ISSN: 2639-0108

Research Article

Advances in Theoretical & Computational Physics

Relationships between Parkinson's disease Risks and Four Biomarkers of Type 2 Diabetes Disease, Insulin Resistance via FPG, Glycemic Control via HbA1c and eAG, Hyperglycemia Intensity using viscoplastic Energy Model of GHMethod: Math-Physical Medicine (No. 960, VMT #359, 11/21/2023)

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Submitted: 2023, Dec 04; **Accepted:** 2024, Jan 08; **Published:** 2024, Jan 24

Citation: Hsu, G. C. (2024). Relationships between Parkinson's disease Risks and Four Biomarkers of Type 2 Diabetes Disease, Insulin Resistance via FPG, Glycemic Control via HbA1c and eAG, Hyperglycemia Intensity using viscoplastic Energy Model of GHMethod: Math-Physical Medicine (No. 960, VMT #359, 11/21/2023). *Adv Theo Comp Phy, 7*(1), 01-07.

Abstract

The interplay of diet quality and portion control significantly impacts body weight, a pivotal factor in type 2 diabetes (T2D) progression. T2D is marked by four key biomarkers, including insulin resistance (via morning fasting glucose - FPG), glycemic control (via daily averaged glucose - eAG), quarterly glycemic control (via HbA1c levels), and hyperglycemia situation control (via hyperglycemia intensity - HyGI). Here, ***his HyGI is calculated as the product of averaged glucose above 180 mg/dL multiplied by the frequency of glucose above 180 mg/ dL.*** *This study delves into the author's Parkinson's disease (PD) risks linked to the aforementioned four T2D biomarkers, drawing from personal data collected over past six years, from 5/1/2018 to 11/20/2023. Traditional statistical analysis reveals strong correlations (ranging from 65% to 91%) between the author's PD risk and his four influential T2D biomarkers. Furthermore, the author employs the space-domain viscoplastic energy (SD-VMT) method from advanced engineering to uncover hidden relationships and dynamics (i.e. energies) between these T2D biomarkers and the author's annual PD risk output.*

In summary, *traditional statistical correlations unveiled significant associations between the author's PD risks and his four T2D biomarkers:*

- ***PD vs. HbA1c: 89%***
- ***PD vs. FPG: 86%***
- ***PD vs. eAG: 91%***
- ***PD vs. HyGI: 65%***

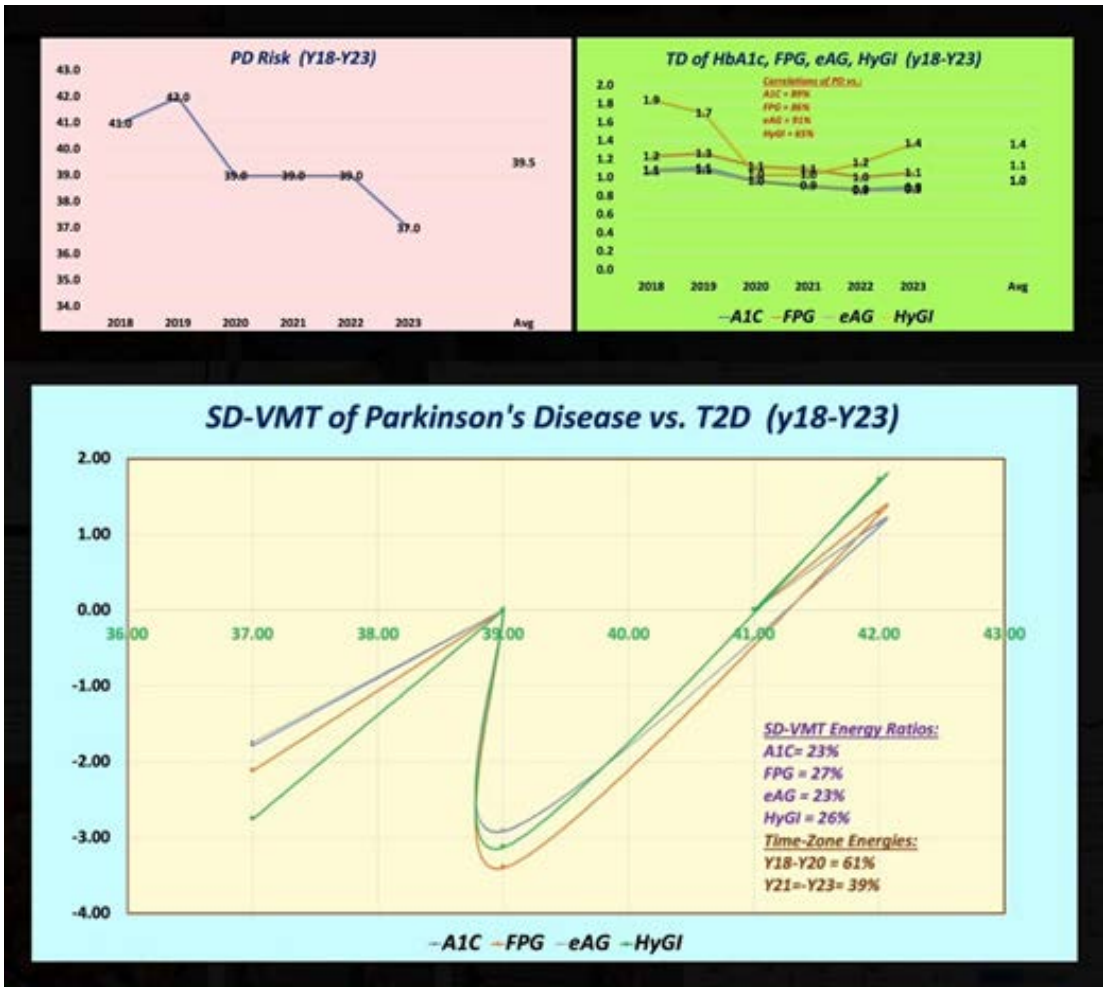
These differ markedly from the low positive correlations (14% to 41%) between his cancer risks and the same T2D biomarkers, reflecting distinct characteristics in the risk waveforms of these two diseases.

Using SD-VMT energy results from advanced engineering, four energy contribution margins on PD risks from four T2D biomarkers were identified:

- ***Energy from HbA1c: 23%***
- ***Energy from FPG: 27%***
- ***Energy from eAG: 23% - Energy from HyGI: 26%***

Key message

The author's T2D conditions are indeed linked to his risks of developing into Parkinson's diseases. Insulin resistance, as indicated by FPG, contributes the most energy to PD risks (27%), followed by hyperglycemia intensity (26%), and the routine glucose indicators: quarterly HbA1c at 23% and daily eAG at 23%. ***Notably, despite hyperglycemia frequency representing only 2% of the total glucose dataset, it still contributes 26% of the total impact or energy on his overall PD risks.***



1. Introduction

The interplay of diet quality and portion control significantly impacts body weight, a pivotal factor in type 2 diabetes (T2D) progression. T2D is marked by four key biomarkers, including insulin resistance (via morning fasting glucose - FPG), glycemic control (via daily averaged glucose - eAG), quarterly glycemic control (via HbA1c levels), and hyperglycemia situation control (via hyperglycemia intensity - HyGI). Here, ***his HyGI is calculated as the product of averaged glucose above 180 mg/ dL multiplied by the frequency of glucose above 180 mg/ dL.***

This study delves into the author's Parkinson's disease (PD) risks linked to the aforementioned four T2D biomarkers, drawing from personal data collected over past six years, from 5/1/2018 to 11/20/2023.Traditional statistical analysis reveals strong correlations (ranging from 65% to 91%) between the author's PD risk and his four influential T2D biomarkers. Furthermore, the author employs the space-domain viscoplastic energy (SD-VMT) method from advanced engineering to uncover hidden relationships and dynamics (i.e. energies) between these T2D biomarkers and the author's annual PD risk output.

2. Biomedical Information

The following sections contain excerpts and concise information drawn from multiple medical articles, which have been meticulously reviewed by the author of this paper. The author has adopted this approach as an alternative to including a conventional reference list at the end of this document, with the intention of optimizing his valuable research time. It is essential to clarify that these sections do not constitute part of the author's original contribution but have been included to aid the author in his future reviews and offer valuable insights to other readers with an interest in these subjects.

3. Parkinson's and Diabetes (from an article published in UK)

Diabetes is a chronic condition affecting 4.5 million people in the UK. Research indicates there is a relationship between Parkinson's and diabetes, with some recent data suggesting treatment or prevention of diabetes may also reduce the risk of Parkinson's or affect the progression of the condition.

3.1 What is Diabetes?

Diabetes is a medical condition where blood sugar levels (or glucose) in the body are too high. We all need glucose – it is a source of energy for our bodies to function properly. Our bodies break down the glucose from the food that we eat or drink, and this is released into the bloodstream. A hormone called insulin – which is produced by an organ called the pancreas – acts like a key to unlock the cells' ability to absorb glucose from the bloodstream through the cell wall. The glucose that is absorbed is then used as energy. It is the pancreas that senses the right amount of the hormone insulin needed to be released for this whole process to function properly.

With diabetes, this process is faulty. There are two types of diabetes. Type 1 diabetes is a condition in which the pancreas produces little or no insulin, and it usually starts early in life. In Type 2 diabetes – which accounts for 95% of diabetes cases – cells stop recognizing and responding to insulin, and this is referred to as ***insulin resistance.***

With insulin resistance, glucose levels in the body rise after we have eaten, the pancreas detects the rising levels of glucose and produces more insulin to reduce glucose levels. When glucose levels continue building in the blood, this is referred to as ***glucose intolerance.***

3.2 Is there a Link Between Parkinson's and Diabetes?

For a long time researchers have known that there is a close relationship between Parkinson's and diabetes; a significant proportion of people with Parkinson's have glucose intolerance and some also live with the added burden of diabetes.

Insulin also does its job of controlling glucose levels in the brain. ***Insulin has been shown to impact dopamine levels – dopamine is a chemical released in the brain and used to send messages between nerve cells.*** Research shows that insulin also helps with our cognitive function – the ability to think clearly, to learn, and remember. Notably, defects in insulin processes in the brain may contribute to Parkinson's. Research has suggested that ***people with diabetes are around 40% more likely to develop Parkinson's than those without diabetes.***

In addition, ***individuals with Parkinson's who are diabetic often have a more rapid progression of their symptoms, so careful management of both conditions is important.*** Currently, one in 15 people in the UK has Type 2 diabetes, and that number is increasing; the risk of developing Parkinson's in a person's lifetime is also growing. Therefore, it is important that we try to understand the relationship between the two conditions, and whether certain Type 2 diabetes medications might, in turn, be able to slow the progression of Parkinson's.

4. Pathophysiological Explanations of Parkinson's disease and Certain Biomarkers of type 2 Diabetes, such as Insulin Resistance via FPG, Diabetic Control via HbA1C and eAG, and Hyperglycemia Intensity

It is important to note that while there is evidence suggesting a potential relationship between PD and type 2 diabetes, the exact mechanisms by which these conditions intersect are still a topic of ongoing research. Further studies are needed to fully elucidate the underlying pathophysiological links and to identify potential therapeutic targets for addressing both conditions simultaneously.

The potential pathophysiological connections between ***Parkinson's disease (PD) and type 2 diabetes (T2D),*** including explanations involving insulin resistance (FPG), diabetic control (HbA1C and eAG), and hyperglycemia intensity (HyGI), are complex and have implications for the interactions between the two conditions. Here are the potential links between these parameters and the pathophysiology of PD and type 2 diabetes:

4.1 Insulin Resistance via FPG

Insulin resistance, a hallmark of type 2 diabetes, may also play a role in Parkinson's disease. Studies have suggested that insulin resistance and impaired insulin signaling pathways in the brain could contribute to the development and progression of PD.

Insulin signaling is important for neuronal function and survival, and disruptions in insulin signaling pathways may contribute to neurodegeneration in PD.

Elevated fasting plasma glucose (FPG) levels are indicative of insulin resistance, a key feature of type 2 diabetes. Insulin resistance leads to reduced cellular responsiveness to insulin, leading to increased blood glucose levels.

Insulin resistance has been linked to neuroinflammation, oxidative stress, and mitochondrial dysfunction, which are implicated in the pathophysiology of Parkinson's disease.

In the context of PD, insulin resistance may contribute to neuronal dysfunction and degeneration, potentially exacerbating the neurodegenerative process seen in the condition.

4.2 Diabetic Control via eAG and HbA1C

Daily averaged glucose (eAG) is a marker of daily averaged value of glycemic control of a T2D patient. Hemoglobin A1C (HbA1C) is a marker used to assess long-term (e.g. a quarter or 90-120 days) glycemic control in individuals with diabetes. Elevated eAG or HbA1C levels reflect chronic hyperglycemia and are associated with increased risks for diabetes-related complications.

Chronic hyperglycemia has been linked to systemic inflammation, oxidative stress, and impaired mitochondrial function, all of which have been implicated in the pathophysiology of Parkinson's disease.

Poor diabetic control, as indicated by high HbA1C levels, may contribute to the progression of neurodegeneration observed in PD through shared pathophysiological mechanisms.

4.3 Hyperglycemia Intensity (HyGI)

Hyperglycemia intensity (HyGI) is defined as the value of the averaged hyperglycemia value (above 180 mg/ dL) multiplied by the occurrence frequency percent of hyperglycemia. Intensive hyperglycemia, reflected in daily averaged glucose levels and hyperglycemia intensity, can have systemic effects on inflammation, oxidative stress, and cellular damage.

Hyperglycemia has been implicated in promoting oxidative stress and inflammation in the brain, contributing to neurodegeneration associated with Parkinson's disease.

Intensive hyperglycemia may exacerbate neuroinflammation and oxidative stress, which are implicated in the pathophysiology of PD, potentially leading to accelerated disease progression.

4.4 Inflammation

Chronic low-grade inflammation is a feature of both type 2

diabetes and Parkinson's disease. Inflammation in the brain, known as neuroinflammation, has been implicated in the pathogenesis of PD.

In type 2 diabetes, systemic inflammation and the release of proinflammatory cytokines may have effects on the brain and could potentially contribute to the development or progression of Parkinson's disease.

4.5 Mitochondrial Dysfunction

Mitochondrial dysfunction, which is observed in both type 2 diabetes and Parkinson's disease, may represent a common underlying mechanism linking the two conditions.

Impaired mitochondrial function can lead to increased oxidative stress and compromised energy production, which may contribute to the degeneration of dopaminergic neurons in the brain, a hallmark of Parkinson's disease.

In summary, the potential pathophysiological connections between Parkinson's disease and type 2 diabetes, including the roles of insulin resistance, diabetic control, and hyperglycemia intensity, involve shared mechanisms such as inflammation, oxidative stress, and mitochondrial dysfunction. These interrelated factors may contribute to the progression of both conditions and their potential interaction. Understanding the intricate relationships and potential paths for intervention may provide insights into managing both Parkinson's disease and type 2 diabetes, particularly in cases where they coexist. However, further research is needed to fully elucidate the specific pathophysiological links and potential therapeutic implications.

5. MPM Background

To learn more about his developed
GH-Method: math-physical medicine (MPM) methodology, readers can read the following three papers selected from his published 760+ papers. The first paper, No. 386 (Reference 1) describes his MPM methodology in a general conceptual format. The second paper, No. 387 (Reference 2)

outlines the history of his personalized diabetes research, various application tools, and the differences between biochemical medicine (BCM) approach versus the MPM approach. The third paper, No. 397 (Reference 3) depicts a general flow diagram containing ~10 key MPM research methods and different tools.

6. The Author's Diabetes History

The author was a severe T2D patient since 1995. He weighed 220 lb. (100 kg) at that time. By 2010, he still weighed 198 lb. with an average daily glucose of 250 mg/dL (HbA1C at 10%). During that year, his triglycerides reached 1161 (high risk for CVD and stroke) and his albumin-creatinine ratio (ACR) at 116 (high risk for chronic kidney disease). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding the need for kidney dialysis treatment and the future high risk of dying from his severe diabetic complications.

In 2010, he decided to self-study endocrinology with an emphasis on diabetes and food nutrition. He spent the entire year of 2014 to develop a metabolism index (MI) mathematical model. During 2015 and 2016, he developed four mathematical prediction models related to diabetes conditions: weight, PPG, fasting plasma glucose (FPG), and HbA1C (A1C). Through using his developed mathematical metabolism index (MI) model and the other four glucose prediction tools, by the end of 2016, his weight was reduced from 220 lbs. (100 kg) to 176 lbs. (89 kg), waistline from 44 inches (112 cm) to 33 inches (84 cm), average fingerpiercing glucose from 250 mg/dL to 120 mg/dL, and A1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes-related medications since 12/8/2015.

In 2017, he achieved excellent results on all fronts, especially his glucose control. However, during the preCOVID period, including both 2018 and 2019, he traveled to ~50 international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control caused by stress, dining out frequently, post-meal exercise disruption, and jet lag, along with the overall negative metabolic impact from the irregular life patterns; therefore, his glucose control was somewhat affected during the two-year traveling period of 2018-2019.

He started his COVID-19 selfquarantined life on 1/19/2020. By 10/16/2022, his weight was further reduced to ~164 lbs. (BMI 24.22) and his A1C was at 6.0% without any medication intervention or insulin injection. In fact, with the special COVID-19 quarantine lifestyle since early 2020, not only has he written and published ~500 new research articles in various medical and engineering journals, but he has also achieved his best health conditions for the past 27 years. These achievements have resulted from his non-traveling, low-stress, and regular daily life routines. Of course, his indepth knowledge of chronic diseases, sufficient practical lifestyle management experiences, and his own developed high-tech tools have also contributed to his excellent health improvements.

On 5/5/2018, he applied a continuous glucose monitoring (CGM) sensor device on his upper arm and checks his glucose measurements every 5 minutes for a total of 288 times each day. Furthermore, he extracted the 5minute intervals from every 15minute interval for a total of 96 glucose data each day stored in his computer software.

Through the author's medical research work over 40,000 hours and read over 4,000 published medical papers online in the past 13 years, he discovered and became convinced that good life habits of not smoking, moderate or no alcohol intake, avoiding illicit drugs; along with eating the right food with wellbalanced nutrition, persistent exercise, having a sufficient and good quality of sleep, reducing all kinds of unnecessary stress, maintaining a regular daily life routine contribute to the risk reduction of having many diseases, including CVD, stroke, kidney problems, micro blood vessels issues, peripheral nervous system problems, and even cancers and dementia. In addition, a long-term healthy lifestyle can even "repair" some damaged internal organs, with different required time-length depending

on the particular organ's cell lifespan. For example, he has "self-repaired" about 35% of his damaged pancreatic beta cells during the past 10 years.

7. Energy Theory

The human body and organs have around 37 trillion live cells which are composed of different organic cells that require energy infusion from glucose carried by red blood cells; and energy consumption from laborwork or exercise. When the residual energy (resulting from the plastic glucose scenario) is stored inside our bodies, it will cause different degrees of damage or influence to many of our internal organs.

According to physics, energies associated with the glucose waves are proportional to the square of the glucose amplitude. The residual energies from elevated glucoses are circulating inside the body via blood vessels which then impact all of the internal organs to cause different degrees of damage or influence, e.g. diabetic complications. Elevated glucose (hyperglycemia) causes damage to the structural integrity of blood vessels. When it combines with both hypertension (rupture of arteries) and hyperlipidemia (blockage of arteries), CVD or Stroke happens. Similarly, many other deadly diseases could result from these excessive energies which would finally shorten our lifespan. For an example, the combination of hyperglycemia and hypertension would cause micro-blood vessel's leakage in kidney systems which is one of the major cause of CKD.

The author then applied Fast Fourier Transform (FFT) operations to convert the input wave from a time domain into a frequency domain. The y-axis amplitude values in the frequency domain indicate the proportional energy levels associated with each different frequency component of input occurrence. ***Both output symptom value (i.e. strain amplitude in the time domain) and output symptom fluctuation rate (i.e. the strain rate and strain frequency) are influencing the energy level (i.e. the Y-amplitude in the frequency domain).***

Currently, many people live a sedentary lifestyle and lack sufficient exercise to burn off the energy influx which causes them to become overweight or obese. Being overweight and having obesity leads to a variety of chronic diseases, particularly diabetes. In addition, many types of processed food add unnecessary ingredients and harmful chemicals that are toxic to the bodies, which lead to the development of many other deadly diseases, such as cancers. For example, ~85% of worldwide diabetes patients are overweight, and ~75% of patients with cardiac illnesses or surgeries have diabetes conditions.

In engineering analysis, when the load is applied to the structure, it bends or twists, i.e. deform; however, when the load is removed, it will either be restored to its original shape (i.e, elastic case) or remain in a deformed shape (i.e. plastic case). In a biomedical system, the glucose level will increase after eating carbohydrates or sugar from food; therefore, the carbohydrates and sugar function as the energy supply. After having labor work or exercise, the glucose level will decrease. As a result, the exercise burns off the energy, which is similar to load removal in the engineering case. In the biomedical case, both processes of energy influx and energy dissipation take some time which is not as simple and quick as the structural load removal in the engineering case. Therefore, the age difference and 3 input behaviors are "dynamic" in nature, i.e. timedependent. ***This time-dependent nature leads to a "viscoelastic or viscoplastic" situation. For the author's case, it is "viscoplastic" since most of his biomarkers are continuously improved during the past 13-year time window.***

Time-dependent output strain and stress of (viscous input*output rate):

Hooke's law of linear elasticity is expressed as:

Strain (ε: epsilon)
= Stress (σ: sigma) / Young's modulus (E)

For biomedical glucose application, his developed linear elastic glucose theory (LEGT) is expressed as:

PPG
(strain) =
carbs/sugar (stress) * GH.p-Modulus (a positive number) + post-meal walking ksteps * GH.w-Modulus (a negative number)

Where GH.p-Modulus is reciprocal of Young's modulus E.

However, in viscoelasticity or viscoplasticity theory, the stress is expressed as:

Stress
= viscosity factor (η: eta) * strain rate (dε/dt)

Where strain is expressed as Greek epsilon or ε.

In this article, in order to construct an "ellipse-like" diagram in a stressstrain space domain (e.g. "hysteresis loop") covering both the positive side and negative side of space, he has modified the definition of strain as follows:

Strain
= (body weight at certain specific time instant)

He also calculates his strain rate using the following formula:

Strain rate
= (body weight at next time instant) - (body weight at present time instant)

The risk probability % of developing into CVD, CKD, Cancer is calculated based on his developed metabolism index model (MI) in 2014. His MI value is calculated using inputs of 4 chronic conditions, i.e. weight, glucose, blood pressure, and lipids; and 6 lifestyle details, i.e. diet, drinking water, exercise, sleep, stress, and daily routines. These 10 metabolism categories further contain ~500 elements with millions of input data collected and processed since 2010. For individual deadly disease risk probability %, his mathematical model contains certain specific weighting factors for simulating certain risk percentages associated with different deadly diseases, such as metabolic disorderinduced CVD, stroke, kidney failure, cancers, dementia; artery damage in heart and brain, micro-vessel damage in kidney, and immunity-related infectious diseases, such as COVID death.

Some of explored deadly diseases and longevity characteristics using the ***viscoplastic medicine theory (VMT)*** include stress relaxation, creep, hysteresis loop, and material stiffness, damping effect ***based on time-dependent stress and strain*** which are different from his previous research findings using ***linear elastic glucose theory (LEGT) and nonlinear plastic glucose theory (NPGT).***

8. Resu

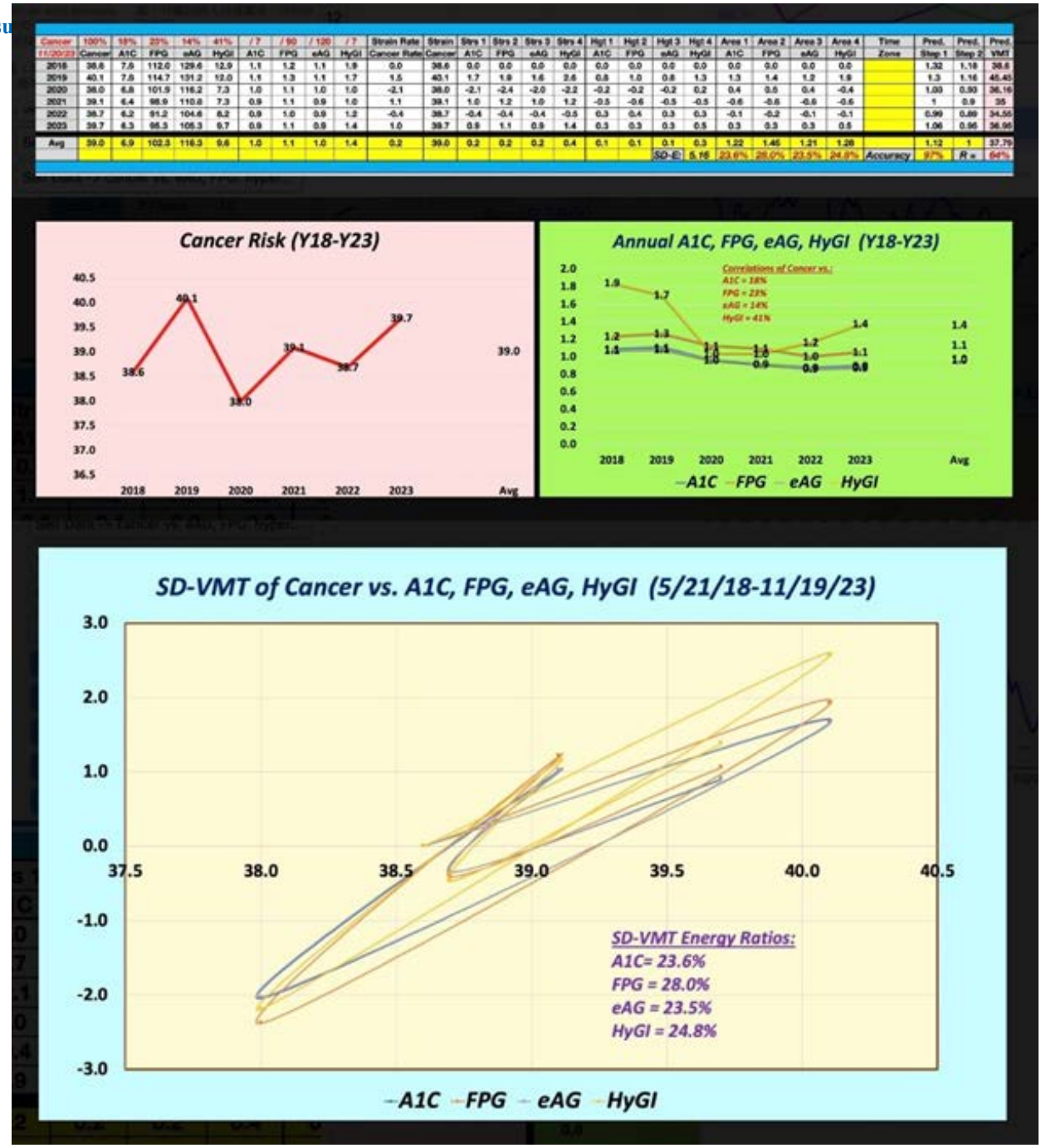


Figure 1: Data table, Time-domain curves and SD-VMT energies.

9. Conclusions

In summary, traditional statistical correlations unveiled significant associations between the author's PD risks and his four T2D biomarkers:

- ***PD vs. HbA1c: 89%***
- ***PD vs. FPG: 86%***
- ***PD vs. eAG: 91%***
- ***PD vs. HyGI: 65%***

These differ markedly from the low positive correlations (14% to 41%) between his cancer risks and the same T2D biomarkers, reflecting distinct characteristics in the risk waveforms of these two diseases. Using SD-VMT energy results from advanced engineering, four energy contribution margins on PD risks from four T2D biomarkers were identified:

- ***Energy from HbA1c: 23%***
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10. Key message

The author's T2D conditions are indeed linked to his risks of developing into Parkinson's diseases. Insulin resistance, as indicated by FPG, contributes the most energy to PD risks (27%), followed by hyperglycemia intensity (26%), and the routine glucose indicators: quarterly HbA1c at 23% and daily eAG at 23%. ***Notably, despite hyperglycemia frequency representing only 2% of the total glucose dataset, it still contributes 26% of the total impact or energy on his overall PD risks.***

References

For editing purposes, majority of the references in this paper, which are self-references, have been removed for this article. Only references from other authors' published sources remain. The bibliography of the author's original self-references can be viewed at www.eclairemd.com. Readers may use this article as long as the work is properly cited, and their use is educational and not for profit, and the author's original work is not altered.

For reading more of the author's published VGT or FD analysis results on medical applications, please locate them through platforms for scientific research publications, such as ResearchGate, Google Scholar, etc.