – 4
 - 1 = not at all and 4 = very much so
- Items categorized into 6 sub-groups: State Somatic, State Cognitive, State Total, Trait Somatic, Trait Cognitive, and Trait Total.
- The sum of each sub-groups was calculated based on the responses received.

Table 2

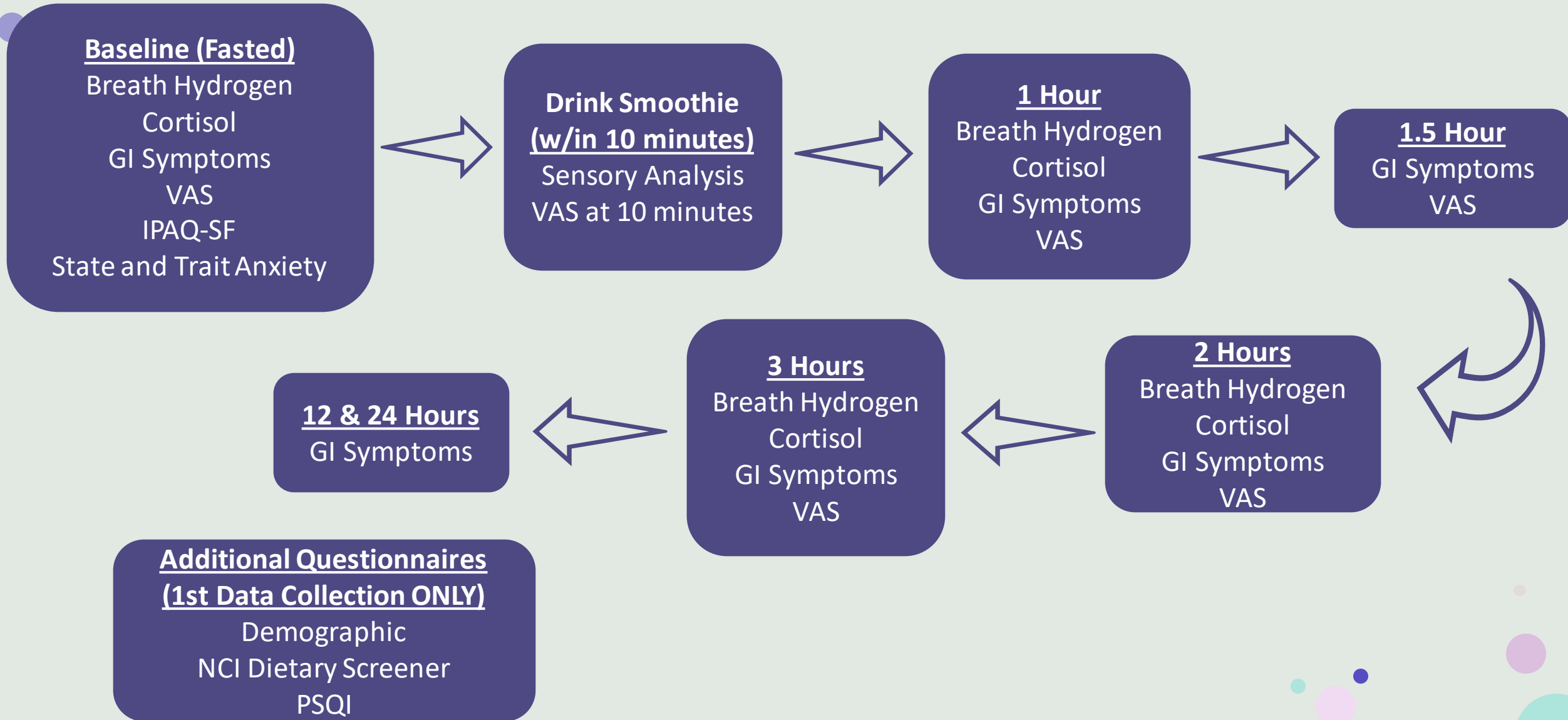
Standardized Factor Loadings for Four-Factor Model in a Patient Sample (N = 567)

Item	State–Cognitive	State–Somatic	Trait–Cognitive	Trait–Somatic
STICSA State				
1. Heart beats fast.		.67		
2. Muscles are tense.		.57		
3. Feel agonized over problems.	.65			
4. Think others won't approve.	.57			
5. Can't make up mind.	.51			
6. Feel dizzy.		.62		
7. Muscles feel weak.		.62		
8. Feel trembly and shaky.		.71		
9. Picture future misfortunes.	.74			
10. Can't get thoughts out of mind.	.76			
11. Trouble remembering things.	.50			
12. Face feels hot.		.56		
13. Think worst will happen.	.73			
14. Arms and legs feel stiff.		.58		
15. Throat feels dry.		.61		
16. Avoid uncomfortable thoughts.	.55			
17. Irrelevant thoughts intruding.	.76			
18. Breathing is fast and shallow.		.69		
19. Cannot control thoughts.	.75			
20. Butterflies in the stomach.		.65		
21. Palms feel clammy.		.62		
STICSA Trait				
1. Heart beats fast.				.64
2. Muscles are tense.				.63
3. Feel agonized over problems.			.70	
4. Think others won't approve.			.57	
5. Can't make up mind.			.50	
6. Feel dizzy.				.62
7. Muscles feel weak.				.66
8. Feel trembly and shaky.				.72
9. Picture future misfortunes.			.72	
10. Can't get thoughts out of mind.			.77	
11. Trouble remembering things.			.46	
12. Face feels hot.				.55
13. Think worst will happen.			.70	
14. Arms and legs feel stiff.				.63
15. Throat feels dry.				.60
16. Avoid uncomfortable thoughts.			.50	
17. Irrelevant thoughts intruding.			.78	
18. Breathing is fast and shallow.				.66
19. Cannot control thoughts.			.72	
20. Butterflies in the stomach.				.56
21. Palms feel clammy.				.57

Note. STICSA = State–Trait Inventory for Cognitive and Somatic Anxiety. All factor loadings were significant at $p < .05$. Items are derived from *State–Trait Inventory for Cognitive and Somatic Anxiety (STICSA)—State Version*, by Melissa J. Ree, Colin MacLeod, Davina French, and Vance Locke, 2000, Perth, Australia: The University of Western Australia. Copyright 2000 by Melissa J. Ree, Colin MacLeod, Davina French, and Vance Locke. Reprinted with permission.

METHODS

CZ



Statistical Analysis

AE

- SPSS IBS Version 28
- Descriptive statistics: Means \pm SD
- AUC
- Multiple Repeated Measures ANOVA with LSD post-hoc
- ANOVA
- Pearson r and Spearman rho Correlation Coefficients
- Significance was set to $p < 0.05$





Results and Discussion

Results – Sensory

- No significant differences between the 3 treatments for each of the categories – good thing!

Average Scoring for Each Sensory Attribute Between Treatments

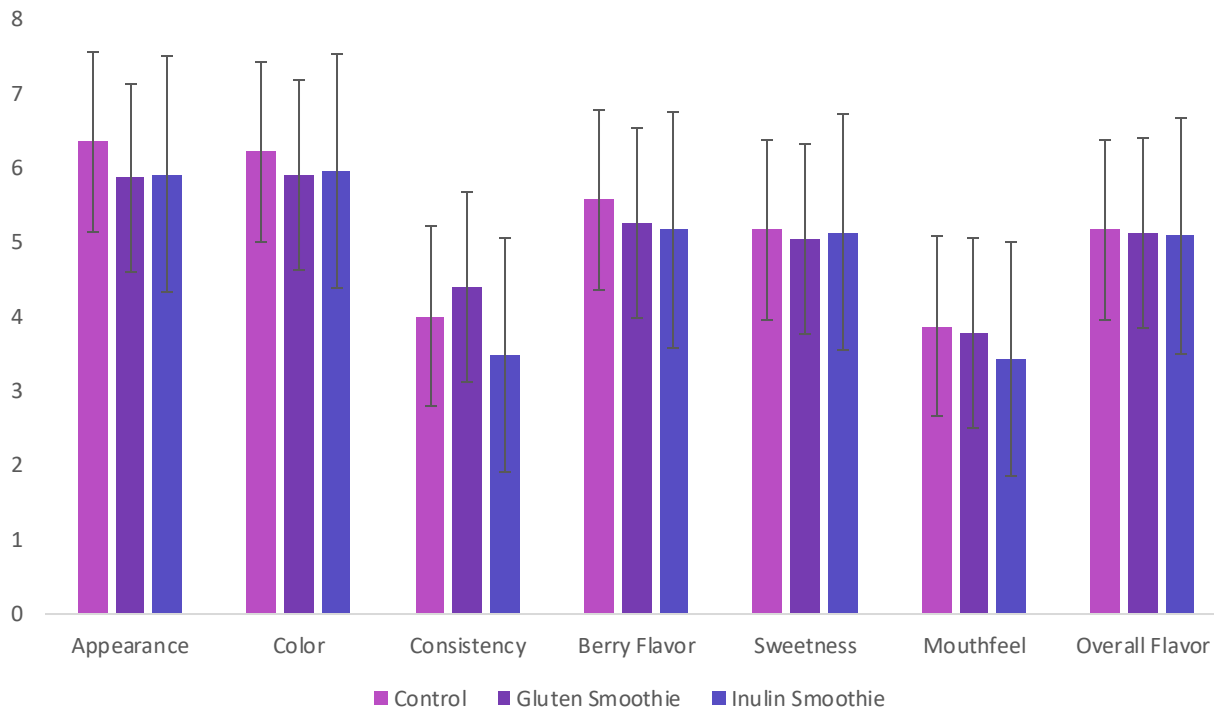


Figure 1. Average scoring for each category between treatments.

Table 1. Descriptive Statistics for Sensory Attributes Based on Treatment

	Control	Gluten	Inulin
Appearance	6.35 ± 0.33	5.87 ± 0.94	5.91 ± 1.63
Color	6.22 ± 1.36	5.91 ± 0.81	5.96 ± 1.59
Consistency	4.00 ± 2.09	4.39 ± 2.07	3.48 ± 2.17
Berry Flavor	5.57 ± 0.62	5.26 ± 1.29	5.17 ± 0.97
Sweetness	5.17 ± 1.15	5.04 ± 0.95	5.13 ± 1.39
Mouthfeel	3.87 ± 1.94	3.78 ± 1.91	3.43 ± 1.89
Overall Flavor	5.17 ± 0.97	5.13 ± 0.94	5.09 ± 1.45

Results – Satiety

- There was a significant difference in AUC for hunger between control and inulin treatments (MD=-6.18; p=0.024).
- There were significant differences in AUC for fullness between control vs inulin (MD=5.96; p=0.026) and gluten vs inulin treatments (MD=6.74; p=0.016).
- Expected results for inulin

Figure 2. Mean AUC Satiety Scores in Non IBS Participants

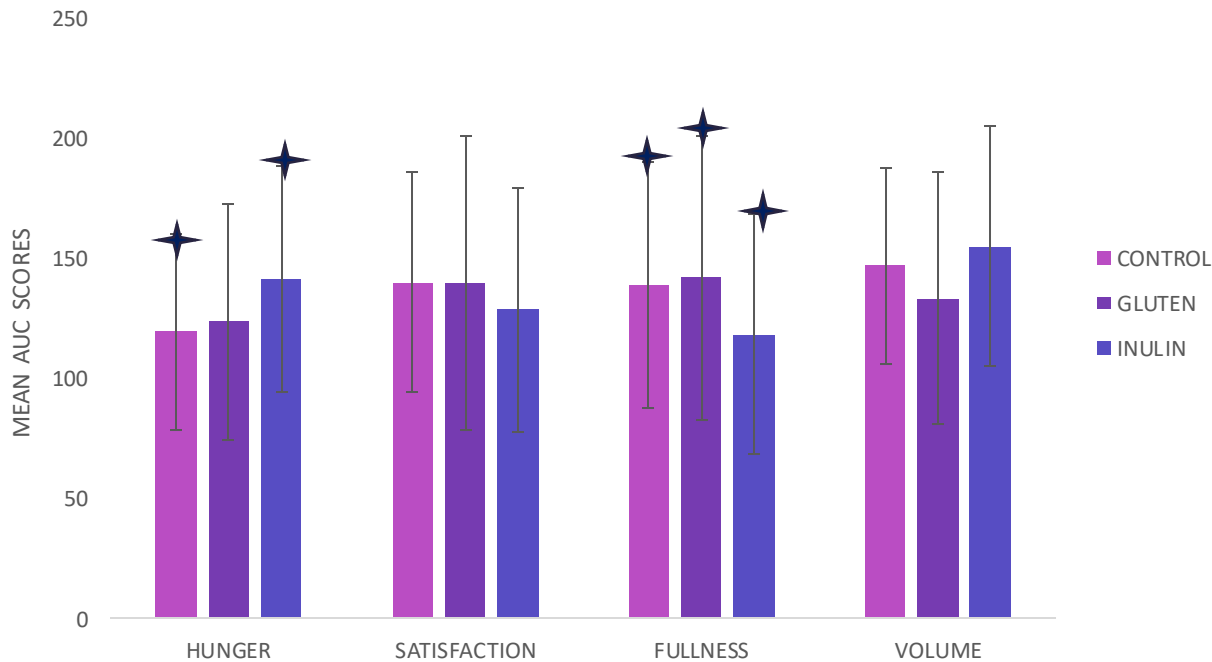


Table 2. Differences in Satiety AUC Between Treatments in Non-IBS Participants

(n=24)	CONTROL	GLUTEN	INULIN	F	p
HUNGER	119.90 ± 40.82	123.77 ± 49.14	141.52 ± 47.01	3.428	0.041*
SATISFACTION	140.18 ± 45.63	139.90 ± 60.94	128.70 ± 51.0	1.371	0.264
FULLNESS	139.30 ± 51.21	142.05 ± 58.95	118.45 ± 49.83	4.623	0.015*
VOLUME	147.30 ± 40.75	133.49 ± 52.38	155.27 ± 49.73	2.442	0.098

Results – Breath Hydrogen

- There were no differences in breath H⁺ between treatments
- No 20ppm response for any treatment
- Expected results for gluten
- Inulin in healthy participants and at the 5g level

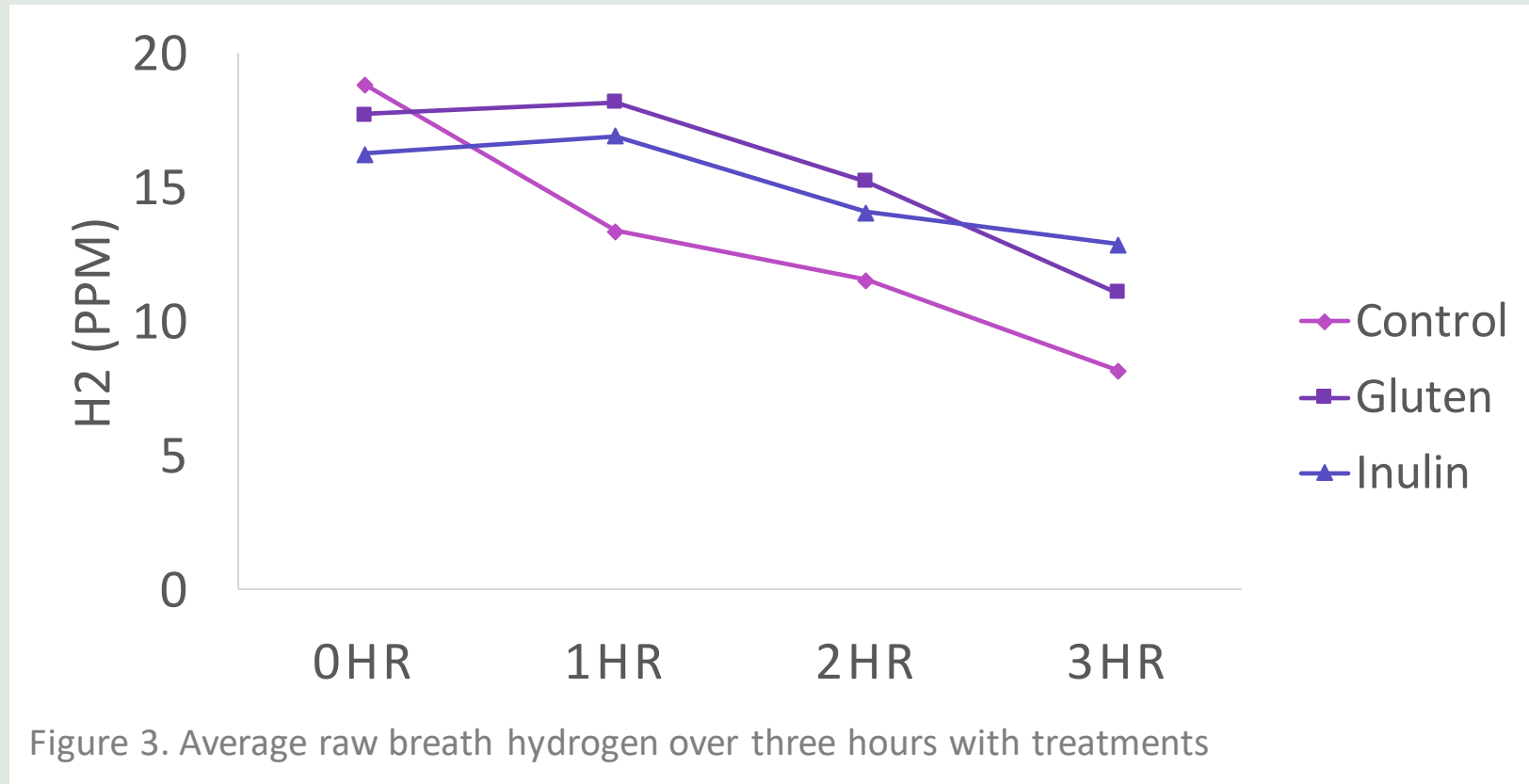


Table 3. Differences in Breath Hydrogen AUC Between Treatments

(n=24)	Control	Gluten	Inulin	F	<i>p</i>	η^2
Breath H ⁺ (ppm)	3.96 ± 19.45	12.31 ± 32.57	11.81 ± 26.67	1.273	0.29	0.052

Results - GI Symptoms

Table 4. Differences in GI symptoms Total AUC Between Treatments

(n=24)	Control	Gluten	Inulin	F	<i>p</i>	η^2
Bloating	8.18 ± 14.42	4.45 ± 8.90	9.27 ± 14.65	2.202	0.122	0.087
Nausea	1.73 ± 5.80	1.45 ± 6.41	2.19 ± 8.70	0.100	0.765	0.004
Gas	7.45 ± 12.28	3.75 ± 6.06	8.35 ± 13.92	1.948	0.154	0.078
Constipation	5.44 ± 12.90	2.14 ± 6.15	4.44 ± 9.68	0.820	0.391	0.034
Rumbling	7.68 ± 10.95	7.58 ± 12.56	8.29 ± 13.28	0.053	0.912	0.002
Cramping	1.41 ± 2.87	1.94 ± 6.40	3.15 ± 9.31	0.686	0.434	0.029
Diarrhea	3.32 ± 6.84	1.64 ± 3.82	1.76 ± 6.74	0.851	0.434	0.036
Total	35.91 ± 37.38	20.00 ± 30.31	37.45 ± 47.62	3.388	0.042	0.128

- GI symptoms differed between gluten and inulin treatments, with gluten producing fewer GI symptoms
- Unclear connection between gluten and GI symptoms compared to control

Results – Cortisol

- Within standardized ranges and similar to previous research
- Control treatment had lower cortisol concentrations at all time points
 - Impact of waking time?

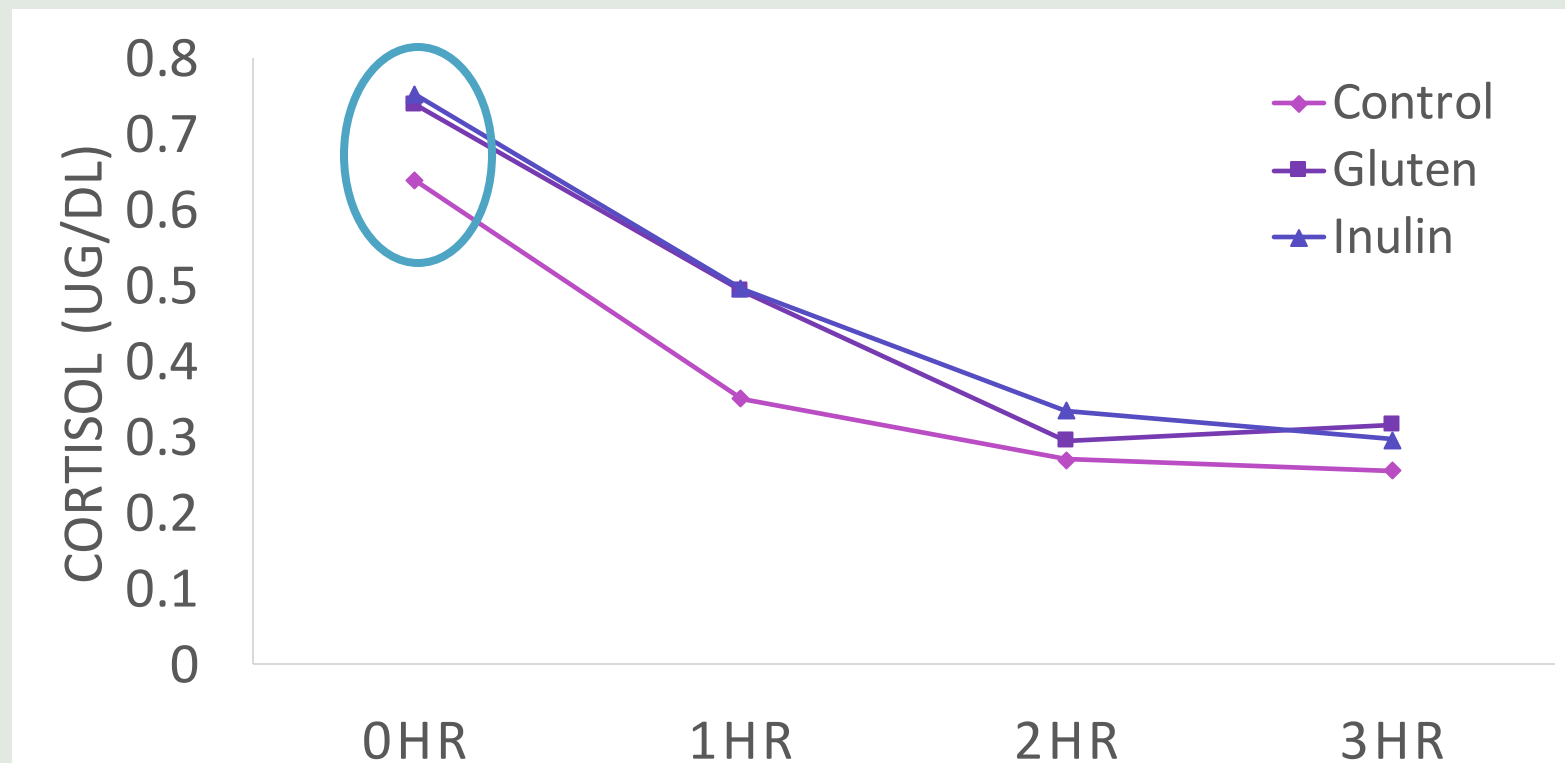


Figure 4. Average Cortisol Values Over Three Hours Based on Treatment

Table 5. Differences in Cortisol AUC Between Treatments

(n=24)	Control	Gluten	Inulin	F	p	η^2
Cortisol ($\mu\text{g}/\text{dL}$)	1.06 \pm 0.38	1.32 \pm 0.47	1.36 \pm 0.67	3.852	0.039	0.143

Results - State & Trait Anxiety

- There was no difference between the 3 treatments in any of the groups. ($p > 0.05$)
 - This is one of the first studies to examine state and trait anxiety. Our study showed low state and trait anxiety levels.
- Click to add text

(n=24)	Control	Gluten	Inulin	F	p
StSom	14.21 ± 3.62	14.29 ± 4.43	13.21 ± 2.62	0.717	0.492
StCog	15.75 ± 5.60	14.83 ± 5.78	14.50 ± 4.38	0.359	0.699
StTot	29.96 ± 7.89	29.13 ± 8.78	27.71 ± 5.95	0.534	0.589
TrSom	14.71 ± 3.87	14.42 ± 4.53	14.36 ± 4.96	0.039	0.961
TrCog	19.50 ± 6.94	17.13 ± 7.23	16.50 ± 6.24	1.295	0.281
TrTot	34.21 ± 9.76	31.54 ± 10.89	30.63 ± 10.11	0.789	0.458

Results - Sleep



Table 7. PSQI Score for Non-IBS Subjects

Variable	Non-IBS (n=24) M ± SD
Sleep PSQI	5.75 ± 2.95

- **PSQI Score > 5 = Poor Sleep**
- On average, our participants have poor sleep quality however we did not find any statistical significance in the data.
- Sleep is not statistically related to increased GI distress
- The population in this study had better-quality sleep-in comparison to other similar studies, however on average a "poor" quality of sleep was noted.

Results-Physical Activity Non-IBS

- There was no difference between the 3 treatments in any of the groups. ($p > 0.05$)
- Physical activity minutes and METs did not correlate breath hydrogen levels
- Physical activity levels were not comparable to other studies

Table 8. Differences in Physical Activity METS Between Treatments

(n=24)					
Treatment	Control	Gluten	Inulin	<i>F</i>	<i>p-value</i>
Vigorous Mets	54.76 ± 41.61	47.62 ± 39.07	48.10 ± 37.71	0.245	0.783
Moderate Mets	17.26 ± 11.22	23.17 ± 35.96	32.62 ± 67.83	0.718	0.492
Walking Mets	18.56 ± 19.17	36.67 ± 50.76	26.91 ± 28.98	1.564	0.217

Results – Dietary Intake

- There was no correlation of any dietary intake variable to breath hydrogen or GI symptoms.
- Recommended Intake:
 - Fruits: 2 cups per day
 - Vegetables: 2-3 cups per day
 - Whole grains: 3-6 oz
- Averages of other college students:
 - Fruit: 1.175 cups
 - Vegetable: 0.935 cups
 - Overall produce: 2.2 cups

Table 9. Descriptive Statistics of Dietary Intake of Non-IBS Participants

Variable	Non-IBS (n=24)
Fruit (cups)	1.22 ± 0.57
Vegetables (cups)	1.17 ± 0.66
F&V (cups)	2.87 ± 0.94
Dairy (cups)	2.52 ± 1.40
Added Sugar (teaspoons)	16.29 ± 4.33
Whole Grain (ounces)	0.98 ± 0.45
Fiber (grams)	18.48. ± 4.04

Limitations

AW

- Mostly college students
- Long duration of data collection (spanning D block, Summer, and Fall/early Spring Semesters)
- Participants were not asked about all medications that could have impacted gut motility
- People may have had functional GI issues and self-selected into the study
- We relied on many subjective measurements – Physical activity, sleep, diet, anxiety, satiety
- Didn't measure/control for what participants ate following their readings

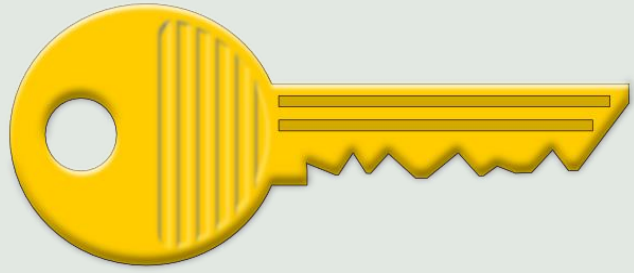


Future Research

AE

- Increase amounts of Gluten and Inulin to see if there are larger effects
- Try and collect data in a shorter period (over 3 months rather than a year)
- Could try Gluten and Inulin in different Food Matrices (solid)
- Control for food intake after consuming the smoothie – GI symptoms
- Standardize saliva collection to 30 minutes after waking for cortisol
- Try to physically measure some variables like PA and sleep
- Include more participants of different ages, races/ethnicities





Main Take Away Points/Summary

CZ

- One of the 1st studies to examine cortisol response and breath H⁺ levels.
- In this sample of participants, the restriction of gluten and inulin in the diet (at 5 grams) is not warranted, as neither treatment produced a significant increase in breath hydrogen or GI symptoms.
- Consumption of 5g of inulin resulted in a decrease in hunger and an increase in fullness.
- Lifestyle Variables
 - No correlations were found between diet, physical activity, sleep, anxiety, and breath hydrogen and GI symptoms for any treatment.
- More research is needed as the relationship between cortisol, breath hydrogen, and GI symptoms is still unclear.

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