

The GH-Method

Viscoelastic or Viscoplastic Glucose Theory (VGT #161): Impact of Metabolism, Glycemic Fluctuation, and Hypoglycemia on the Risk of Developing Dementia for a Type 2 Diabetes Patient Using GH-Method: Math-Physical Medicine (No. 754)

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Keywords: Viscoelastic; Viscoplastic; Alzheimer's dementia; Metabolism; Hypoglycemia; Glycemic fluctuation; Type 2 diabetes; Dementia

Abbreviations: AD: Alzheimer's dementia; GF: glycemic fluctuation; FD: frequency domain; MPM: math-physical medicine

1. INTRODUCTION

The author has been researching dementia over the past four years. Recently, he has read many published articles about Alzheimer's dementia (AD). He was inspired by some of them and decided to utilize the GH-Method: math-physical medicine (MPM) with his collected big data of health conditions and lifestyle details to recalculate his own risk probability of developing dementia conditions due to a combination of metabolism index, glycemic fluctuation (GF), and hypoglycemia rate. He also decides to use his recently developed viscoelastic & viscoplastic glucose theory (VGT) model and glucose density model with his recent 4+ years collected data of GF, i.e. glycemic fluctuations, (maximum glucose minus minimum glucose within a day, usually varies from about 82 mg/dL to 110 mg/dL) and his hypoglycemia data density % (glucose less than 70 mg/dL) to dig deeper into his risk probability of developing dementia conditions.

For the metabolism index (MI) portion of his research, the basic concept and approach are remarkably similar to his previous research studies of risks regarding stroke, cardiovascular disease (CVD), chronic kidney disease (CKD), diabetic retinopathy (DR),

and cancers. However, this specific dementia article has included data of both GF and hypoglycemia collected during the past 4+ years from 5/8/2018 to 10/20/2022 which are calculated from his collected continuous glucose monitoring sensor data (288 CGM data per day).

Over the past 13 years, the author has self-studied and conducted medical research with a focus on type 2 diabetes and its related complications. But, certain types of dementia can also be related to diabetes. For example, some research scientists even named Alzheimer's dementia "type 3 diabetes". More information can be found in the section of methods.

The author was diagnosed with type 2 diabetes (T2D) in 1995. Since then, he has realized that the root cause of his diabetes and its many complications are a direct result of his poor lifestyle beginning in early 1980. In 2010, he initiated his own study and research on endocrinology with a special interest in diabetes, he made a vow to himself that within 10 years, he would learn and understand his personal health situation and the related medical issues using his ready learned academic knowledge from 7 different universities, including mathematics, physics, engineering, and computer science, despite

his lack of formal training in biology and chemistry. During the past 13 years, he has spent over 40,000 hours and read more than 4,000 published medical papers. He researched four of his chronic diseases and their induced complications, including obesity, type 2 diabetes (T2D), hyperlipidemia, hypertension, CVD, CKD, diabetic neuropathy, foot ulcer, bladder infection, diabetic retinopathy, hypothyroidism, diabetic constipation, diabetic skin fungal infection. Thus far, he has had no sign of either cancer or dementia. But these two groups of diseases are his primary concern and major interest in terms of disease understanding and prevention.

After a decade of self-study and research on internal medicine, he finally realized that the biomedical system is the most sophisticated and complicated system he has ever dealt with. The human body is an “inner space or inner universe” with many interrelated and mutually-influenced organs inside. Studying internal medicine is like exploring a “black box” that has so many dynamically changing and interrelated organs and diseases are hidden inside. This situation is quite similar to the “outer space or outer universe” which includes many mutually-influenced planets. The human body has 37.2 trillion live cells which are “organic” and change constantly. This is vastly different from the “inorganic” materials that the author studied at schools and practiced as a professional engineer for 37 years. These living cells go through many different lifecycles and developmental stages, such as birth, growth, sickness, damage, healing, splitting, mutation, rebirth, and death. They are very different from the engineering materials, such as steel, concrete, rubber, copper, silicon, soil, ice, and ocean water which were utilized in his past working experiences in various systems of aerospace, defense, computers, nuclear power plants, semiconductors chips, electronic devices, mechanical and structural designs.

During his continuous self-study of medicine and medical research work, he has finally understood and also identified a major highway of his medical research direction and its moving path. This main highway starts from lifestyle through metabolism and immunity, then through various metabolic-induced diseases, and finally reaches death or longevity. This transportation route has guided him to expand his interests and

research efforts from diabetes to many other related medical branches, such as cardiology, nephrology, neuroscience, dementia, and cancers. For example, numerous published medical articles have clearly indicated the path of dementia prevention is through lifestyle management. (Even cancers have approximately 45.2% cases related to various metabolic disorders and poor lifestyles.).

The above descriptions have outlined the author’s background and personal philosophy in conducting his medical research work on dementia.

The author estimates 65% to 70% of deaths from various diseases are either directly or indirectly related to metabolic disorders which are linked to poor lifestyle in most cases. In other words, death-causing diseases have a common root cause, which is lifestyle. Unfortunately, so many patients are seeking a “quick fix” or a “miracle” from their medical doctors. In fact, there is no “quick fix” or “permanent repair” for many endocrinological diseases, particularly when they have resulted from long-term damaged internal organs, including the brain. The author believes that lifestyle management combined with strong willpower and persistence is the only way to deal with the root cause of many diseases, including dementia, at the most fundamental level.

Another medical paper that has caught his attention and also made a deeper impression on him is: “The Presence of Dementia as one of the Diabetic Complications: Hyperglycemia, Hypoglycemia and Glycemic Fluctuation are Associated with the Development of Dementia” written by Kaneto on the Journal of Alzheimers Disease Parkinsonism. This is a well-written article regarding the connection between diabetes and dementia, particularly due to factors like chronic hyperglycemia, repeated hypoglycemia, and large amplitude of glycemic fluctuations (GF). Being a mathematician and engineer, this article’s qualitative biochemical descriptions of dementia’s biophysical phenomena are excellent. However, those linguistic descriptions lack support from quantitative proof with sufficient data. Therefore, it could not totally satisfy his own curiosity about questions like: “to what degree do the glycemic fluctuation (GF) and hypoglycemia influence dementia?” In other words, he was

searching for a presented quantitative proof instead of just a linguistic description of the connection between glucose and dementia, specifically with GF, hyperglycemia, and hypoglycemia. This curiosity has driven him to research the same subject deeper and wider using his MPM model, VGT model, and data density model.

There are three extra risk estimation models involving both GF and hypoglycemia.

(1) The first case is using MI (assigned weight of 85%), GF (assigned weight of 10%), and hypoglycemia (assigned weight of 5%) in his calculating formula of dementia risk, his averaged dementia risk percentage is then increased by 3% to 60% in comparison with the original dementia risk of 57% using only MI scores and other related factors during the period of 4+ years from 5/8/2018 to 10/20/2020.

(2) The second case is using MI (assigned weight of 80%), GF (assigned weight of 10%), and hypoglycemia (assigned weight of 10%) in his calculating formula of dementia risk, his averaged dementia risk percentage is then increased by 2% to 59% in comparison with the original dementia risk of 57% using only MI scores and other related factors during the period of 4+ years from 5/8/2018 to 10/20/2020.

(3) The third case is using MI (assigned weight of 38%), GF (assigned weight of 46%), and hypoglycemia (assigned weight of 16%) in his calculating formula of dementia risk, his averaged dementia risk percentage is then increased by 15% to 72% in comparison with the original dementia risk of 57% using only MI scores and other related factors during the period of 4+ years from 5/8/2018 to 10/20/2020.

In summary, the inclusion of glucose fluctuations (GF) and Hypoglycemia into the calculation would increase his averaged dementia risk by a range of 2%, 3%, or 15% depending upon the assigned weighting factor. Numbers do not lie and they indeed reflect part of the reality of his life during this period.

This study is a continuation of Papers No. 372 and No. 435.

2. METHODS

2.1 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 700+ 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 the 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.

2.2 Alzheimer's dementia (AD)

The following paragraphs in this sub-section are excerpts from different published papers about dementia.

“What is the relationship between diabetes and dementia?” by Andrew E. Budson, MD on Harvard Health Publishing of Harvard Medical School on July 12, 2021:

“It has been known for many years that type 2 diabetes increases your risk for strokes and heart disease. More recent studies have shown that diabetes also increases your risk of dementia. What has not previously been investigated, however, is whether the age of onset of diabetes makes a difference in your risk of developing dementia.

New research about the age at diabetes onset and the risk of developing dementia

A newly published study examined the association between the age of onset of diabetes and the development of dementia using a large, ongoing cohort study. The cohort was established in 1985–88 among 10,308 employees aged 35 to 55 years (33% women, 88% white) in London-based government departments. Data on diabetes exposure, including fasting glucose and the Finnish Diabetes Risk Score, were obtained at ages 55, 60, 65, and 70. (The Finnish Diabetes Risk Score includes age, family history of diabetes, personal history of

elevated blood glucose, fruit and vegetable consumption, blood pressure medication, physical activity, body mass index, and measured waist circumference.) (The author's note: these factors have been included in his metabolism model for dementia.)

Dementia due to any cause was the primary outcome measure. In addition to diabetes, they also examined the effects of age, sex, race, smoking, alcohol consumption, physical activity, fruit and vegetable consumption, high blood pressure, body mass index, coronary heart disease, heart failure, stroke, medications, and the Alzheimer's risk factor gene, apolipoprotein E.

The long-term effects of diabetes on dementia

From 1985 to 2019, 1,710 cases of diabetes and 639 cases of dementia were recorded. For every 1,000 people, examined yearly, the rates of dementia were 8.9 in those without diabetes at age 70. Comparable rates of dementia for those with diabetes were 10.0 for those with onset up to five years earlier, 13.0 for six to 10 years earlier, and 18.3 for more than 10 years earlier. These striking results clearly show that the earlier you develop diabetes, the greater (about two times higher) your risk is for developing dementia.

How diabetes can lead to dementia?

There are multiple reasons why years of type 2 diabetes may lead to dementia. One reason is related to the effects that diabetes has on the heart, as heart health is related to brain health. Heart disease and elevated blood pressure are both associated with strokes that, in turn, can lead to dementia. However, strokes do not appear to be the complete answer, as some studies found that diabetes led to an increased risk of dementia even when strokes were controlled for.

Another factor relates to the episodes of hypoglycemia that commonly occur in diabetes. Although tight control of blood sugars has been proven to reduce the long-term risks of heart disease and strokes, tight control can also lead to hypoglycemia, memory loss, and dementia. Here, the reason is likely because low blood sugars are known to damage the hippocampus — the memory center of the brain.

One of the more intriguing hypotheses is that diabetes directly causes Alzheimer's disease. Indeed, Alzheimer's disease has even been called "type 3 diabetes" because of the shared molecular and cellular features between diabetes and Alzheimer's. For example, insulin plays a critical role in the formation of amyloid plaques, and insulin is also involved in the phosphorylation of tau, which leads to neurofibrillary tangles. In other words, whereas insulin resistance in the body can lead to type 2 diabetes, insulin resistance in the brain can lead to the plaques and tangles of Alzheimer's disease.

Reduce your risk of diabetes and dementia

The good news is that you can reduce your risk of type 2 diabetes — and your risk of dementia. Speak with your doctor today about whether the following lifestyle modifications would be right for you. Note that these life changes are helpful even if you have a diagnosis of diabetes or prediabetes.

- Engage in aerobic exercise for at least 30 minutes each day, five days each week.
- Eat a Mediterranean-style menu of foods.
- Maintain a healthy body weight.
- Treat high blood pressure.
- Treat high cholesterol.
- Don't smoke.

Lastly, social activities, a positive attitude, learning new things, and music can all help your brain work at its best and reduce your risk of dementia. (The author's note: these lifestyle factors have also been considered in his metabolism model for dementia.)”

The overall picture of dementia:

“Alzheimer's dementia is the most common form of dementia, and probably the best studied. Alzheimer's disease is on the rise in the United States, and the facts are daunting. According to the Alzheimer Association's 2020 Alzheimer's Disease Facts and Figures report, approximately 5.8 million Americans age 65 and older currently have the Alzheimer dementia (AD) disease, with this number expected to triple over the next 30 years, and nearly two-thirds of those are women. It's the sixth leading cause of death in the United States—a ranking that's

expected to skyrocket as the US population ages (reference 2).

And it's not just an American problem. The WHO estimates there are about 50 million people across the globe living with dementia, with nearly 10 million cases being added each year (Reference 3). According to a review published in *Therapeutic Advances in Chronic Disease*, this number is projected to increase to 75 million by 2030, and to 135 million by 2050.

The cost of dementia in the worldwide healthcare system is currently more than \$800 billion and is expected to mushroom to \$2 trillion by the year 2030, and that does not account for the costs associated with informal caregiving. As a matter of fact, over 16 million Americans care for patients with Alzheimer's or other dementias, without pay."

Dementia and lifestyle:

"The following news is based on an analysis of data collected over 8 years from almost 200,000 adults aged 60 and over in the UK (Reference 4). This study was conducted by researchers from the UK (University of Exeter Medical School, University of Oxford, University College London, The Alan Turing Institute), the US (University of Michigan, Veterans Affairs Center for Clinical Management Research in Michigan), Australia (University of South Australia), and Germany (University of Hamburg, Hamburg Center for Health Economics). The study was published in the peer-reviewed *Journal of the American Medical Association (JAMA)*.

There are measures we can take individually to help combat the problem. According to the authors of the aforementioned review, almost half of all dementia cases can be attributed to a small number of modifiable lifestyle risk factors, including smoking, obesity, and physical inactivity.

The research project used volunteers who completed questionnaires at the start of the study about their lifestyles, and researchers looked at their DNA to see who carried genetic variations that have been associated with increased risk of Alzheimer's – the most common type of dementia.

The researchers found that among participants who had a higher genetic risk of getting dementia, only about 11 in every 1,000 with healthier lifestyles developed the condition during follow-up, compared with about 18 in every 1,000 with unhealthy lifestyles.

Overall, however, the findings are good news. We cannot change our genetics, but this study suggests that regardless of this, changing our lifestyles could help everyone reduce their dementia risk. This large UK cohort study has suggested that a healthy lifestyle can reduce overall dementia risk, even in people with genetic risk factors for Alzheimer's disease (Reference 5). The *Daily Telegraph* reported, "Bad dementia genes can be overcome through healthy living, study finds". The newspaper reports that regular exercise, not smoking, drinking sensibly, and eating a healthy diet have been found to reduce the risk of getting dementia even if a person has a higher genetic risk of developing the condition."

Glycemic fluctuations & dementia:

The following is an excerpt from an article by Kaneto, Kinoshita, Shimoda, and Kaku, "The Presence of Dementia as one of the Diabetic Complications: Hyperglycemia, Hypoglycemia and Glycemic Fluctuation are Associated with the Development of Dementia".

"Mainly, there are two types of dementia; one type is Alzheimer's disease and another type is vascular dementia. Chronic hyperglycemia and repeated hypoglycemia are closely associated with the onset and/or development of dementia. It is well known that the presence of diabetes mellitus leads to various complications such as microangiopathy (nephropathy, retinopathy, neuropathy) and macroangiopathy (ischemic heart disease, stroke). Dementia is often complicated in elderly subjects with diabetes and thereby thought to be one of diabetic complications. Indeed, it was reported that the incidence of Alzheimer's disease and vascular dementia was significantly higher in subjects with diabetes compared to non-diabetic subjects. It has been suggested that in the diabetic state chronic hyperglycemia leads to the formation and accumulation of advanced glycation end products in the brain which could lead to the development of dementia [8] (Figure 1). In

addition, while it is known that hyperglycemia and subsequent oxidative stress reduce insulin signaling in various insulin target tissues [9,10], insulin receptors are highly expressed in the brain as well [11]. It was reported that such reduction of insulin signaling in the brain induced hyper-phosphorylation of Tau protein and accumulation of beta amyloid protein both of which are well known as main characteristics in Alzheimer's disease [8,12-14] (Figure 1). In subjects with diabetes, there are several macro- and micro-angiopathy. Diabetic macroangiopathy (e.g. atherosclerosis) leads to the onset of cerebrovascular disease such as stroke which is closely associated with the development of vascular dementia. In addition, diabetic microangiopathy brings out brain ischemia which is also closely associated with the onset and progression of vascular dementia (Figure 1).

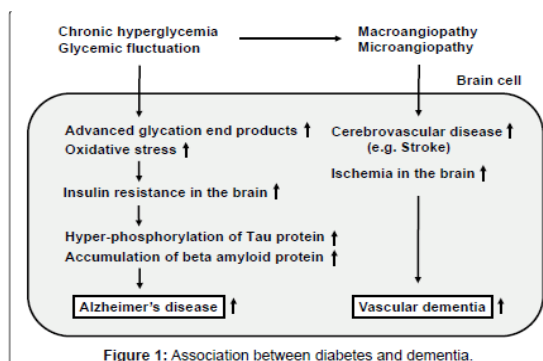


Figure 1: Association between diabetes and dementia.

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There was also a significant linear association between an increased risk of dementia and an increased number of hypoglycemia. It is known that recurrent hypoglycemia causes brain damage, especially in the cerebral cortex and hippocampus. There is a kind of vicious cycle between the frequency of hypoglycemia and the development of dementia including both Alzheimer's disease and vascular dementia (Figure 2).

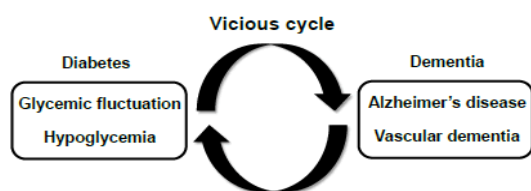


Figure 2: Vicious cycle between diabetes and dementia.

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It was reported that the risk of Alzheimer's disease and vascular dementia was significantly associated with postprandial glucose levels but not fasting glucose levels [7]. These data support the hypothesis that the fluctuation of blood glucose levels is likely associated with the development of various types of dementia. It has been reported that the glycoalbumin (GA)/hemoglobin A1c (HbA1c) ratio is a good marker for the fluctuation of blood glucose levels regardless of glycemic control situations [20].

The fluctuation of blood glucose levels, but not the incidence of hypoglycemia, was significantly associated with the decrease of cognitive impairment in this study. In order to avoid the onset and/or development of dementia, we should be careful about reducing the fluctuation of blood glucose levels in addition to avoiding hypoglycemia. Taken together, glycemic fluctuation is closely associated with the onset of and/or progression of dementia in elderly subjects with type 2 diabetes. We should avoid glycemic fluctuation especially in elderly subjects with type 2 diabetes to avoid the development of dementia.

Dementia is often complicated in elderly subjects with diabetes mellitus and thereby thought to be one of the diabetic complications. Not only chronic hyperglycemia and repeated hypoglycemia but also the fluctuation of blood glucose levels is associated with the onset and/or progression of dementia in elderly subjects with diabetes mellitus."

2.3 The author's diabetes history

The author was a severe type 2 diabetes patient since 1996. 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. 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 finger-piercing 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 pre-COVID 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 self-quarantined life on 1/19/2020. By now, 4/10/2021, his weight was further reduced to ~165 lbs. (BMI 24.4) and his A1C was at 6.2% without any medication intervention or insulin injection. In fact, with the special COVID-19 quarantine lifestyle since early 2020, not only has he written 200 new research articles and published a total of 400 medical papers in various medical and engineering journals, but he has also achieved his best health conditions for the past 26 years. These achievements have resulted from his non-traveling, low-stress, and regular daily life routines. Of course, his in-depth 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 5-minute intervals from every 15-minute interval for a

total of 96 glucose data each day stored in his computer software.

Through the author's own medical research work over 40,000 hours 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 well-balanced nutrition, persistent exercise, having a sufficient and good quality of sleep, reducing all kinds of unnecessary stressors, 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 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.

2.4 Metabolism data for dementia

The author used his collected data since 2012 with different stages. Since 1/1/2012, he recorded his daily weight, glucose, and walking steps. Since 2013, he started to collect his blood pressure and lipid (cholesterols) data. In 2014, he developed a mathematical model of metabolism which includes stress, sleep, daily life routines, and more. Since 5/1/2015, he started to gather his carbs/sugar intake amount and post-meal walking steps for diabetes concerns. The data collected in the earlier years was reconstructed to provide a more complete picture based on his scattered numbers.

For example, the social connection category includes the number of contacts of real (face-to-face) and virtual (online), quality of social connection, frequency of social contacts with family members, relatives, friends, colleagues, acquaintances, and certain stresses induced by social networking. One specific example is that during the COVID-19 quarantine period in 2020, a virtual connection is the major form of communication between individuals. But this new and easy way of social networking could introduce more stress into people's relationships, such as stress-induced by over-debated information sharing and intensive online discussion of political debates. All these factors can affect individual scores in

the social and stress categories, including sleep.

In 2014, he developed the metabolism index model, by using the topology concept of advanced mathematics and finite-element modeling techniques of structural engineering, he developed a mathematical model of a metabolism index system that includes 4-categories of disease control (body outputs) and 6-categories of lifestyle management (body inputs). He started to collect his personal detailed data on 1/1/2012. To date, he has collected more than 2 million pieces of data regarding his health and lifestyle.

For example, among these 10 categories and their associated ~500 elements, the sleep category has nearly 10 elements, including sleep hours, wake-up time, and deep sleep hours, while the stress category has more than 40 elements, including physical, emotional, financial, social, environmental, and others.

Finally, he further assembled those 10 categories (with ~500 detailed elements) and combined them into two new terms: the metabolism index (MI), which is a combined daily score to show the body's health situation, and general health status unit (GHSU), which is the 90-day moving average number to show the trend. He also identified a "break-even line" at 0.735 (73.5%) to separate his metabolism conditions between healthy (below 0.735) and unhealthy (above 0.735).

For the new dementia category of the social network, inter-relationship, and mental activities, such as meditation and yoga, he must establish a subjective measurement method and give a relative score for each year based on his memory.

2.5 Glycemic fluctuation & hypoglycemia data for dementia

Since 5/8/2018, the author started his glucose collection every 5 or 15 minutes time intervals using a CGM sensor device on his upper arm. He uses the highest glucose within a day (maximum) minus the lowest glucose within the same day (minimum) as his glucose fluctuation (GF) value.

He then developed a data density program to calculate the occurrence rate for the glucose values below 70 mg/dL (i.e. hypoglycemia) over the daily total glucose occurrences (for example 96 for measurements at every 15 minutes or 288 for measurements every 5 minutes).

Note: For a more detailed description, please refer to the "consolidated method" section which is given at the beginning of the special issue.

3. RESULTS

Figure 1 shows the input items and data associated with the MI model and the output of Dementia risk % based on the MI model from Y2012 to Y2022.

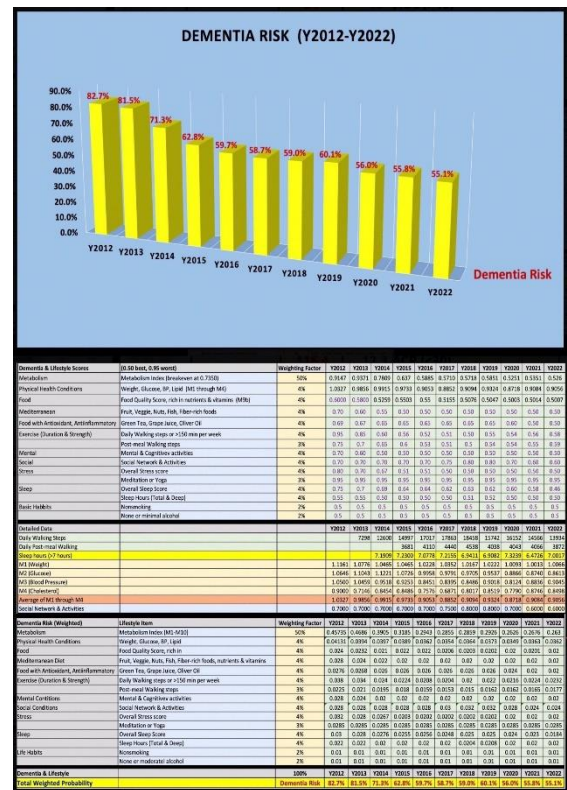


Figure 1: Input items and data associated with MI model and the output of dementia risk % based on the MI model from Y2012 to Y2022.

Figure 2 depicts GF, normalized GF (divided by 96 mg/dL), and Hypoglycemia % from Y2018 to Y2022.

Figure 3 reflects his VGT input panel, associated items with MI from Y2018 to Y2022, and an article on risk factors of dementia from www.alzheimer.ca/brainhealth.

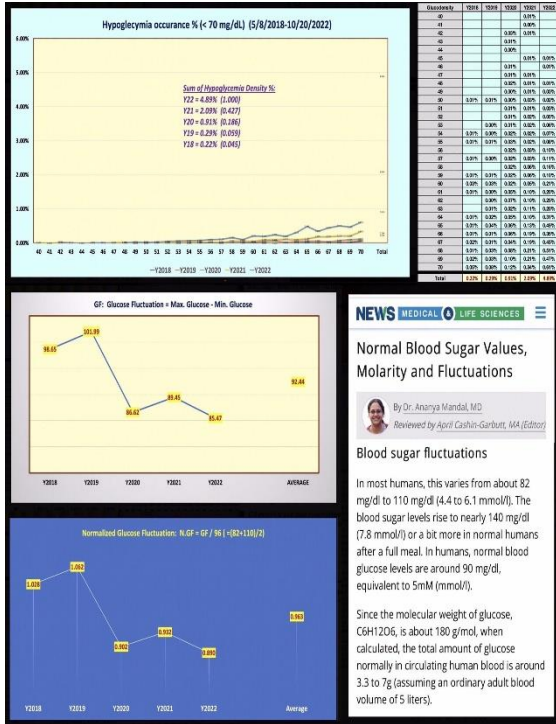


Figure 2: GF, normalized GF (divided by 96 mg/dL), and hypoglycemia % from Y2018 to Y2022.

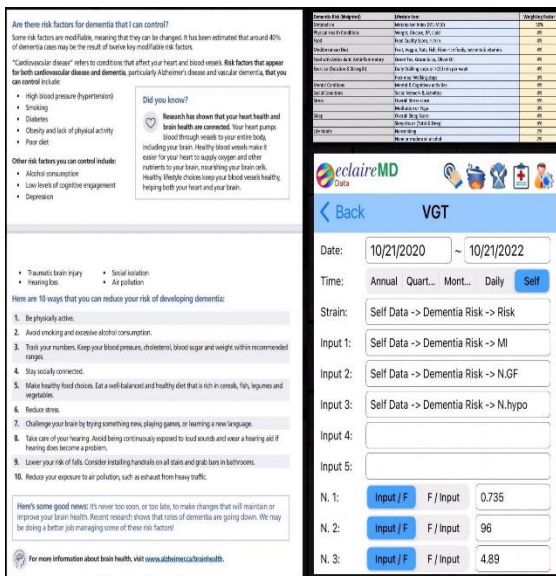


Figure 3: VGT input panel, associated items with MI from Y2018 to Y2022, and an article of risk factors of dementia from www.alzheimer.ca/brainhealth.

Figure 4 displays the time-domain and space-domain diagrams with VGT analysis results from Y2018 to Y2022.

Figure 5 reveals 3 estimated dementia risk % using 3 different contribution weighting factors versus the dementia risk % based on MI alone, from Y2018 to Y2022.

Figure 6 illustrates measured dementia risk % versus hypothetical dementia risk %

resulting from improvements in both GF and Hypoglycemia control in Y2022.

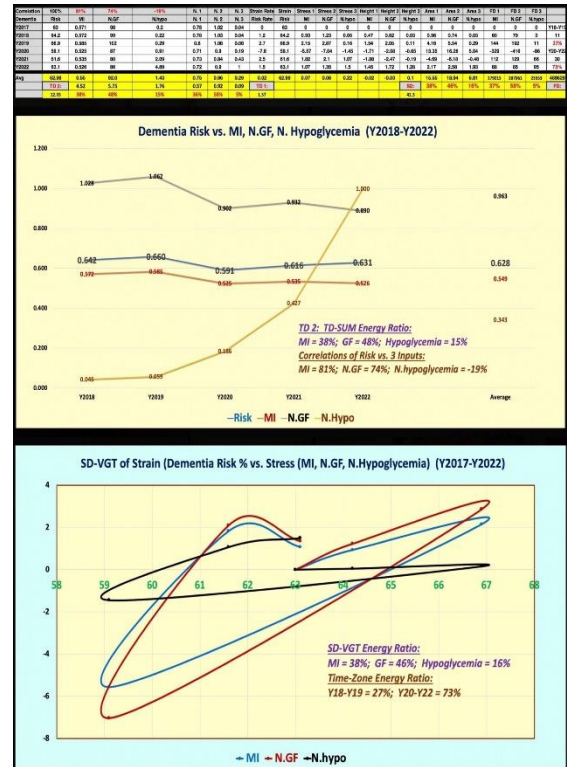


Figure 4: Time-domain and space-domain diagrams with VGT analysis results from Y2018 to Y2022.



Figure 5: 3 estimated dementia risk % using 3 different contribution weighting factors versus the dementia risk % based on MI alone, from Y2018 to Y2022.

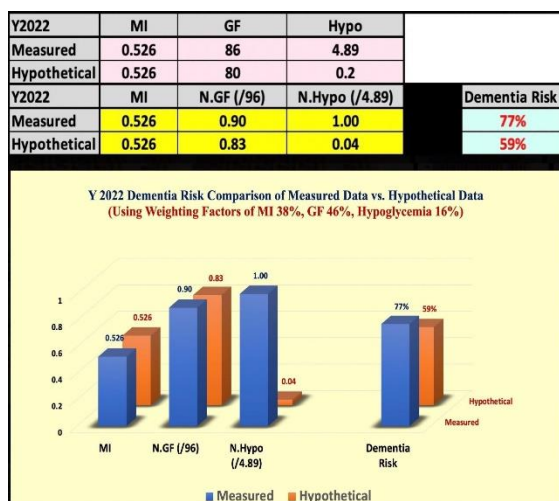


Figure 6: Measured dementia risk % versus hypothetical dementia risk % resulted from improvements on both GF and hypoglycemia control in Y2022.

4. CONCLUSION

This study is a continuation of his published paper No. 372: “Relative changes of risks on having Alzheimer’s dementia based on metabolism and lifestyle factors using GH-Method: math-physical medicine”, and No. 435: “Glycemic fluctuation impact on the risk probability of developing dementia in addition to metabolic influences for a diabetes patient using GH-Method: math-physical medicine”.

There are 3 summarized conclusions:

(1) Waveform characteristics: Regarding the overall trend of his data waveforms, such as the single output of dementia risk %, and those three inputs of MI score, GF data, and hypoglycemia density %, he has noticed the following prominent findings. First, over these 11 years from Y2012 to Y2022, his dementia risk percentages and his MI scores are continuously reduced year after year (with an extraordinarily high correlation coefficient of 99.7%). It should also be noted that these risk percentages are only showing the “relative picture”, not in the format of “absolute” numbers. This finding is a direct result of his continuous effort to improve his metabolism through his stringent lifestyle management. Second, over 4+ years from 5/8/2018 to 10/20/2022 using his collected data of CGM sensor gluces, the downward decreasing pattern of the GF curve is very similar to the downward decreasing pattern of the dementia risk curve (correlation is 79%). However, the upward-increasing pattern of the Hypoglycemia curve is opposite

to the downward-decreasing pattern of the dementia risk curve (correlation is -19%). This observation has also supported what Dr. Ebson said in his Harvard article: “Although tight control of blood sugars has been proven to reduce the long-term risks of heart disease and strokes, tight control can also lead to hypoglycemia, memory loss, and dementia”. By 2018, the author’s overall glucose situation had been well under control through his stringent lifestyle management program, without any medication intervention. However, this same tight glucose control has also pushed his hypoglycemia rate from 0.22% in 2018 to 4.89% in 2022. Particularly, in 2022, his combined dementia risk% of 61%-78% is 11%-42% higher than his MI single factor dementia risk of 55% which mainly resulted from his high hypoglycemia rate of 4.89% in 2022. Again, from now on, he must be very careful watching out for this upward trending pattern of his hypoglycemia conditions.

(2) Dementia risk models and data: Regarding the overall trend of his risk probability of having dementia, he was pleased to discover the following two conclusions: First, his risk percentages based on the MI model are continuously being reduced year over year. For example, his MI data are: 91.5% in 2012, 57.2% in 2018, and 52.6% in 2022; and his dementia risk based on MI is: 82.7% in 2012, 59.0% in 2018, and 55.1% in 2022. This encouraging finding is a direct result of his constant effort to improve his metabolism through lifestyle management. Second, when he includes GF and hypoglycemia into the calculating formula, then his dementia risk percentages are further increased: If using assigned weights of MI (85%), GF (10%), hypoglycemia (5%), his averaged dementia risk percentage is then increased by 3%; if using assigned weights of MI (80%), GF (10%), hypoglycemia (10%), his averaged dementia risk percentage is then increased by 2%; if using MI (38%), GF (46%), and hypoglycemia (16%), his averaged dementia risk percentage is then increased by 15% during the period of 4+ years from 5/8/2018 to 10/20/2020.

(3) What if improvements in Y2022: If the author makes improvements on both his GF and hypoglycemia control by maintaining them at the lowest level during the period from 2018 to 2022, i.e. GF at 80 mg/dL and hypoglycemia at 0.02%, his dementia risk for

2022 would be reduced from 77% of the measured case to 59% of a hypothetical case, a reduction of 18% on his dementia risk.

In summary, the inclusion of glucose fluctuations (GF) and hypoglycemia into the calculation would increase his averaged dementia risk by a range of 2%, 3%, or 15% depending upon those three different assigned weighting factors. Numbers do not lie and they indeed reflect part of the reality of his life during this period.

The most important finding and useful tip for the author himself are that, from now on, he must be ultra-careful watching out for his hypoglycemia conditions, particularly before falling asleep. He can prepare some chocolate at the bedside to prepare for the situation of low glucose before he falls asleep.

5. REFERENCES

For editing purposes, the majority of the references in this paper, which are self-

references, have been removed. Only references from other authors' published sources remain. The bibliography of the author's original self-references can be viewed at www.eclairemd.com.

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For reading more of the author's published VGT or FD analysis results on medical applications, please locate them through three published special editions from the following three specific journals:

- (1) Special Issue. The GH-Method. (<https://www.theghmethod.com>).
- (2) Journal of Applied Material Science & Engineering Research (contact: Catherine).
- (3) Advances in Bioengineering and Biomedical Science Research (contact: Sony Hazi).

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