Ultra-Processed Food, Glucose Homeostasis, And The Gut Microbiota

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***Abstract*—The gut microbiota maintains a significant role in the health of digestion, immune system regulation, protection of the gut barrier, and disease risk. While remaining incomplete, previous studies' characterization of the microorganisms of the gastrointestinal tract highlights the dominant influence of lifestyle, in addition to the genetics of a host, on microbial communities. Ultra-Processed Food (UPF) is a large component of present-day eating attitudes, yet it is associated with imbalance in the composition of the gut microbial community, referred to as dysbiosis, as well as disruption to glucose homeostasis. It is expected that baseline and postintervention chemical analyses of data collected reveal a UPF diet's harmful effects on gut microbiota composition and glucose homeostasis, thus increasing the risk of Type 2 Diabetes (T2D). Thus, this study aims to establish proof of concept of the individual effect of diet, specifically UPF intake, on the gut microbiota and glucose homeostasis. Following a two-week standardized diet of 59% UPF, in a two-months investigation, 50 mid-life adults aged 40-65 will be assigned to one of two groups incorporating dietary restrictions of 0% or 81% UPF intake. This understanding of UPF's relationship to gut well-being can serve a significant role in mitigating the severity, if not reducing the risk of occurrence, of various related pathological conditions as well as expand current approaches to prevention strategies and management of T2D and such diseases.**

Keywords—ultra processed foods, glucose homeostasis, gut microbiota

Introduction

Components of Ultra-Processed Food (UPF) are associated with alterations in the gut microbiota: microorganisms of the digestive tract which help regulate glucose levels and insulin sensitivity. This suggests its role in accelerating gut-associated chronic diseases of advanced age, specifically Type 2 Diabetes (T2D), which is a condition of insulin resistance. Therefore, understanding the impact of UPF on the maintaining of stable blood glucose levels, or glucose homeostasis, is critical to the advancement of preventative initiatives in healthcare, especially for those at greater risk for T2D and other nutrition-related diseases prevalent in middle age. This research proposal will replicate a study from Capra et al. (2024) of a controlled feeding trial guiding dietary behaviors of two mid-life adult groups, aged 40-65, towards UPF consumption. Through a 5 point OGTT, 3-Day Stool Collection, and a 7-Day CGM, baseline and postintervention glucose and insulin concentrations, glycemic control, SCFA production, and inflammatory biomarkers will be acquired and biochemically assessed, and body weight will be measured similarly. **This project aims to address the following question: What is the influence of Ultra-Processed Food consumption on mid-life adults' insulin sensitivity and gut microbial composition and function, and how does this relate to Type 2 Diabetes?** In other words, what is the role of a highly commercially processed or UPF-heavy diet in causing an improper response to insulin in mid-life adults and disrupting their gut microbiota's diversity and ability to manage glucose, and how does this connect to an increased risk of T2D, a chronic disease?

Methods

Participants: The participants are 50 mid-life adults (aged 40–65). Eligibility requirements are: stable weight, body mass index below 35, sedentary or recreationally active, nondiabetic, and no major gastrointestinal disorders or dietary restrictions

Data are collected at baseline and postintervention to diets. The following variables are collected: Body Weight (BW), 5-Point Oral Glucose Tolerance Test (OGTT) - to assess glucose and insulin concentration, 3-Day Stool Collection (SC) - to measure SCFA and fecal calprotectin, lactoferrin, and lipocalin-2 presence, and 7-Day Continuous Glucose Monitor (CGM) - to monitor 24 hour glycemic control.

Daily measures of BW are taken in the following system.Week 0: 5-Point OGTT, 3-Day SC, 7-Day CGM. Week 2: 5-Point OGTT, 3-Day SC, 7-Day CGM. Week 8: 5-Point OGTT, 3-Day SC, 7-Day CGM

Diet Assignment started with a Lead-in (2 weeks) with random assignment to either 59% energy from

UPF or No or High UPF (6 weeks). Group #1: 0% energy from UPF • Group #2: 81% energy from UPF.

Diet Delivery was Monday-Saturday visits with Breakfast only supervision. Daily meals and snacks prepared in portable cooler.

Providing a lead-in diet ensures standardization to eliminate potential effects of previous dietary factors on results. The Mifflin-St. Jeor equation in addition to self-reported physical activity will also be used to determine each participant's energy needs in order to maintain a eucaloric diet for all. Further contributing to the effectiveness of this study is measuring dietary compliance through recording uneaten foods, which attributes change to the controlled diet. The following shows sample meals used in the study.

Sample Meals			
	0% UPF	Standardized	81% UPF
Breakfast	remove orange juice and milk and replace with homemade pancakes		keep milk and berries, and add syrup
Lunch	remove ketchup		replace with more processed meat
Dinner	add more vegetables		replace with fried chicken
Snack	replace with peanut butter rice cakes, and add fruit		add a glass of milk, fruit, peanut butter, and gummies
Optional	replace all with their healthier alternative, and remove berries		add more processed deli meat and cheese

Daily sample meals for each controlled diet acquired from Capra et al. (2024). **Results & Discussion**

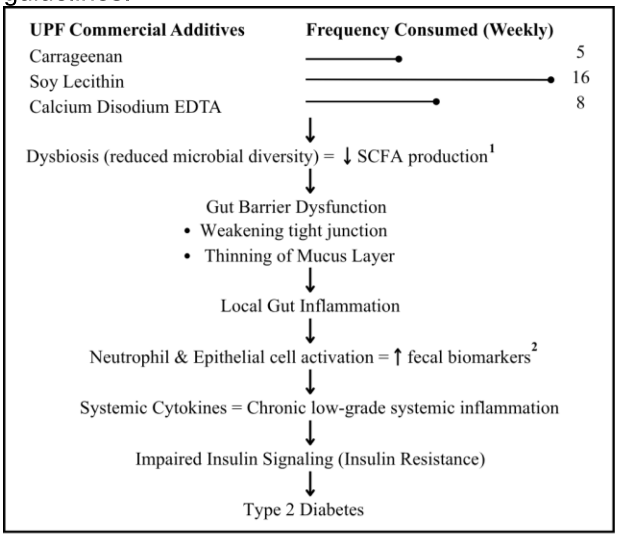
Diet delivery supervision will lead to increased adherence and Week 2 assessments will reveal a limited participant variability and better allocate postintervention results to UPF effects. The following are the outcomes.

Average 5-Point OGTT Glucose and Insulin Concentrations				
	Baselines & 0% UPF Postintervention		81% UPF Postintervention	
Time (min)	Glucose (mg/dL)	Insulin (μIU/mL)	Glucose (mg/dL)	Insulin (μIU/mL)
0	70-90	2-10	100-125	10-25
30	110-140	30-60	140-180	60-120
60	120-150	40-80	160-220	100-200
90	90-130	20-60	150-210	80-180
120	70-110	5-30	140-199	40-120

Data values collected from the 5-Point Oral Glucose Tolerance Test (OGTT) across weeks 0, 2, and 8 yielded averages that reflect an increased range in 81% UPF post-intervention glucose and insulin concentrations. Compared to baseline measurements, this would suggest impaired metabolic regulation with a type 2 diabetes trajectory.

Average 7-Day CGM Metrics		
Metric	Baseline & 0% UPF Postintervention	81% UPF Postintervention
Time in Range (70-140 mg/dL)	>90%	60-75%
Time Above Range (>180 mg/dL)	<5%	15-25%
Glucose Variability (CV%)	<20%	25-35%
Overnight Glucose Stability	Stable	Variable

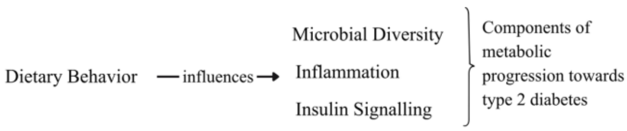
Data values collected from the 7-Day Continuous Glucose Monitor (CGM) identify abnormal average percentages that deviated from healthy metric guidelines.



A Model of the acceleration of UPF effects into Type 2 Diabetes. Postintervention 3-Day Stool Collection Measures (SC) for a 81% UPF diet group will reveal a decrease in (1) short chain fatty acids including acetate, propionate, and butyrate and an increase in (2) biomarkers such as calprotectin, lactoferrin, and lipocalin-2.

Future Implications

UPF should be seen and promoted as a dietary choice that can improve health. Results portray proof-of-concept for increased UPF uptake causing gut microbiota dysbiosis and impairment in glucose homeostasis. Thus the following should be acknowledged:



Making healthier food choices, such as increasing unprocessed foods which have no commercial additives, will reduce the risk of early diabetes development.

Above image is Capra et al. (2024) sample of an unprocessed meal. There is a Minimal Cost Difference such that the UPF diet: $9.72/day vs. Non-UPF diet: $10.23/day. Since 45% - 50% of Midlife Adults (40-65 Years Old) Are Prediabetic the following are important outcomes. A heightened awareness of the direct ties of dietary choices on diabetic predisposing factors can inform appropriate dietary guidelines and T2D prevention strategies for this age group. Reducing UPF components, such as emulsifiers and non-nutritive sweeteners which impact gut microbial composition and function, can slow down the acceleration of age-related decline of beta-cell function, insulin secretion, insulin sensitivity, and elevated levels of pro-inflammatory cytokines. Implementation of preventative strategies against type 2 diabetes can decrease risk of chronic diseases that dysbiosis of the gut microbiota plays a role in the pathophysiology of, including colitis, low-grade chronic inflammation, and metabolic and cardiovascular disease.

References

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