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Diabetes is a Complex Neurological, Multisystemic, Multipathological and Polygenomic Disorder: the Use of Strannik Software as an Effective Modality to Illustrate Its Complexity

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Abstract

This paper illustrates that the brain is a biophysical entity in which both sensory and biological input sustain its biophysical and computational function. This leads to the conclusion that the brain works in a multi-level and coherent manner to optimise and/or regulate the body's multi-systemic stability and function.

It further illustrates that the 'optimisation of blood glucose levels' exhibits the characteristics of a neurally regulated physiological system in which blood glucose levels are regulated between higher and lower limits i.e. 4-8 mmol/l blood glucose; that types 1 and 2 diabetes are comorbidities thereby explaining the inaccuracies reported when diagnosing diabetes; that under pathological conditions mainly in the pancreas, but also as a result of pathological onset in adjacent organs and systems, there is an imbalance between insulin expression and insulin reactivity which leads to increased or decreased blood glucose levels, elevated blood viscosity, the onset of free radical reactions, the subsequent production of complex glycated proteins/lipids and metabolites, altered colour perception.

Moreover such precise knowledge; which is embodied in Grakov's mathematical model of the relationship between sense perception, brain function, the autonomic nervous system and physiological systems, and pathological onset; can be applied to screen the patient's health (as Strannik Virtual Scanning) and/or as a neuro modulation type technique (as Strannik Light Therapy) to treat autonomic dysfunction and the range of comorbidities experienced by diabetic and obese patients.

Abbreviations

SVS: Strannik Virtual Scanning; SLT: Strannik Light Therapy; LTP: Long Term Potentiation; HGH: Human Growth Hormone; GABA: Gamma Amino Butyric Acid; CBT: Cognitive Behavioural Therapy; NLP: Neurolinguistic Programming; IRP2: Insulin Receptor Protein2; GP: General Practitioner; LGN: Lateral Geniculate Nucleus

Introduction

This paper sets out to provide a coherent explanation for the phenomena of unstable blood glucose levels taking into account the complexity of psychological and physiological phenomena which accompany 'Diabetes Mellitus'. It considers the influence of sensory input and/or perception, and/or cognition; that the brain functions as a neuro modulator which regulates the autonomic nervous system and physiological systems; and how autonomic dysfunction is accompanied by pathological onset. This is significant for a variety of reasons e.g. misdiagnosis of the condition leads to further diagnostic tests which have significant additional costs, overlooking other medical conditions which may be more significant and which indirectly influence blood glucose levels, poor therapeutic outcomes, inconvenience and discomfort to the patient's health, the continued need for medication and further consultations with their GP, etc.

Our relationship with our environment and how we respond to sensory input

The human is a creature of habit. We can be influenced to do things and adopt patterns of behaviour which alter and/or simplify the complexity of our lives e.g. what we eat and drink, how we eat and drink, where we eat and drink, with whom we eat and drink, how much we eat and drink, etc.

Through our senses we are predisposed to favour particular experiences, foods, music and fashions often involving colour(s) e.g. a deep shade of red is known to stimulate appetite and is occasionally painted on the walls of a savvy restaurant whilst a pastel shade of green slows heartbeat and is occasionally to be found on the walls of a cardiac ward in hospital; however our sense perception and colour preferences change with pathological onset e.g. the onset of diabetes is accompanied by changes of blue-yellow colour perception.

We are subject to the complex influences of industries which, through advertising programmes, seek to persuade us to alter our patterns of behaviour, and hence purchase the products which they produce, manufacture and sell e.g. red or white meat, acidified and/or alcoholic beverages, processed foods including sugars and oils, cereals and carbohydrates, etc.

We make decisions, which are not based upon fact because we simply do not have the time to examine facts but instead upon our perception of the facts and how we are expected to behave i.e. whether we perceive that it is the appropriate thing to do; and we are guided by the complex opinions which we have built up throughout our lives

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and which are based upon what we have seen, read, viewed, heard and/or discussed with our peers. Our sensory experiences sculpt our neural connectivity and multilevel function by mechanisms, memories and opinions, which are still to be fully understood or defined e.g. whether rational or emotional, which are influenced by the autonomic nervous system. As a result, we are almost powerless to make a choice in our lives which has not been shaped by vested interests yet every aspect of the body's function and our behaviour is fundamentally biochemical i.e. our physiology, and how the brain influences, and/or is influenced by, the viscera; is influenced at different levels, in particular at the psychosomatic level, which influences our conscious thought patterns; and at the somatic level which influences our subconscious thought patterns, processes and mechanisms.

Somehow our psychosomatic and somatic function is the product of a precise and sophisticated biological and structural relationship, which includes the reaction kinetics at the molecular level, however there is not yet a clear accepted understanding of this relationship. Indeed, such is the complexity of this subject that it has perplexed the leading minds of our time e.g. Kandel, Brenner, Noble, and others; who have sought in their published works to explain the fundamental mechanisms by which the body is organised and regulated [1].

The process of physiological adaptation to our environment

The sub-division of most medical research into sub-units, known as reductionism, ensures that there is not any significant research into the fundamental whole-body mechanisms by which the body functions and is regulated. Most medical research is not intended to develop an understanding of how the body functions but instead to develop techniques which have commercial potential whereas a precise understanding of how the body functions e.g. a neurosimulation technique, would conceivably reduce the complexity and cost of healthcare. Nevertheless there are several research areas which are devoted to such an approach e.g. neurology and neuroscience, psychology, sports physiology, systems biology [2], complementary and alternative medicine, biofeedback/neurofeedback/neuromodulation.

Consider how humans live in different climates, at different altitudes, and in different environments. Those who live at altitude, in the Andes or Tibet, have higher levels of red blood cells in order to transport oxygen around the body, or create more energy using less oxygen, or have widened blood vessels which improve blood flow. Those who live in extremely cold regions, the Inuit, have a diet which is high in meat and fat which enables them to better deal with low temperatures and, in South-East Asia, the Bajau are able to dive to the seabed because their bodies produce higher levels of hemoglobin i.e. there is a neurological mechanism which assesses the physiological response to environmental parameters, to which the body is exposed, alters the genetic expression of hemoglobin, and, through its relationship with long-term memory, enables the body to adapt to its environment. This is significant because the brain receives biochemical input from the visceral organs and continuously regulates the body's physiological parameters in order to optimize its systemic stability by continuously adjusting the various metabolic processes which are involved in the regulation of metabolic rate and hence maintain a suitable environment in which the brain can function effectively.

Claude Bernard considered that the internal environment of organism is constant with the existence of control processes to achieve such 'homeostasis' and envisaged future mathematical modeling and/or neurosimulation simulation applications [3]. Moreover, the body is such a highly regulated entity that the possibility of mathematical modeling its function appears to be plausible i.e. if the complex nature and structure of its function were to be understood.

Every medical condition, without exception, comprises a range of pathologies which can be defined in terms of its genotype i.e. the rate at which the genes express particular protein(s); and its phenotype i.e. the rate at which the expressed protein(s) react with their substrates which is influenced by stress. In the case of diabetes and obesity this has overcome our ability to live and sustain a healthy life with the result that longevity is now declining in the most wealthy economies [4], fertility throughout the world is in decline [5], and expenditure on healthcare throughout the world continues to increase i.e. the GP and their patients needs to be educated in order to make the choices which enable us to live long, healthy and happy lives.

Accordingly, the aim of this article is to summarise the complex range of factors which influence the occurrence of diabetes and diabetic comorbidities and to further elucidate the complex neurological origins of such conditions.

A Review of The evidence-base Regarding Calorific Intake and Energy Expenditure

Regarding diabetes and obesity, the healthcare professions are in agreement that the body regulates its calorific intake i.e. if we consume more energy (via food and drink) than we expend (via exercise) our weight will increase. There are numerous examples which support this general and eminently logical conclusion e.g.

- **The quantity of food portions is significant** - if we place large portions on our plate there is an imperative to eat the full allocation [6]. The Japanese often use the term 'Hari Hachi Bu' to direct and/or advise that we should eat until we are just 80% full.

- **How we serve the food is significant** - it influences the rate at which we digest the food e.g. an emulsified or blended soup is digested more slowly than an unblended soup [7].

- **How we eat the food is significant** - if we eat a calorie-rich meal in a short period, and/or whether the meal is accompanied by an acidified or alcoholic beverage [8] - which influences the availability of essential minerals which are stored in the body, in particular Mg, Ca and Zn which are often essential catalysts in metabolically significant processes [8].

- **Who we are is significant** - e.g. our genes and or gender/whether male or female and/or our racial origins [8,9]; whether young or old; and/or our exposure to gene-altering moieties e.g. viruses and virus-like particles [10,11]; and/or our exposure to acidity [12-14].

The observation that the genetic profile which is required to express insulin can differ between racial groups with differing genetic profiles illustrates that diabetes is a polygenomic indication i.e. that gene conformation is a more significant factor than the chemical nature and/or structure of the gene(s) [10].

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• **How much we consume is significant** - someone who has an energy intense job/elevated metabolic rate requires greater sustenance than someone who has a sedentary lifestyle e.g. a computer programmer, social media consultant, etc. In general, if we consume more calories than we expend through physical activity and/or elevated metabolic rate; then our weight will increase [15]. (An additional ca. 3500 calories leads to ca. 500 grams increased weight i.e. a standard 51 gram branded snack bar each day can be expected to increase your weight by up to ca. 1 kg each month).

• **What we eat and drink is significant** - if we drink water, or acidified, alcoholic or caffeinated beverages with a snack or meal [16].

• **Diets must include fats** - because some vitamins are fat-soluble whilst others are water-soluble. Fats and carbohydrates are both metabolised into energy, by different metabolic processes, and have different diabetic significance e.g. that a balanced fat/carb diet (avoidance of high fat and/or high carb diets) is often appropriate in dietary control [17-19].

• **The taste of our food is significant** - the merest thought of food is often sufficient to make us salivate and produce enzymes required for early mastication/digestion whilst the taste buds detect the sweet tastes from foods containing glucose and/or other sugars and stimulate the neurological process by which the brain initiates the supply of insulin [20,21].

• **The calorie loading of our food is significant** - whether we consume large quantities of 'carbs' e.g. pasta, potatoes, rice, bread, etc; or whether we consume a vegetarian, vegan or Mediterranean diet. Large amounts of carbs increase the required levels of insulin - the body fluctuates between hyperglycaemia and hypoglycaemia - therefore a balanced diet should include foods which are slower to digest, require lower levels of insulin, and stabilise blood glucose levels over longer periods [22].

• **Foods which are difficult to digest often require greater levels of digestive acidity.** The production of elevated levels of digestive acidity may exceed the combined ability of the pancreas and duodenum to neutralise excess acidity with the result that pH in the intestines cannot be maintained at indicatively pH 6.5-7.0 and leads to pathological onset in the digestive tract, altered levels of intestinal flora, etc [23].

• **Where we eat is significant** - if we eat in a fast food outlet we are likely to eat more rapidly - the calorific load is consumed in a short period - the consequence being greater fluctuations in insulin and blood glucose levels i.e. hyperglycaemia followed by hypoglycaemia [24]; whereas if we eat more slowly, perhaps over an extended period the relative calorific load is less (the Mediterranean diet). Intriguingly the colour red, perhaps on the walls of a good restaurant, has been shown to stimulate appetite.

• **Where and how we live is significant** - our exposure to light stimulates the pituitary gland which in turn stimulates the thyroid gland and hence influences our metabolic rate; through the pineal gland the levels of ROS scavengers, the antioxidants melatonin and serotonin; and via the skin the level of cholecalciferol (vitamin D3) which influences immune function i.e. exposure to natural sunlight is essential.

• **When we eat is significant** - the body requires a stable series of mealtimes - typically breakfast, lunch and an evening meal. Eating carb. rich meals later in the evenings, elevates blood glucose levels, alters predisposition to sleep and/or the onset and duration of sleep, and is invariably accompanied by increased weight [25].

• **If we sleep later** - (night-owls and/or parents of newborns) or do not enough good quality sleep it becomes harder to regulate body weight [26,27].

• **Where we sleep is significant** - if our bed is uncomfortable or if we have issues which prevent is getting good quality sleep e.g. having hearing problems perhaps from living alongside a noisy road, having a nasal infection or problem, having a spinal problem.

• **If we develop problems in the sexual organs perhaps as a result of a hysterectomy to treat endometriosis** - the body is increasingly unable to regulate blood glucose levels (non-pancreatic diabetes) [28].

• **What and how we exercise** - exercise elevates metabolic rate and hence our ability to metabolise surplus weight [29,30].

…….and to illustrate the somatic consequences of varying degrees of hyper indulgence:

• Why do we engage in hyper indulgent behaviour?- eating and drinking too much of the wrong things over a short/long period expands the volume of the stomach and digestive tract [31]; and which, at its extreme, requires corrective bariatric surgery.

• **How we regulate our weight by dietary means following periods of weight-gain ?** [31,32] - it takes time for the body to adjust to lower levels of food intake and adjust to a lower weight.

Nevertheless, despite the immense body of experiential medical research, there is not yet an accepted recognition of how this plethora of psychosomatic factors influences the body's stable function i.e. at the somatic level; however that the human body is an intensely regulated organism is not in dispute. Every second in every day for ca 70-80 years throughout our lives; from birth throughout our many and various developmental phases until our death; there is a neural mechanism which continuously receives sensory and biological data; which regulates body temperature, the circulation of blood, breathing and/or the supply of oxygen to the brain, blood pressure, blood glucose, intercellular and digestive pH, digestion, elimination of toxins and wastes, and all other essential physiological functions.

Cognitive changes, in particular of sense perception have pathological origins. Perhaps the most convincing explanation to date has been incorporated in the Strannik technology, which is based upon the first mathematical model of the relationship between sense perception, brain function, the autonomic nervous system and physiological systems [16,33-36], and pathological onset; and how this can be applied to screen (as Strannik Virtual Scanning) diabetes and a broad range of other indications [31,40,41], and/or treat (as the neuro modulation technique Strannik Light Therapy (SLT)) their autonomic dysfunction [37-41].

The Body is continuously regulated and Functions at Different Levels of Physiological Significance

Our ability to express proteins and other biologically significant

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moieties declines as we age. By the time we are 75 years we express as little as 10% of the insulin which we expressed when we were in our prime but we do not drop dead. It is only when our demand for insulin exceeds the supply and/or reactivity of insulin (and/or other physiologically significant proteins) that there is a problem i.e. the genetic expression of insulin declines to the extent that it is unable to sustain the required demand for insulin. This illustrates the existence of a multi-level mechanism, acting at the psychosomatic and somatic levels, which continuously regulates and adjusts the stable and coherent function of the autonomic nervous system, physiological systems and ultimately cellular and molecular biology.

The evidence suggests the involvement of the neuro sensory pathways, the brain, neural networks and vagus nerve in the body's function e.g. (i) the role of neural networks in memory and learning [42,43], in diabetes [44-46]; (ii) the effect of stimulating the vagus nerve as a way of regulating blood glucose levels and (iii) that the magnitude and/or longevity of exposure to a psychological/ psychosomatic or somatic factor(s) influences the body's function at different levels of physiological significance i.e. the brain functions in some ways as a parallel processor e.g. the communication between the two halves of the brain which appears to influence our emotional intelligence [47-49]; and in other cases as a serial processor in which the brain functions at different levels of physiological significance, perhaps enabling much greater serial processing when freed from the constraints imposed by emotional processing [50]. Nevertheless, there is not yet a consensus of opinion re what the brain does and how it does it.

The physiological significance of the brain-wave states

The brain-wave states are recognised to be physiologically significant i.e. the magnitude and/or longevity of exposure to stress has neurological and visceral significance. The gamma state (ca. 30-60hz) is associated with subliminal imaging i.e. sensory perception of our environment [51]; the beta state (ca. 15-30 hz) is associated with physical activity and/or movement and/or function [52,53]; the alpha state (ca. 8-15 hz) is associated with sensory input and/or associative thought [54]; however there are no precedents which illustrate that these brain wave states function independently i.e. independently of each other or independently of the theta and delta states which function throughout each 24 hour cycle. The only exception is that in cases of severe trauma (coma) the brain will shut down most, if not all, brain wave activity with the exception of the delta state i.e. the different EEG frequency states are an interdependent and essential element of the body's function [55]. Moreover biochemical changes e.g. resulting from the administration of pharmacological substances, alters the EEG states [56]. This illustrates the existence of a dynamic biophysical relationship which involves the brain's biology, its function, and/or the prevailing brainwave (EEG) state(s) e.g. if we give a stimulant (caffeine, nicotine or adrenaline) or a sedative (ethyl alcohol).The gamma, beta and alpha states characterise the psychosomatic state whereas the theta and delta states characterise the somatic subconscious state. Moreover there are no precedents of the brain functioning independently of the body in the absence of the delta state. Accordingly what is the significance of the somatic state and how is this significant re the diagnosis and/or treatment of diabetes?

The Influence and significance of sleep

The delta oscillations, without which the body cannot function, are particularly associated with the function of the autonomic nervous system. The evidence indicates that the delta (ca. 1-4 hz) and theta states (ca. 4-8 hz) are implicated in the physiological mechanisms which are linked to the body's health, function, stability and survival e.g. during sleep the majority of time is spent in the delta state and hence is associated with the body's complex reparative and regulatory mechanisms [57].

'Sleeping is the second (after being awake) state of active life. Accounting for the information which is absorbed during the day; preparation of the controlling programme for the next day; check-up of the condition of organs and tissues; correction of controlling signals' Grakov IG

Lack of sleep is associated with declining health [58] and pathological onset e.g. of diabetes and obesity, and with poorer fixation and recall of memories thereby implicating the hippocampus and processes such as Long-Term Potentiation (LTP) which is associated with fixation of memories [59,60]. This indicates that sleep performs a physiological significant role and that particular sleep phases are associated with the transfer of memories from the hippocampus to the cerebral cortex i.e. from short term memory to long-term memory, elimination of neurotoxins which is supported by the observation that the brain shrinks during sleep [61,62], the production of HGH; the balance of melatonin and serotonin by the pineal gland; levels of the primary neurotransmitters e.g. gaba, N-acetyl Choline, Nor-epinephrine, dopamine; and the many and various secondary neurotransmitters e.g. beta-endorphin, peptides, secretins, gaseous signalling molecules, amino-acids, etc.

Sleep exhibits the characteristics of a neurally regulated physiological system [63]. Emergent pathologies in any of the organs in this system, and often in adjacent systems, influences the quality and quantity of sleep e.g. in the endocrine glands, spinal cord, ears, nose, etc. It is characterised by the terms hyper and hypo e.g. hypersomnia and/or hyposomnia. There is no other way of explaining why the brain has such immense computing power other than to consider that the brain functions as a neuro modulator which continuously emits and receives sensory and biological datahowever this does not yet define the precise significance of the theta state which appear to be associated with pain and fixation of memories (LTP) [64], perhaps as a limiter of extreme function detecting cellular changes prior to failure.Lack of sleep is accompanied by an increase in levels of neurotoxins which influence the prevailing brain wave state(s) and lead to pathological onset [65].

Further reflections upon the body's multi-level function

The gamma and beta states are associated with the most basic experience - perceiving our environment, the alpha state is associated with the accumulation of memories i.e. of thought or imagination, the theta state is associated with physiological or psychological 'pain' i.e. limits of behaviour/cellular damage which is the most significant learning state, and the delta state is associated with cellular/organ damage and/or repair and/or physiological regulation.

Consider how someone responds with greater urgency to different

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Table 1: Therapy *vs* Brain wave state.

Therapy	Frequency State	Notes
Exercise	beta/alpha/theta/delta	activity-based
CBT	alpha	thought-based
NLP	alpha	thought-based
Yoga	alpha/theta	has a calming effect
Meditation	alpha/theta	expert meditators claim to meditate as low as delta
Hypnosis	theta	binaural-beat induced Theta EEG-activity
		(https://www.monroeinstitute.org/article/3704)
Neuromodulation (Strannik)	theta/delta	acts upon systemic stability/autonomic dysfunction
Sleep	theta/delta	stimulates production of HGH, melatonin, etc
Coma	delta	focus upon neuro-reparative processes

levels of stimuli e.g. a spoken instruction, an irritated instruction, an angry instruction perhaps accompanied by an elevated punishment e.g. a smack, and an explosion of anger and physical punishment e.g. tissue damage or even a broken bone. The significance and/or retention of the memory increases with the degree of the stimulus. The stress experienced at such levels of stimuli influences our ability to concentrate and memory, whilst the memory of physical damage e.g. of a broken leg, is never erased.

The issues can be illustrated by comparison with therapies (note 1) and/or neurological states and/or precedents e.g. CBT, NLP, yoga, meditation, sleep, coma (Table 1). Cognitive therapies influence thought patterns at the cognitive level but have little or no direct effect upon the subconscious somatic levels, however therapies and techniques which influence at the deepest somatic level, the delta state, also influence at the psychosomatic level and have a calming, relaxing effect upon behaviour whilst lack of sleep leads to increasingly manic behaviour [66-68].

The delta and theta states are the dominant neurological states. Traumatic events of varying magnitude or longevity, increased weight and advancing age, influence the stable and coherent function of the autonomic nervous system which influences organ function and is accompanied by changes of cellular and molecular biology e.g.

- Why someone who experiences severe trauma e.g. a bereavement, divorce, or work-related stress, experiences a range of pathological 'symptoms' e.g. heart conditions, aches and pains, migraine/headaches, digestive complaints/ulcerative conditions, etc. The stress is the cause whilst the range of emergent pathologies are the consequences of the problem and often decline when the patient comes to terms with their trauma;

- Why someone who eats and drinks too much of the wrong things becomes diabetic and/or obese e.g. alcoholic [69], acidic [70-72] beverages. The cause of their condition is that they eat and drink too much of the wrong things, for psychosomatic and/or somatic reasons, whilst the resulting diabetes and/or obesity (and the level of HbA1c, blood glucose, etc) is the consequence;

- Stress leads to autonomic dysfunction which leads to changes of molecular and cellular biology, organ biology, the stable and coherent function of the physiological systems, and the process by which the brain regulates and is influenced by changes of autonomic stability;

- But also that blood glucose is a neurally regulated physiological system in which the brain regulates the coherent function of a network of organs with the specific purpose of regulating blood glucose level(s) within optimum limits [73], typically between 4-8mmol/litre;

- and how changes of molecular biology influence the function of the brain and subsequent behaviours e.g. how anti-depressive medication influences brain biology and function [74].

Figure 1 illustrates how biological input, received through the visceral organs, influences the function of the brain which in turn influences the stable and coherent function of the neural networks, physiological systems, organs, and cellular and molecular biology; how sensory input e.g. as stress, alters this dynamic relationship leading to pathological onset (genotype and phenotype) and behavioural change; and how pathological onset leads to changes of sense perception.

This bidirectional flow of 'data' is particularly evident in the diabetic in whom the hypothalamus activates multiple pathways e.g. how levels of leptin (Figure 1) [75-77], insulin, fatty acids, and ghrelin, influence feelings of appetite, hunger, and satiety; and it illustrates how someone prescribed psychotropic medication will often gain weight. The genetic expression of pre-pro-insulin, pro-insulin and insulin (type 1 diabetes) in the pancreas influences brain function and how we experience hunger yet the availability and, in particular, the reactivity of insulin is influenced by how the brain manages the stress response. The elevated levels of acidity arising from exposure to stress (Note 2) influences the rate at which insulin reacts with its reactive substrate IRP2 (insulin resistance), the subsequent entrance of blood glucose into the cell, and its conversion into energy.

Accordingly the therapeutic application of specific EEG states [78] - as brainwave entrainment, brainwave coherence, neuro modulation, neuro feedback or biofeedback, and/or vagal nerve stimulation - has the potential to modulate brain function and hence improve or recover the stable and coherent function of the autonomic nervous system, physiological systems, organs, etc.

The influence of sensory and biological input upon brain function and the medical syndrome diabetes mellitus

The brain receives visual input via the retina (rods and cones) and optic nerve which transmits visual information to the brain, in particular to the Lateral Geniculate Nucleus (LGN), and to the visual cortex in the occipital region at the rear of the brain. It also transmits information to other thalamic brain regions including the pretectal nucleus, midbrain nuclei and suprachiasmatic nucleus; however altered biochemistry(s) e.g. due to the application of drugs applied to the eye to treat glaucoma and of many medical conditions; are associated with changes of colour perception. This indicates the

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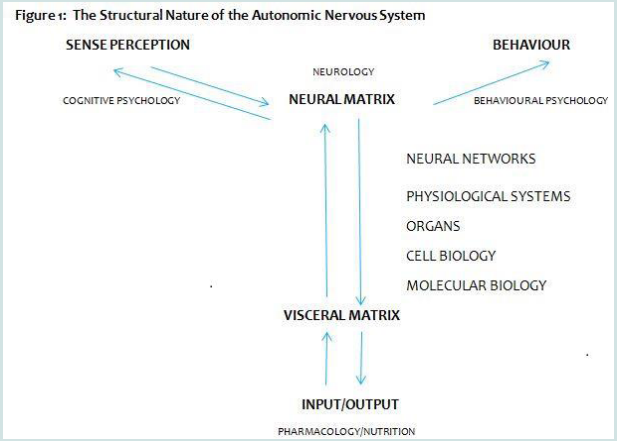

Figure 1: Illustrates how biological input, received through the visceral organs, influences the function of the brain which in turn influences the stable and coherent function of the neural networks, physiological systems, organs, and cellular and molecular biology; how sensory input e.g. as stress, alters this dynamic relationship leading to pathological onset (genotype and phenotype) and behavioural change; and how pathological onset leads to changes of sense perception.

presence of a biological/pathological mechanism which alters colour perception. In addition the brain receives sensory input via the sensory organs e.g. via the retina, which influences the magnocellular and parvocellular pathways in the LGN (widely researched in dyslexia [79-81]) and which has pathological origins [81]. This receipt of sensory data via the amygdala [82,83], converts stress into its pathological coordinates; via the hippocampus influencing regulation of the autonomic nervous system and short-term memory; and the hypothalamus before forwarding information to the cerebral cortex (Note 3).

That the magno and parvo-cellular pathways are significant is evident by noting that loss of vision may occur as a result of brain damage e.g. when these pathways are damaged or destroyed [84,85], and due to the effect of drugs, and pathological onset. Almost all medical conditions, drugs and vaccines influence sense and/or colour perception. Moreover the mechanism which alters colour perception incorporates various parameters of the autonomic nervous system e.g. the ratio of oxyhemoglobin and deoxyhemoglobin in the blood [86]. This is consistent with sense perception having autonomic (pathological) origins i.e. which are genetic and non-genetic (lifestyle-related and/or phenotypic).

Such observations link what we see to the function of the optic nerve whilst the influence of biological/pathological changes links how well we see sensory input, in particular colour and visual contrast, to the presence of pathological factors upon the function of the amygdala, hippocampus, etc.

Changes of colour perception in the diabetic are therefore linked to the function of the autonomic nervous systemand, in particular [87-90], the emission of biophotons being emitted by proteins and other biologically active and significant moieties as they react with their reactive substrates e.g. proteins, enzymes [91,92].

The brain is also fed nutritional input from the visceral organs however it is worth considering whether nutrition can be of value i.e. if the body is short of a particular component this demonstrates that the body's physiology is no longer able to retain this component e.g. a vitamin or mineral. The pathological state becomes the stable base state. Irrespective, this is significant because of the structural relationship in which changes of molecular biology i.e. of genotype and phenotype (note 4) are associated with cellular biology, organ function, the coherent function of the organ networks (the physiological/functional systems) and brain function (conceivably via the neural networks).

This relationship between brain function, the autonomic nervous system and physiological systems, and cellular and molecular biology becomes particularly evident in diabetes and obesity - because the regulation and optimisation of blood glucose is that of a neurally regulated physiological system. This is significant for reasons outlined below:

(i) Type 1 diabetes is commonly associated with the coherent function of >20 genes to express pre-pro-insulin which metabolises rapidly into 'insulin' (the rate is influenced by prevailing pH and level and bioavailability of essential minerals) however the issue is complicated by the observation that the spectrum of genes which express pre-pro-insulin in the Caucasian often differs from the spectrum of genes which express pre-pro-insulin in different racial groups i.e. that the chemical profile of the genes is only part of the mechanism by which the genes express particular proteins (Figure 2) [10-12.93.94].

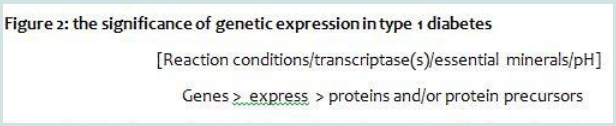

Figure 2: Illustrates how under normal circumstances the genes function in a coherent manner to express a particular protein however this is a chemical reaction which must be influenced by the prevailing levels and reactivity of transcriptase(s) which are often dependent upon the prevailing levels of Mg and Zn. Changes to thegenetic spectrum alters gene conformation [10] and the prevailing energetics and influences the extent to which the genes will express a particular protein..

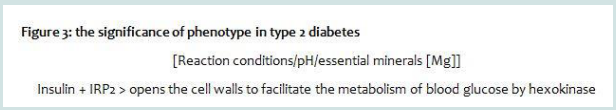

Figure 3: illustrates that the reaction of insulin with its receptor protein IRP2 is a Magnesium dependent reaction which is dependent upon the prevailing pH, the nature of the acidity, and the level of Mg.

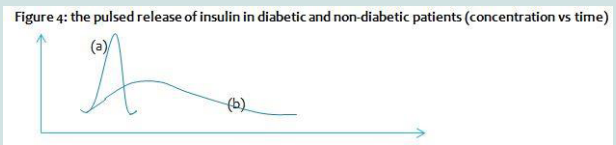

Figure 4: Illustrates how insulin is released in diabetic and non-diabetic patients e.g. the pulsatile release of insulin in the non-diabetic; (b)the pulsatile release of insulin in the diabetic. Studies report the pulsatile release of insulin every 3-5 minutes in the healthy patient and up to 15 minutes in the diabetic patient..

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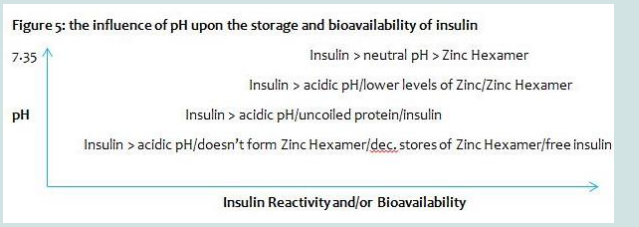

Figure 5: Illustrates how at neutral pH insulin exists in its coiled reactive state and/or is stored as the Zinc Hexamer. As intercellular acidity increases the level and bioavailability of Zinc declines, insulin becomes less coiled and the levels of insulin which are stored as the Zn Hexamer declines. As intercellular acidity declines still further insulin becomes increasingly uncoiled and unreactive with the result that stores of Zn Hexamer in the pancreas decline and need to be supplemented by therapeutic doses of insulin.

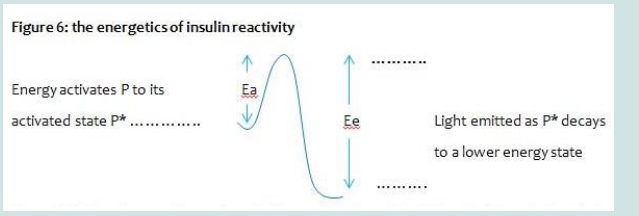

Figure 6: Illustrates how proteins, such as insulin, require to be activated from their base state to their reactive state by energy before they can react. Moreover when insulin reacts it releases energy in the form of light as it decays from its reactive state to its unreactive base state.

Figure 2 illustrates how under normal circumstances the genes function in a coherent manner to express a particular protein however this is a chemical reaction which must be influenced by the prevailing levels and reactivity of transcriptase(s) which are often dependent upon the prevailing levels of Mg and Zn. Changes to the genetic spectrum alters gene conformation [10] and the prevailing energetic and influences the extent to which the genes will express a particular protein.

(ii) Type 2 diabetes is commonly associated with the rate or level at which the genetically expressed insulin reacts with its reactive substrate IRP2. This lack of reactivity is commonly referred to as 'insulin-resistance' so what would make insulin 'resist' reacting with its reactive substrate? (Figure 3).

Figure 3 illustrates that the reaction of insulin with its receptor protein IRP2 is a Magnesium dependent reaction which is dependent upon the prevailing pH, the nature of the acidity, and the level of Mg.

(iii) This raises two significant issues: (a) type 1 and type 2 diabetes are considered to be independent of each other yet they are clearly two consecutive steps in the sequence by which the body metabolises blood glucose. One follows the other which explains why there is often misdiagnosis of type 1 as type 2 and vice versa: because type 1 and type 2 are coexistential comorbidities [95,96]; and (b) what are the factors which could influence the genetic expression of pre-pro-insulin, protein coiling and the reaction of insulin in its coiled state with the insulin precursor IRP2: because pH influences the prevailing levels and/or redox states/bioavailability of essential minerals (in particular of Mg, Zn and Cr) which are essential components in the etiology of diabetes.

(iv) Many metabolic processes involve the essential minerals Mg and Zn. In the case of genetic expression, transcriptase enzymes often require Mg and Zn to be part of their structure and/or to facilitate the genetic expression of pre-pro-insulin. If there is an insufficiency of Mg and Zn the rate of genetic expression can reasonably be expected to decline (Figure 2) [97].

(v) Insulin is a polar entity with -COOH and -NH2 groups at its extremities therefore its chemical/spatial structure/conformation i.e. whether coiled and reactive, or uncoiled and un-reactive, must inevitably be influenced by the prevailing level of intercellular pH.

(vi) Pro-insulin is stored by the pancreatic beta-cells as the zinc-insulin hexamer. It enables insulin to be released in a pulsatile manner according to instructions passed by the brain [98-100]. There is an inverse relationship between the levels of acidity and the storage of the zinc-insulin hexamer. As acidity increases the pulsatile release of insulin extends over a longer period (Figure 4).

Figure 4 illustrates how insulin is released in diabetic and non-diabetic patients e.g. the pulsatile release of insulin in the non-diabetic; (b) the pulsatile release of insulin in the diabetic. Studies report the pulsatile release of insulin every 3-5 minutes in the healthy patient and up to 15 minutes in the diabetic patient.

(vii) The reaction of insulin with its receptor protein is a Mg dependent reaction therefore lower levels of Mg will reduce the rate at which this reaction proceeds (Figure 3) [101].

Accordingly, and in order to explain the significance of this issue it is important to recognise the various dietary and lifestyle factors which influence the regulation of intercellular acidity/pH and consequences thereof.

(viii) Elevated levels of intercellular acidity influences the ability of the pancreas to store insulin as the zinc-insulin hexamer (Figure 5).

Figure 5 illustrates how at neutral pH insulin exists in its coiled reactive state and/or is stored as the Zinc Hexamer. As intercellular acidity increases the level and bioavailability of Zinc declines, insulin becomes less coiled and the levels of insulin which are stored as the Zn Hexamer declines. As intercellular acidity declines still further insulin becomes increasingly uncoiled and un-reactive with the result that stores of Zn Hexamer in the pancreas decline and need to be supplemented by therapeutic doses of insulin.

(ix) At elevated acidity the levels of free radical reactions increase and lead to the onset of glycation reactions e.g. of glycated haemoglobin, insulin, albumin, LDL-cholesterol, etc. There is no evidence that glycation reactions occur at pH 7.35-7.45 or above [102];

(x) The body's inherent bioluminescence is generated by the absorption and release of biophotons of light by proteins (and/or

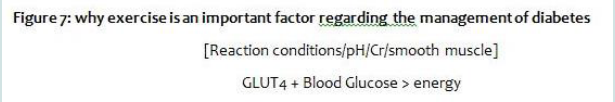

Figure 7: Why exercise is an important factor regarding the management of diabetes.

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other bioactive moieties and/or substrates) as they are elevated to their reactive state and subsequently react with their reactive substrates and then decay to their less reactive or base state(s) (Figure 6).

Figure 6 illustrates how proteins, such as insulin, require to be activated from their base state to their reactive state by energy before they can react. Moreover when insulin reacts it releases energy in the form of light as it decays from its reactive state to its unreactive base state.

Such a phenomena, which is recognised in chemistry and astronomy [73], has both diagnostic and therapeutic significance. It explains how changes of colour perception accompany the onset and progression of diabetes [69-75]; how this can be applied to screen for types 1 and 2 diabetes, and related diabetic comorbidities; and how light can be applied with therapeutic effect [37,38,41]. It enables a cognitive diagnostic technique based upon this observation or principle to track the emergence of type 1 and 2 diabetes from its presymptomatic origins [33-41]; and conceivably at greater levels of sensitivity, accuracy and significance than current diagnostic tests (Note 5).

(xi) When exercising, in order to lose weight, the body consumes energy from the blood and associated reserves e.g. in the liver and muscles as glycogen. Depletion of these reserves, because we exceed the levels stored in the blood and muscles or because we exercise at a rate which consumes more energy than can be supplied from the blood, leads to the conversion of stored body fat from adipose or fatty tissues into fatty acids, or is released as CO_2 following its metabolism.

Significantly the metabolism of blood glucose in smooth muscle is a Cr-dependent reaction therefore the condition/fitness of the smooth muscle, and the prevailing levels and bioavailability of Cr is a factor in the conversion of blood glucose into energy (Figure 7) [103,104].

The metabolism of blood glucose takes place in the smooth muscle. This is a Cr dependent reaction and hence is dependent upon the prevailing intercellular pH. Poor muscle tone, elevated intercellular pH and low levels of essential minerals, often accompanies being diabetic and overweight, and hence influences the patient's energy levels.

(xii) Moreover non-pancreatic forms of diabetes often occurs in patients who have a range of ailments in other organs e.g. following a hysterectomy or due to emergent pathologies in the endocrine organs. The terms hyper/hypo-glycaemia, and acidosis/alkalosis, suggests that blood glucose and pH exhibit the characteristics of neurally regulated physiological systems i.e. networks of organs are regulated by the brain to function coherently and thereby maintain blood glucose and pH within optimal limits.

(xiii) Protein uncoiling e.g. of insulin 'resistance', is not unique to diabetes and hence to our perception of hunger but is also associated with other dietary hormones: leptin (leptin-resistance) which is associated with our feelings of appetite (in the brain), and ghrelin (ghrelin-resistance) which is associated with feelings of satedness (in the gut).

(xiv) The consumption of excess amounts of food leads to expansion of the digestive organs, in particular of the stomach, which influences the levels of ghrelin and feelings of satedness, hence the use of bariatric surgery to treat those with severely extended stomachs [31].

In normally healthy patients excess glucose levels are stored as acyl triglycerides and other complex fatty acids/lipids however the build-up of such moieties in diabetic patients, in particular omega-6 and saturated fatty acids, are pro-inflammatory and associated with pathological onset whilst others are less/anti-inflammatory e.g. eicosapentaenoic acid and docosahexaenoic acid [105].

The pathological significance of pH

Under acidic conditions free radical/oxidative stress reactions initiate the conversion of excess glucose and other free sugars (e.g. fructose, galactose, etc) into glycated metabolites of proteins e.g. glycated haemoglobin [106], glycated LDL cholesterol, glycated insulin, glycated albumin, advanced glycation end products, etc.

A significant body of evidence links elevated levels of free iron with the etiology of diabetes [107,108]; free radical reactions occur in the eye [109]; and, significantly, that antioxidants have a therapeutic effect [110,111].

Increased blood viscosity arising from elevated levels of blood glucose, glycated proteins and other viscosity enhancing (thickening) moieties e.g. elevated blood cell count; influences the ability of the heart to deliver blood throughout the blood and peripheral blood vessels [112,113], and hence influence the function of the brain, lungs, brain, kidneys [114], liver, etc; and how pathological onset in any of the visceral organs (in particular the pancreas, pituitary, thyroid and adrenal glands, heart kidneys, liver, etc) influence the stable and coherent function of the physiological systems which are directly implicated in the regulation of blood glucose e.g. sleep, pH, blood pressure (Figure 1).

Moreover, as each organ is a component in the various organ networks (physiological systems) which are designed to regulate key functional parameters, this illustrates the interplay between the various physiological systems e.g. pH, blood glucose, blood pressure, temperature, blood cell count [115,116], breathing, sexual function, blood volume, elimination of toxins and/or wastes, and ultimately with what we eat and drink. In diabetes, the most significant physiological systems are the regulation of blood glucose, pH and sleep [63,117-119].

Many medical conditions have a neurological basis or are influenced by the function of the brain. In scoliosis it is recognised that the condition often has neurological origins [120]. In cancer research the study of neuro-oncology is based upon recognition that the brain plays a role in the onset of cancer. In the study of diabetes, in particular in neuroendocrinology, there is recognition of the influence of the brain and the endocrine glands. The brain, in particular (but not exclusively) the hypothalamus, controls the secretion of pituitary gland hormones, which influence numerous interconnections involving the endocrine and nervous system(s). This illustrates the convergence of the neurological paradigm with the biomedical paradigm because the brain and endocrines (adrenal, pituitary and thyroid glands/organs) are component organs in many of the body's physiological and/or functional systems.

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There is also a relationship between the different physiological systems and the organs in each system e.g. that patients who undergo a hysterectomy often have problems regulating blood glucose (non-pancreatic diabetes); whilst recent research has indicated that glucose can trigger sleepiness after a meal by triggering neurons in the hypothalamus which participate in the regulation of sleep [121]. This illustrates how instability in one physiological system can influence the stability and function of other physiologically adjacent systems and/or organs. Moreover the observation that there is a neural network which connects various areas of the cerebral cortex to the adrenal gland illustrates the link between brain function [122], the neural networks, the autonomic nervous system and pathological onset.

Current research is now exploring the connection between neural networks and diabetes although restricted to artificial neural networks which perhaps illustrates an adherence to current etiology rather than a fundamental consideration, or understanding, of the complex nature of diabetes however there is now an emerging consensus that the brain is involved in the management of diabetes, in particular via the hypothalamus and the autonomic nervous system although the focus of research appears to be focused upon the changes which occur as a result of pathological onset rather than considering the fundamental control mechanism provided by the brain [47,123-125].

The issue is complicated as researchers invariably continue to seek a 'magic bullet' which can be used to provide an immediate 'fix' e.g. via a drug, or an electric stimulus via implants which are attached to the nervous system; and thereby ignore the complex nature of the body's function i.e. the neural regulation of the autonomic nervous system and physiological systems, and how it is naturally influenced by sensory input.

Strannik Case Studies

The Strannik technology is based upon a precise and sophisticated neural simulation and/or mathematical model of how the brain receives sensory input, and how such sensory data sets can influence brain function and the regulation of the autonomic nervous system, physiological systems, organs, and cellular and molecular biology. We report in this paper a series of case studies, reported by medical doctors at the study clinics, in which diabetic patients have been screened and treated using the Strannik technology:

In the following case studies Strannik Virtual Scanning was used, alongside other diagnostic tests and observations by the GP, to determine the patient's health before determining the specific parameters required for a course of Strannik Light Therapy i.e. which was appropriate for their condition.

Patient: male; 55 y.o.

Diagnosis: weight 104 kgs, essential hypertension. After forty sessions of the additional 'overweight protection' SLT course the patient's weight declined by 21 kilos, cardiovascular indices stabilised, sleep and work efficiency restored.

Patient: female; 65 y.o.

Diagnosis: weight 93 kgs. The patient was diagnosed with dyscirculatory encephalopathy, hearing loss, sinusitis, calcium deficiency, hepatitis A, cholecystitis, pancreatitis, cardiomyopathy, heart arrhythmia, iron deficiency, gastroduodenitis, irritable bowel syndrome, osteochondrosis with neurological symptoms. The organism was unable to maintain normal levels of blood glucose, circulating blood volume and blood pressure. Nine organs were organically changed. The client was prescribed the 'anti-aging' and the 'overweight protection' SLT courses. After a course of SLT the patient's condition had improved, the organic changes of the organs were absent, and weight reduced to 84 kgs, a loss of 9kgs.

Patient: male; 64 y.o.

Diagnosis: diabetes; diabetic angiopathy; kidney failure. After 14 days of using the SLT program, the cardiologist reduced the dose of insulin injected from 32 to 22 units.

Patient: male; 50 y.o.

Diagnosis: diabetes. Blood sugar test revealed 8 mmol/liter; reduced to 6.5 mmol/litre after a course of SLT.

Patient: female; 55 y.o.

Diagnosis: weight 78 kgs. By the 50th day of the anti-aging SLT course the patient's weight declined by 5 kgs without any special diet.

Patient: male; 53 y.o.

Diagnosis: weight 85 kgs. The patient complained of heart pain, headache caused by changes of arterial tension; and infarction of posterior wall of the left ventricle of the heart. After first month of the 'anti-aging' SLT course, vision improved; blood pressure stabilized at 120/75, the patient stopped taking medicine.

Patient: female; 53 y.o.

Diagnosis: weight 87 kgs. The patient complained of excess weight and essential hypertension. After 20 sessions of SLT course, the patient's weight declined by 11 kgs and 12 cms around the waist; had lack of appetite; arterial tension stabilized.

Patient: female; 43 y.o.

Diagnosis: diabetes, type 2, weight 96 kgs, prescribed insulin. After the 'anti-aging' SLT course, the patient's weight declined by 5 kgs, working efficiency increased, blood sugar level reduced, sugar and ketone bodies in urine were absent, diuresis reduced. The patient stopped taking insulin, now taking antihyperglycemic drugs.

Patient: male; 79 y.o.

Diagnosis: swollen foot (diabetic foot ulcer), type 1 diabetic, lack of mobility. After 3-6 months of SLT his swollen foot was no longer swollen and he had fully recovered his mobility.

Patient: male; 23 y.o; narcotic dependence.

Diagnosis: diabetes, 1 type, heavy form, diabetic encephalopathy, polyneuropathy, microangiopathy, blood glucose at 10-17 mmol/l. The patient was receiving up to 40 units per day of insulin. After 5 sessions of SLT the level of sugar in the blood was lowered to 5 mmol/l, and was accompanied by hypoglycaemia. It stabilized at 7-8 mmol/l. The insulin dose and drug dependency were decreased.

Conclusion

The traditional view or etiology of diabetes is based upon consideration of the effectiveness of the pancreas to express pre-

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pro-insulin and the reactivity of insulin, commonly referred to as 'insulin-resistance'however the author suggests in this paper specific shortcomings with the prevailing etiology of diabetes mellitus:

(i) Diabetes is considered to be a problem which is solely associated with the function of the pancreas whereas the evidence suggests that it is a multisystemic, multipathological and polygenomic disorder;

(ii) Diabetes is considered to be a problem of the pancreas whereas the evidence suggests that it is a problem associated with the neural regulation of the physiological system which regulates blood glucose levels and hence that pathological onset in organs and related systems i.e. other than the pancreas, may influence blood glucose levels;

(iii) Diabetes is considered to be two distinct pathologies in which impaired genetic expression of insulin and subsequent insulin reactivity are the most common diabetic symptoms yet the evidence suggests that in most cases diabetes is a problem of type 1 AND type 2 diabetes i.e. the two conditions are co-existential morbidities, thereby illustrating that there is a need for more sophisticated ways of diagnosing diabetes;

(iv) Understanding the fundamental mechanisms by which the brain regulates blood glucose levels has significant diagnostic and therapeutic potential.

An increasing body of evidence illustrates that the brain plays a fundamental role regulating the function of the autonomic nervous system [126,127], and its effect upon energy balance and glucose homeostasis i.e. through its relationship with the physiological systems, organs and/or tissues. That it involves how the senses function is clearly evident but it must also include e.g. the role of the amygdala (receives and processes sensory data), hypothalamus (generates neuroendocrine output/hormones), brain stem, hippocampus (short-term memory) [128], cerebral cortex (long-term memory) [129], and the transmitting mechanism - the vagus nerve; which are implicated in this enormously sophisticated process; and hence which play an immensely significant role in the regulation of blood glucose levels by the coherent and biodynamic function of the brain with the pancreas, endocrines, etc. [130-133].

The case studies presented illustrate how such knowledge can be applied with therapeutic effect to achieve outcomes which appear to be beyond that which is possible using drugs (which treat the symptoms and fail to take into account the complexity of the condition) and which has the potential to enhance how the patient is screened and/or treated. Examples are presented of how this can be used to treat weight problems, diabetic foot ulcer, high blood pressure, erectile dysfunction, mental health issues, and influence cognitive decline and/or the aging process.

This illustrates the existence of a complex neurally regulated mechanism - a regulated network of organ networks - which continuously monitors and adjusts levels of all physiologically significant parameters including, but not limited to, blood glucose i.e. that the multilevel function of the brain is the dominant characteristic which via the senses continuously monitors and adjusts our nutritional requirements (that under normal non-pathological conditions that the brain is able to exert an extraordinarily fine level of control of calorific intake); yet is continuously influenced at the psychosomatic level by the effect of stress upon brain function and the autonomic nervous system, and by emergent pathologies (of genetic and/or non-genetic origins) in the visceral organs in this and other physiological systems.

Moreover the rate of supply of food is as critical to the flow of energy as the rate of supply of insulin, perhaps more so. If the supply of calories increases significantly this stimulates the supply of insulin whereas under acidic conditions normal or elevated levels of insulin will be accompanied by feelings of appetite and hunger. The issues are complicated by variations of acidity which alter protein reactivity, in particular (but not solely) of leptin, insulin and ghrelin which influence our feelings of appetite, hunger and satedness; and the emergence of pathological onset in other organs and systems e.g. explaining the phenomena of non-pancreatic diabetes in which the patient e.g. following a hysterectomy, has problems regulating blood glucose levels.

In light of the issues reviewed in this paper the author makes the following conclusions and/or recommendations e.g.

- Insulin is supplied mainly by the pancreas but also to a lesser extent by other endocrine organs therefore the focus upon the pancreas can only be part of the etiology of diabetes;
- The pancreas is only one of the organs in the physiological system which regulates blood glucose levels therefore pathological onset in other organs within this system must also contribute to variations in blood glucose levels;
- The brain is intimately involved in the regulation of blood glucose levels and dysfunction of this mechanism is experienced as diabetes and comorbidities in other organs and systems;
- Problems of blood glucose regulation (diabetes) may occur in patients with a normally functioning pancreas;
- When considering diabetes from the current perspective, in particular the genetic expression of insulin and 'insulin resistance', type 1 and type 2 diabetes are co-existential comorbidities;
- Protein reactivity e.g. of leptin, insulin and ghrelin (and hence our feelings of appetite, hunger and satedness) - is influenced by the prevailing level of intercellular pH;
- Sleep exhibits the characteristics of a physiological system and hence that lack of good quality sleep influences brain function and autonomic control;
- The brain plays a fundamental role regulating and optimising blood glucose levels, and levels of all the body's essential functional parameters;
- The brain uses a complex mechanism involving frequency and light to regulate the body's autonomic stability and function;
- Knowledge of how the brain functions, which is incorporated in the mathematical model developed by Grakov IG, can be used with significant diagnostic and therapeutic effect, and achieve therapeutic outcomes which are comparable with what can be achieved by biomedicine and in some circumstances are better than can be achieved using drugs

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• Improved autonomic control influences sense perception e.g. feelings of appetite, hunger and satedness;

• The different brain wave states are associated with different levels of cellular and molecular biology;

• Instability in other, apparently unrelated, physiological systems may lead to problems of blood glucose regulation i.e. as the brain seeks to optimise the body's physiological stability.

Conflicts of Interest:

The author is Chief Executive of Mimex Montague Healthcare, a company which is devoted to the commercialisation of the Strannik technology developed by Dr Igor Gennadyevich Grakov.

Notes

[1] many/various techniques have been developed which claim/provide their therapeutic effect by providing stimulation at various EEG frequencies e.g. HeartMath, Strannik Light Therapy, Brightstar Learning, AddBrain, etc; an industry of estimated value USD10-20BN pa (Table 1).

[2] In this paper stress is considered in a wider context than the more usual psychological context i.e. to include the stress of excess weight.

[3] The limbic structure; including the thalamus, hypothalamus, etc; is associated with emotional changes e.g. are widely considered to be associated with hunger, aversion, sexuality, extremes of pleasure and displeasure, aggressiveness, fear, etc.

[4] This paper uses the terms genotype and phenotype to define (i) genotype: the rate and extent to which the genes express a particular protein or other biologically active moiety and (ii) phenotype: the non-genetic component by which the environment and/or stress inhibits the rate at which a particular protein or other biologically active moiety reacts with its reactive substrate (the autonomic response).

[5] The eyes respond to as little as 7*10^2 biophotons per second.

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