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A Hypothetical Communication Model between Brain and Liver Regarding Glucose Production (Both PPG and FPG) Using GH-Method: Math-Physical Medicine (No. 236)

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Keywords: Brain; Liver; Glucose; Postprandial plasma glucose; Fasting plasma glucose

Abbreviations: T2D: type 2 diabetes; PPG: postprandial plasma glucose; FPG: fasting plasma glucose

1. INTRODUCTION

This paper discusses the results of a comprehensive 7-month research project conducted by the author from September 2019 to March 2020. The study aimed to identify a potential internal communication model between the brain via nervous system with certain vital internal organs, namely the liver and stomach. It specifically investigated the production of both postprandial plasma glucose (PPG) and fasting plasma glucose (FPG). The findings of this research offer valuable insights into the intricate relationship between these organs and glucose regulation.

2. METHODS

The author conducted an extensive study using a continuous glucose monitor (CGM) device, collecting 51,511 glucose data points over 682 days, averaging 75.53 measurements daily from May 5, 2018, to March 14, 2020. He has monitored his postprandial glucose (PPG) levels by measuring every 15 minutes for three hours after first-biting of his meals and also measured PPG values two hours post-meal using finger-piercing method.

The focus of this study was to investigate the relationships between food nutritional contents, cooking methods, food material phases, and variations in glucose waveform patterns (PPG curves). Based on careful observations, the author developed a bold hypothese regarding communication model among the brain, stomach, liver, and pancreas through the nervous system, specifically concerning glucose production amount, timing, and pattern. He attempted to validate his hypotheses using big data analytics, mathematical operations, and artificial intelligence tools with extensive data on food and glucose.

The author conducted experiments involving 122 meals with various nutritional ingredients, food preparation techniques, and cooking methods, including soup-based (liquid) and pan-fried (solid) meals.

In the soup-based liquid food group, there were 55 meals, comprising 34 egg meals, 8 squash meals, 8 cabbage meals, and 5 mixed meals. "Broth" in these experiments referred to pasty or clear soup without solid food chunks.

In the pan-fried solid food group, there were 67 meals, including 34 egg meals, 8 squash meals, 8 cabbage meals, and 19 mixed meals. Vegetables were cut into specific sizes for pan-fried meals, while soup-based vegetables were diced into tiny pieces and boiled for a semi-clear or pasty-style broth. For single food material studies, liquid and solid food had identical nutritional ingredients and similar amounts of consumption. In multiple food material meals, there might be minor differences in their ingredient quantities.

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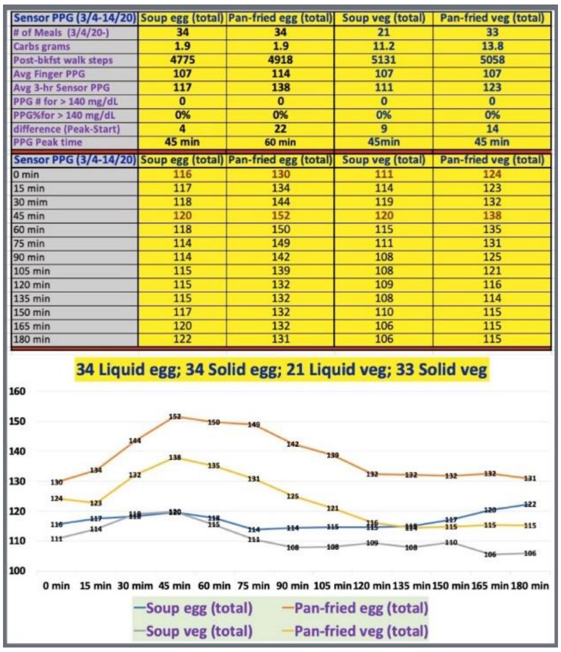
3. RESULTS

In Figure 1, detailed data on both soup-based liquid meals and pan-fried solid meals are presented, including carb/sugar amounts in grams, post-meal walking steps, and PPG values in mg/dL obtained through both finger-piercing and sensor-collected methods (180-minutes and 120-minutes).



Sensor PPG (3/4-14/20)	Soup egg (total)	Pan-fried egg (total)	Soup veg (total)	Pan-fried veg (total)
# of Meals (3/4/20-)	34	34	21	33
Carbs grams	1.9	1.9	11.2	13.8
Post-bkfst walk steps	4775	4918	5131	5058
Avg Finger PPG	107	114	107	107
Avg 3-hr Sensor PPG	117	138	111	123
PPG # for > 140 mg/dL	0	0	0	0
PPG%for > 140 mg/dL	0%	0%	0%	0%
difference (Peak-Start)	4	22	9	14
PPG Peak time	45 min	60 min	45min	45 min

Sensor PPG (3/4-14/20)	Soup egg (total)	Pan-fried egg (total)	Soup veg (total)	Pan-fried veg (total)
0 min	116	130	111	124
15 min	117	134	114	123
30 mim	118	144	119	132
45 min	120	152	120	138
60 min	118	150	115	135
75 min	114	149	111	131
90 min	114	142	108	125
105 min	115	139	108	121
120 min	115	132	109	116
135 min	115	132	108	114
150 min	117	132	110	115
165 min	120	132	106	115
180 min	122	131	106	115

Figure 1: Detailed data of liquid food vs. solid food & detailed data of egg food vs. vegetable food.

Summarized findings include:

(1) Carb/Sugar Amount: Eggs contained 1.9 grams of carbs/sugar, while vegetables ranged from 11.2 to 13.8 grams, aligning with established nutritional knowledge.

(2) Post-Meal Walking: All post-meal walking exceeded 4,000 steps (ranging from 4,800 to 5,100), indicating that exercise's influence on PPG can be disregarded. Notably, the author's body weight remained within the 170-174 lbs. (77-79 kg, BMI 25) range during this experimental period.

(3) Finger-Piercing PPG: Finger-piercing PPG values ranged from 107 mg/dL to 114 mg/dL, suggesting that traditional 2-hour post-meal finger-piercing tests do not yield meaningful insights. This neuroscience research necessitates complete glucose waveform data (either 2-hour or 3-hour periods) for meaningful interpretations and useful results.

In Figure 2, a summarized comparison between solid and liquid meals is presented. Pan-fried solid food displayed significantly higher peak PPG and averaged PPG values compared to soup-based liquid food. It's important to consider variations in starting PPG values (at 0 minutes) due to pre-meal factors. Therefore, comparing the PPG difference between peak PPG and starting PPG is more logical. The PPG difference for solid food was 18 mg/dL with an average sensor PPG of 131 mg/dL, while for liquid food, it was 6 mg/dL with an average sensor PPG of 115 mg/dL. Solid food exhibited a PPG difference three times higher and approximately 14% higher average sensor PPG than liquid food.

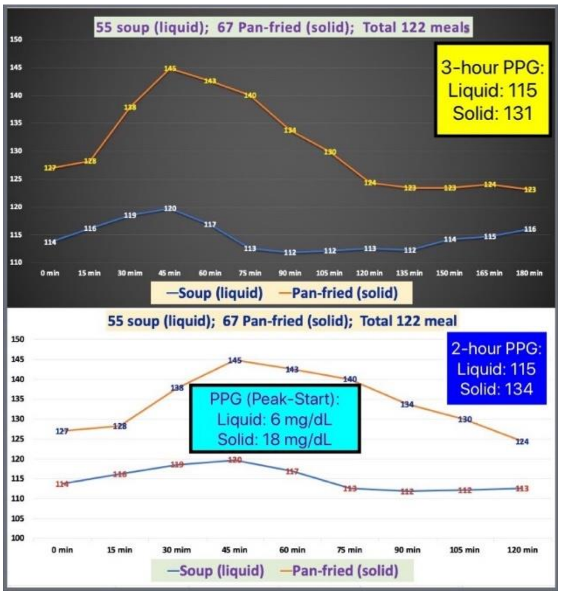


Figure 2: PPG waves comparison between liquid food & solid food (both 3 hours & 2 hours).

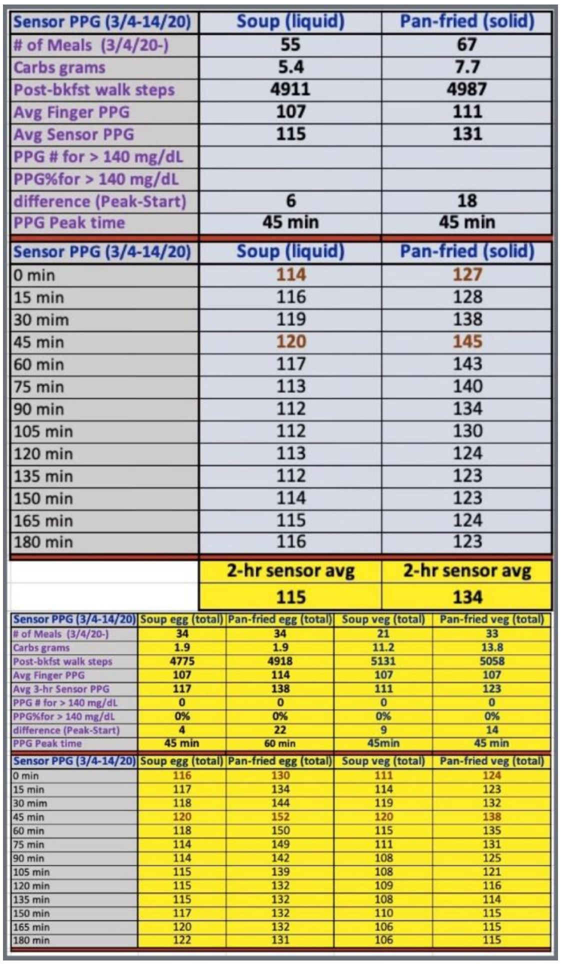
Notably, the average sensor PPG for liquid food over a three-hour period (115 mg/dL) closely resembled the finger-piercing PPG measured at two hours after the first bite of food (107 mg/dL for liquid food and 111 mg/dL for solid food). These findings suggest that liquid food is a safe option for diabetes patients in terms of glucose control.

Figure 2's sensor PPG waveforms (both 3-hour and 2-hour diagrams) provide a clear conclusion for this neuroscience study. Soup-based liquid food consistently yielded lower glucose values than pan-fried solid food. Based on the 122 food experiments, consuming solid food resulted in a range from pre-diabetes to diabetes (averaged PPG 131-134 mg/dL and peak PPG >140 mg/dL), while consuming liquid food-maintained glucose levels within the normal and healthy range, i.e., non-diabetic, as all glucose data remained under 120 mg/dL.

Figure 3 provides a micro-view of detailed data and waveform comparisons between eggs and vegetables (mixed vegetables and meat broth), encompassing both liquid and solid meals. Key observations in this figure include:

1. Generally, the wave heights of vegetables are lower than those of eggs, whether in liquid or solid form.

2. For the wave segment between 120-minutes and 180-minutes, the solid vegetable wave segment closely resembles the egg soup wave segment.



Sensor PPG (3/4-14/20)	Soup (liquid)	Pan-fried (solid)
# of Meals (3/4/20-)	55	67
Carbs grams	5.4	7.7
Post-bkfst walk steps	4911	4987
Avg Finger PPG	107	111
Avg Sensor PPG	115	131
PPG # for > 140 mg/dL		
PPG%for > 140 mg/dL		
difference (Peak-Start)	6	18
PPG Peak time	45 min	45 min

Sensor PPG (3/4-14/20)	Soup (liquid)	Pan-fried (solid)
0 min	114	127
15 min	116	128
30 mim	119	138
45 min	120	145
60 min	117	143
75 min	113	140
90 min	112	134
105 min	112	130
120 min	113	124
135 min	112	123
150 min	114	123
165 min	115	124
180 min	116	123
	2-hr sensor avg	2-hr sensor avg
	115	134

Sensor PPG (3/4-14/20)	Soup egg (total)	Pan-fried egg (total)	Soup veg (total)	Pan-fried veg (total)
# of Meals (3/4/20-)	34	34	21	33
Carbs grams	1.9	1.9	11.2	13.8
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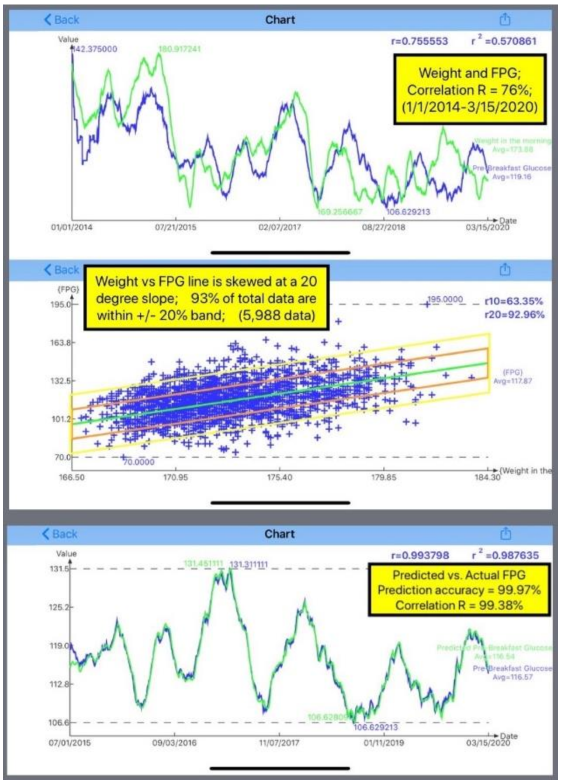
120 min	115	132	109	116
135 min	115	132	108	114
150 min	117	132	110	115
165 min	120	132	106	115
180 min	122	131	106	115

Figure 3: Egg vs. vegetable meals (liquid and solid).

Despite most liquid and solid foods having nearly identical nutritional ingredients, they produce significantly different glucose outcomes. The author grapples with explaining this observed phenomenon, drawing from their accumulated knowledge in traditional food nutrition, internal medicine, and diabetes pathology. This apparent contradiction challenges understanding the intricacies of the relationship between food composition and glucose response.

Figure 4 draws on data collected over the past 6+ years (from January 1, 2014, to March 15, 2020) to reaffirm a discovery made in 2017, highlighting a strong correlation and close association between fasting plasma glucose (FPG) and body weight. The time-series analysis, with time on the x-axis and FPG and weight on the y-axis, reveals a high correlation coefficient of 76%. Furthermore, a spatial analysis, with weight on the x-axis and FPG on the y-axis, irrespective of time, depicts a clustered, skewed cucumber-shaped data cloud at an inclination of approximately 20 degrees. This inclination implies that as weight increases, FPG also increases, and vice versa.



Weight and FPG; Correlation R = 76%; (1/1/2014-3/15/2020)

Weight vs FPG line is skewed at a 20 degree slope; 93% of total data are within +/- 20% band; (5,988 data)

Predicted vs. Actual FPG
Prediction accuracy = 99.97%
Correlation R = 99.38%

Figure 4: Body weight vs. FPG (time-series & spatial analysis).

Based on this finding, the author has developed an FPG prediction model with an impressive 99.97% prediction accuracy and a very high 99.38% correlation coefficient between actual FPG and predicted FPG, as demonstrated in Figure 4. This data reinforces the strong relationship between body weight and fasting plasma glucose, offering valuable insights for predicting and managing FPG levels.

4. HYPOTHESIS

Over the past nine years, the author has accumulated knowledge from both internal medicine and food nutrition, understanding that different glucose levels are influenced by the varying amounts of carbs and sugar in food intake. However, a reasonable explanation is needed for the observed differences between higher PPG values from solid food and lower PPG values from liquid food.

To shed light on this, the author draws from basic physics concepts he learned in junior high school, which recognize three fundamental phases of matter: solid, liquid, and gas (vapor or steam). In the context of this meal study, he deals with two phases: the liquid phase, represented by egg drop soup and mixed vegetable soup, and the solid phase, illustrated by pan-fried eggs or mixed vegetables.

The author has also gathered key insights from his nine years of medical research. First, he has discovered that approximately 70% of energy intake is consumed by our brain and nervous system, challenging the common belief that the heart is the primary energy consumer. Second, the brain stands out as the only internal organ equipped with functions like sense cognition, situational judgment, information processing, decision-making, and the issuance of commands, akin to the central processing unit (CPU) of a computer system. Third, all our internal organs operate synergistically, intricately interconnected, and under the exclusive commands of our brain.

Additionally, the author conducted an experiment involving a specialized IC chip placed on the skin of a human leg, revealing the electronic flow and signal transmission through the nervous system between the brain and leg muscles. This experiment underscored the remarkable capabilities of our brain and nervous system.

Further evidence of the brain's influence on our glucose levels is depicted in Figure 4. In the early morning, when food and exercise have no impact, our brain is aware of our morning body weight and communicates this information to the liver via the nervous system, directing the appropriate production of fasting plasma glucose (FPG) after wakening up.

In relation to postprandial glucose (PPG), the author recognized that glucose is produced by the liver from glycogen, rather than being "directly transformed or converted" from food, as sometimes casually stated by nutritionists and physicians. Glycogen is a substance stored in bodily tissues for carbohydrate storage. Initially, the liver breaks down carbohydrates from our diet and synthesizes glucose. When the body doesn't require immediate energy from glucose, it is stored in the liver and muscles as glycogen.

The author's perspective on this subject draws from his academic background and professional training in mathematics, physics, engineering, and computer science. He views the liver as an operational machine or system which has a "stimulator" (food as input), a "command center" (the brain as the central processing unit), and a "feedback system" (glucose as output). Thus, glucose is not directly "converted" from food; rather, it is "produced, stored, and released" by the liver, even though the liver relies on food as an "energy source" for its functions and as the "raw material" input for glucose production.

Building upon the knowledge discussed earlier and his unique engineering interpretation, the author formulated a hypothesis about glucose production by the liver. This hypothesis centers on the idea that the differences in postprandial glucose (PPG) production, both in quantity and timing, are determined by the specific physical phase of the meal, categorized as either "liquid" or "solid." The final physical phase of a meal directly influences a patient's PPG characteristics, including the height of the glucose peak, the extent of glucose fluctuations, and the shape of the final glucose curve.

Upon the introduction of a particular type of food into the gastrointestinal system, the stomach rapidly sends signals via the central nervous system to inform the brain about the food's arrival and its physical phase, either liquid phase or solid phase. Subsequently, the brain processes these input signals, along with other related biochemical information, makes decisions and issues operational instructions to the liver concerning the quantity of glucose to be produced and the timeframe within which it should be produced. This information processing and order-issuing process is highly "nonlinear" and "dynamic" due to the complex and ever-changing biochemical conditions of food ingredients and biochemical reactions within the human body. This complexity is why the timing of reaching glucose peaks varies depending on the physical phase of the food, such as liquid vs. solid and even within categories like eggs vs. vegetables, and conventional nutrition and diabetes pathology cannot convincingly and clearly explain these observations.

Timing plays a significant role in this process. The author observed from over 5,779 food and glucose data points collected over the past 5+ years that the body typically takes about 10-15 minutes to reach its glucose peak after consuming high-sugar content liquid food, about 30-60 minutes for liquid food, and about 45-75 minutes for solid food. The 15-30-minute delay in reaching the glucose peak for solid food may be attributed to the digestive process.

Simultaneously, the brain communicates with the pancreas, instructing it on how much insulin to produce to counterbalance the excessive glucose generated by the liver. However, for diabetes patients with severely damaged pancreatic beta cells, their insulin production capabilities are impaired. As a result, the most effective approach for these patients is to find practical ways to reduce the production of glucose, for example, insulin shots.

This hypothesis explains the author's math-physical perspective on how the brain communicates with the stomach and liver via the central nervous system regarding the quantity, timing, and waveform pattern of PPG during either a 180-minute or 120-minute period after the first bite of a meal. Lower PPG values and flatter curve patterns from liquid-based meals are associated with the physical phase of the food, akin to drinking tea or water, which does not trigger the brain to increase glucose production.

It’s important to note that type 2 diabetes patients should consistently avoid foods high in carbohydrates, such as starchy grains, flours, corn, and potatoes, as well as foods with high sugar content, like sweetened cakes, ice creams, or sugary beverages.

Hence, this discovery offers an opportunity to "trick" the brain into producing a "lower amount of glucose" for diabetes patients when they consume a soup-based meal, even if the nutritional ingredients are the same as in solid food. This emphasizes the influential role of the brain in managing glucose levels.

Regarding the author's earlier discovery from March 2017, which linked fasting plasma glucose (FPG) to body weight (depicted in Figure 4), it's clear that the brain has a profound influence as it knows the morning body weight and dictates to the liver the appropriate amount of FPG to be produced. Once again, it highlights the power of the brain in regulating glucose levels.

5. CONCLUSION

The author has applied the GH-Method: math-physical medicine (MPM approach) to investigate a Type 2 Diabetes (T2D) patient's glucose production process through a scientific magnifying lens, with a focus on the capabilities of the brain and nervous system. This approach has led to the formulation of a hypothesis suggesting that the brain plays a crucial role in regulating glucose production. If this interpretation holds true, it opens the possibility of "tricking" the brain into reducing post-meal glucose production without compromising essential food ingredients and nutritional balance. Consequently, T2D patients can potentially modify their cooking methods to lower both their peak postprandial glucose (PPG) values and their average PPG levels.

Furthermore, recognizing the strong correlation and direct connection between fasting plasma glucose (FPG) and body weight, it becomes feasible to effectively control FPG levels. As a result, a T2D patient's total glucose levels, encompassing FPG and post-meal PPG values, can be managed more efficiently.

The author aims to share his research findings with fellow medical research scientists, seeking their insights to provide improved interpretations, proper explanations, or additional justifications for the broader medical and healthcare community. This collaborative effort could involve using both the GH-Method MPM approach and traditional biomedical research methodologies, such as biochemical medicine (BCM), to gain a more comprehensive understanding of diabetes management and potentially develop some innovative solutions for T2D patients.