International Scholars Journals

African Journal of Internal Medicine ISSN 2326-7283 Vol. 3 (9), pp. 202-214, October, 2015. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Review

A study of the interaction of the free chemical energy that emanates from the melanin with some intracellular processes

***Miguel J. Iberio, Rockdrigo M. N and Eraclio Coffman Yunes**

Department of Microbiology, Faculty of Medicine, Universidad Veracruzana, Xalapa, Mexico.

Accepted 26 July, 2015

AD is the most common age-related neurodegenerative disorder affecting elderly populations over the age of 65. Characteristic symptoms of AD include progressive memory loss, declining cognition, impaired linguistic function, and dementia. Pathologically, the brain exhibits extensive synapse and neuronal cell loss, as well as the appearance of Neurofibrillary Tangles (NFT) and senile plaques, associated with widespread oxidative stress and damage. Recent research suggests that glucolytic enzymes, that is (GAPDH) that has been studied in relation AD, possesses highly diverse, non-glucolytic functions, as its expression and activity are affected by multiple factors. Taking into consideration the multitude of functions GAPDH can carry out under normal conditions, in addition to a variety of sub-cellular locations, it is not surprising that this enzyme is so often affected by disease pathology.

Key words: Alzheimer, melanin, photosynthesis, glucose, ATP, energy, mitochondria.

INTRODUCTION

The aim of this study is to clarify the interaction of the free chemical energy that emanates from the melanin with some intracellular processes, as it was a previously unknown process. The expression of genes has a fundamental requirement: sufficient free chemical energy into the cell and the findings about epi and metagenetics is a proof, and expression of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) [Brown et al., 2004] is not an exception. By other side the activity of this and any enzyme, requires energy (sufficient intracellular free chemical energy) despite highly diverse, glucolytic or not, functions. Thereby the growing idea that AD is an energy problem is right, overall taking into account our finding that eukaryotic cell is able to take energy from water by means of the intrinsic property of melanin (previously unknown) to split and re-form the water molecule, termed as human photosynthesis by analogy with the irreversible water dissociation that happens in plants.

The thesis of glucose as source of energy has major inconsistencies beginning with the non-yet proved Mitchell's Chemiosmotic Theory about ATP formation, and by other side if it were really glucose energy source, diabetic patients should then be able to fly.

Thereby glucose as an energy source par excellence, although it is a concept deeply rooted, just keep being a model has even become dogma but is not possible to position it as a high-level theory.

ENERGY AND ALZHEIMER´S DISEASE

Brain cells are highly energy dependent for maintaining ion homeostasis during high metabolic activity [Parihar et al., 2007]. Full mitochondrial function is essential to generate ATP (theoretically) from electrons that originate

*Corresponding author. E-mail: miguel _iberio24@gmail.com

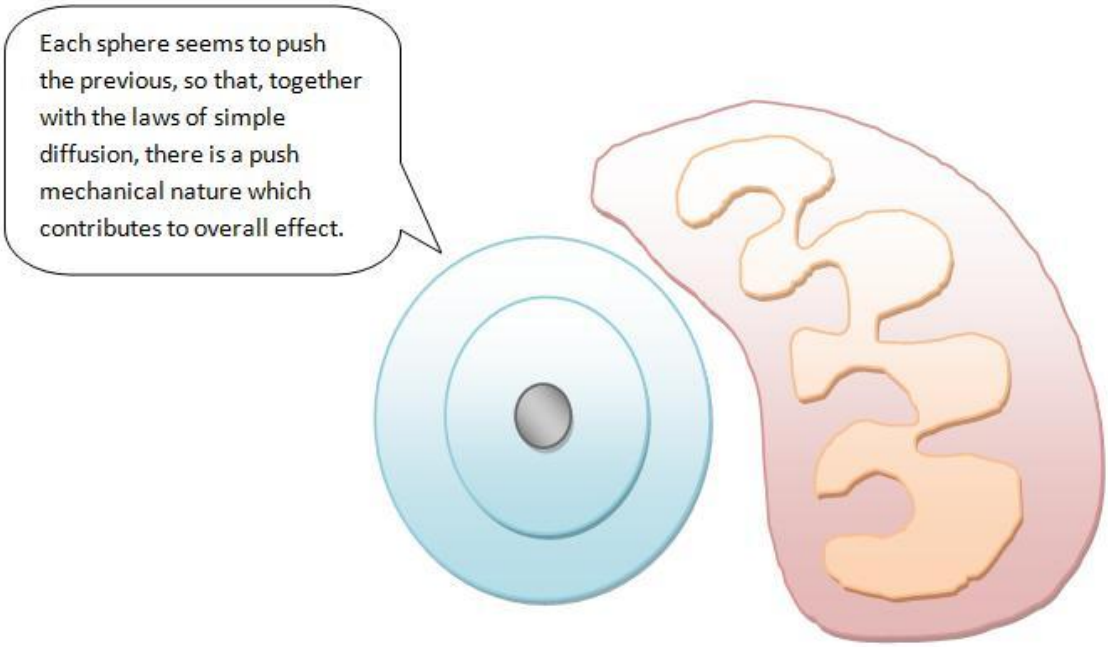

Figure 1. Human photosynthesis is the energy source of the mitochondria.

with the oxidation of NADH. Decreasing brain metabolism is a significant cause of cognitive abnormalities of Alzheimer disease (AD), but it remains uncertain whether this is the cause of further pathology or whether synaptic loss results in a lower energy demand.

But back to the mitochondria, the maintenance of a gradient of protons requires sufficient free chemical energy. When these energy levels are low, mitochondria tend to be depolarized producing thereby higher levels of superoxide anion and other oxidants [Mangialasche et al., 2010]. Theoretically, without a steady supply of ATP molecules, cells die within seconds. More accurately without a stable source of energy the cell dies in a few seconds. Remember that energy is defined as anything that produces a change, whatever it may be.

Human photosynthesis is the energy source of the mitochondria

Energy spreads symmetrically in all directions, as spheres which possess increased each different physicochemical properties, as in the first there will be elevated levels of diatomic hydrogen, which leads to the energy beyond that does not mix with the surrounding water, and also levels high diatomic oxygen which is one of the most stable molecules known, and the next field will contain high levels of re-formed water which flow genre 4 high energy electrons for every two molecules of water re-formed. When levels of free chemical energy within the internal environment of the cell decreases, then the mitochondria tend to be depolarized and therefore generate a greater number of reactive oxygen species (Solis-Herrera, 2013) (Figure 1).

Free chemical energy must be available for the work of synthesizing new cellular material, as neurotransmitters, membrane receptors, maintaining membranes and organelles, active transport [Mikirova et al., 2004], etc. Determination of the concentration of adenosine-5´-triphosphate (ATP) may asses the metabolic (not energy) state in cells. Cellular ATP seems as an important determinant of cell death by apoptosis or necrosis, but not because it is considered (theoretically) the universal currency of energy exchange, because in fact we do not know for sure, since Mitchells chemiosmotic theory, after more than 50 years that was proposed, has not been established conclusively, to date remains more as a study model than a high-level theory.

Proton gradient model of the mitochondrial intermembrane space based on human photosynthesis

Model of the conformation of the proton gradient in the mitochondria inter-membrane space based in our finding of the intrinsic property of melanin to dissociate and re-form the water molecule, producing, therefore, free

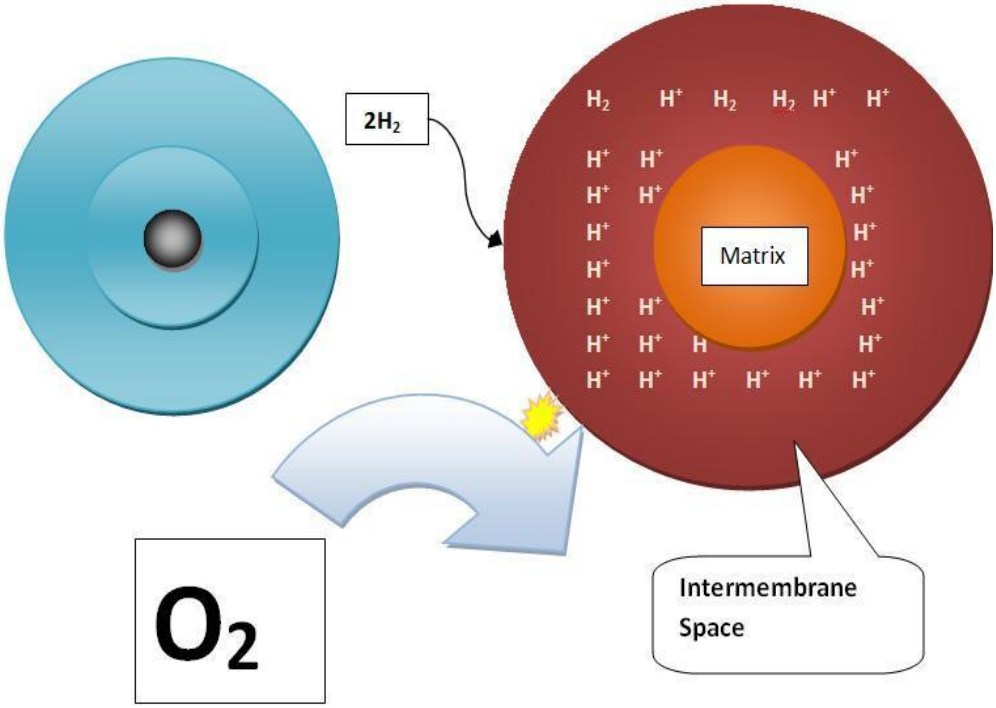

Figure 2. Proton gradient model of the mitochondrial Intermembrane space based on human photosynthesis.

chemical energy. The diatomic hydrogen and oxygen represented in the schema as $2H_2$ and O_2 come from melanin molecule (Dark circle) surrounded by the growing spheres of energy. Do not lose sight that the molecular hydrogen, the ultimate energy carrier, not only in the human body but in the entire universe, does not mix with the water (Solís-Herrera, 2013) (Figure 2).

But yet, in light of the discovery of human photosynthesis, mitochondrial functions should be reconsider. An in depth discussions will not be taken about the ATP, of which there are numerous examples in the literature, I will refer only to certain details that are important as each molecule of ATP the terminal phosphate is added and removed 3 times each minute (Kornberg, 1989: 65). We might think that one of the main functions of mitochondria is the regulation of the phosphate groups (Pi), given that high levels of such is toxic to the cell.

Mitochondria as regulator of the levels of phosphate groups

Phosphate is critical for a vast array of cellular processes. Phosphate is one of the major components of the skeleton, providing mineral strength to bone. Phosphate is an integral component of the nucleic acids that make up DNA and RNA. More important the phosphate groups of ATP are not able to carry the energy required for all cellular functions. Furthermore phosphate functions as a buffer in bone, serum, and urine.

The addition and deletion of phosphate groups to enzymes and proteins are common mechanisms for the regulation of their activity, but this remarkable effect is due to the energy level of the molecules involved (enzymes or proteins) are modified, but not by the alleged energy that carry phosphate groups, but because them changes their relationship with the free chemical energy emanating from the melanin molecule.

Phosphate groups as any molecule actually possesses some degree of energy, but this energy does not have the right characteristics to be part of the equation of life, because the size of it and how could free is not as constant, uniform and unique as energy free chemistry that conducts the melanin.

By other side the study model of the ATP as the universal currency of energy exchange presents serious inconsistencies. For example, suppose that links of low energy are transformed into high-energy phosphate bonds, this required no doubt the presence of sufficient free chemical energy, thereby To create a high-energy bond is essential to have energy that previously, so it is only possible its translocation. Recall that energy is not created or destroyed, only transformed. In other words it is not possible to create a high-energy bond. Secondly, when the molecule of ATP is degraded to ADP also requires the presence of sufficient free chemical energy. So: from which so much energy? Remember that energy

is defined as anything that produces a change, whatever it may be.

ATP: THE PERFECT PHOSPHATE GROUPS CURRENCY FOR THE CELL?

Phosphate is widely distributed and an adequate balance is required for maintaining essential cellular and organ functions [Ohnishi and Razzaque, 2013] and in turn this balance requires the presence of sufficient free chemical energy. Dysregulation of phosphate balance, this may be a response to low or inadequate levels of free chemical energy which always requires the eukaryotic cell to function, and can manifest either in the form of hypophosphatemia or hyperphosphatemia can induce disorders ranging from rickets/osteomalacia to cardiovascular calcification. The more melanin you have a cell; have more affinity for calcium to a thousand times more. Only the bone has a higher affinity, but Calcium is only deposited in mineral form.

A physiologic phosphate balance is delicately maintained by multiorgan cross-talks among the intestine, kidney and bone. But this multi organ cross talk is not for free because it requires the concatenation by multiple chemical sequences that must occur in different parts of the organism in time and form, and of whose synchronization know very little or nothing, as we cannot deny that there is a internal harmony, but we have no clear idea of as is carried out.

Serum phosphate is maintained within certain range by intestinal phosphate absorption [Fukumoto, 2010] (that requires energy), renal phosphate handling (also requires available free chemical energy); and dynamic equilibrium with intracellular phosphate, that indeed requires free chemical energy and ATP but just as phosphate groups (Pi) exchange currency, or phosphate in bone. Renal Phosphate handling is believed to be the main determinant of the serum phosphate level at least in a chronic state. The filtration and reabsorption of phosphate through the kidney are processes that require free chemical energy in steadily and sufficient manner.

SUGAR: A SOURCE OF CARBON CHAINS

Sugar is vital to all organisms. Bacteria, plants, animals and humans use glucose and other sugars as a source of building blocks for synthesis of biomass. Therefore, it is very important to keep the intracellular sugar concentration at the right level.

After taking in glucose into their cells, the cell first attach a phosphate group to the sugar molecule, and this seemingly simple step, phosphorylation, also requires the presence of free chemistry energy. This prevents the glucose from freely leaving the cell. At the same time, the glucose is made available as a building block source in this way. As essential as glucose may be to the cell, in turn, the cell react to excessive sugar levels with a stress response. A mechanism that has been described is that a small RNA molecule leads to a reduction in the quantity of transporter molecules responsible for importing sugar into the cell. Besides that high intra cellular sugar levels activates an enzyme responsible for removing the phosphate group from glucose and other sugars, allowing the sugar molecules to flow practically all by themselves out of the cell.

Sugar or saccharides are essential components of all living things. The biology of saccharide (sugar chains or glycans) is studied by Glycobiology which is defined as the study of the structure, biosynthesis, and biology of saccharide. Glycobiology is fast emerging as a primary field of interest of biomolecular and biomedical research around the globe. Once considered merely supporting structures, the sugars have now been widely recognized to be vital components in running the complex machinery of life itself.

The metabolism (from Greek metabole: to change) of glucose requires free chemical energy, because any change requires energy.

WHEN ATP IS DEGRADED TO ADP ENERGY IS ABSORBED

When the ADP is converted into ATP, the energy is released, and when the ATP goes to ADP then energy is absorbed. Our model is totally opposed to the traditional model based on the chemiosmotic theory of Mitchell. Moreover, both reactions require to be activated by free chemical energy (Solís Herrera, 2013) (Figure 3).

The mitochondria´s electrochemical gradient requires of free chemical energy to form and stay

The mitochondrion itself functions to produce an electrical chemical gradient-somewhat like a battery-by accumulating hydrogen ions in the space between the inner and outer membrane. An electrochemical gradient in an aqueous medium requires the constant presence of free chemical energy, starting for the generation, maintenance and modulation of the process itself and of the involved actors in the series of action or steps necessary to achieve it, such as mitochondrial structure, the corresponding enzymes such as ATP synthase, which consists of a sequence of 500 amino acids, the complexes of the OXPHOS, and so on, thereby each and every one of them requires energy constantly from start to finish, and not only to function properly and thus synchronized with the rest of the processes intra and extra-mitochondrial but also with, in addition; to the energy required to maintain the shape or structure of the molecule in question. These mitochondria particularities

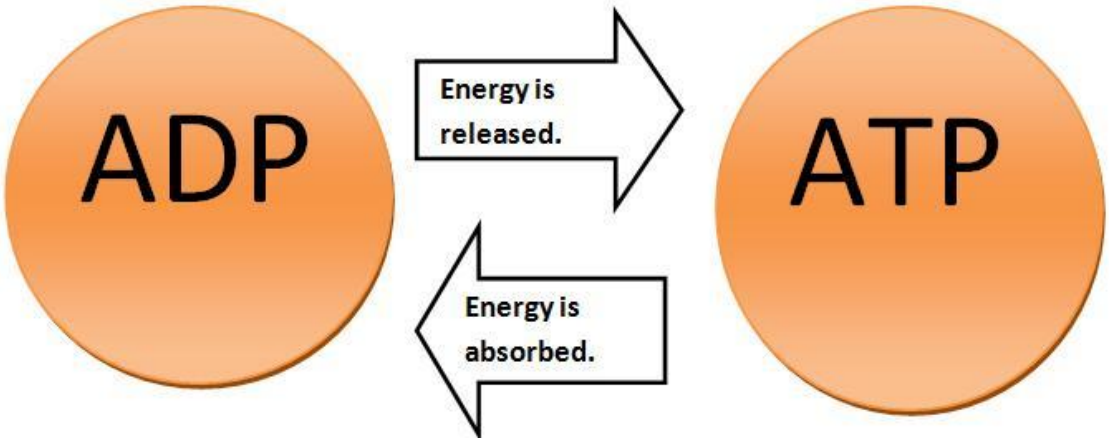

Figure 3. When ATP is degraded to ADP energy is absorbed.

are very consistent with our finding, previously unknown, that the eukaryotic cell is capable of break and re-forms the water molecule. This implies that the human body is able to use water as a source of electrons or energy, which, apart from that was not previously known, breaks the old dogma of glucose as an energy source par excellence to small pieces.

TABLE COMPARING THE FIRST REACTION OF PHOTOSYNTHESIS IN PLANTS AND HUMANS

Photosynthesis in plants involves a series of reactions not yet understood by the plant which fuses the CO_2 with water to form glucose. The lower reaction corresponds to Solis-Herrera cycle. By analogy, the lower reaction we call human photosynthesis, which is completely descriptive term (Solís-Herrera, 2013).

$2H_2O \rightarrow 2H_2 + O_2$

The first step of Photosynthesis plants

$2H_2O \leftrightarrow 2H_2 + O_2 + 4e^-$

The first step of Photosynthesis in humans

How does this potential difference into inter-membrane space serve to reattach the phosphates on ADP molecules? The more protons there are in an area, the more they repel each other. When the repulsion reaches a certain level, the hydrogens ions are forced out of a revolving-door-like structure mounted on the inner mitochondria membrane called *ATP synthase* complexes. This enzyme functions to reattach the phosphates to the ADP molecules, again forming ATP. The ultimate source of building blocks for constructing ATP is food. The average daily intake of 2,500 food calories translates into a turnover of a whopping 180 kg (400 lbs) of ATP. We would be at the miracle of fish and loaves and this on a daily basis. More over: in each and every cell of our body? It is difficult to understand and less to accept, in my opinion we must look for more acceptable explanation from the scientific point of view.

And the amazing ability of the eukaryotic cell to make energy from water through the use of the intrinsic property of the Melanin molecule, a previously unknown fact, to dissociate and re-form the water molecule is a valid conceptual revolution it.

THE COMPLEXITY OF CELL ATP SYSTEM

How adenosine mono-phosphate (AMP) is built up into ATP again illustrates the precision and the complexity of the cell ATP (not energy) system. The enzymes used in glycolysis, the citric acid cycle, and the electron transport system, are all so precise that they will replace only a *single* phosphate. They cannot add *two* new phosphates to an AMP molecule to form ATP.

The solution is an intricate enzyme called *adenylate kinase* which transfers a *single* phosphate from an ATP to the AMP, producing *two* ADP molecules. The two ADP molecules can then enter the normal Krebs cycle designed to convert ADP into ATP.

Adenylate kinase is a highly organized but compact enzyme with its active site located deep within the molecule. The deep active site is required because the reactions it catalyzes are sensitive to water. If water molecules lodged between the ATP and the AMP, then the phosphate might break ATP into ADP and a free phosphate instead of transferring a phosphate from ATP to AMP to form ADP.

To prevent this, adenylate kinase is designed so that the active site is at the *end* of a channel deep in the structure which closes around AMP and ATP, shielding the reaction from water. Often enzymes catalyze the two reactions in series by providing a structural scaffold that

Figure 4. Macro-photography of Melanin, the human chlorophyll (Solís-Herrera, 2013).

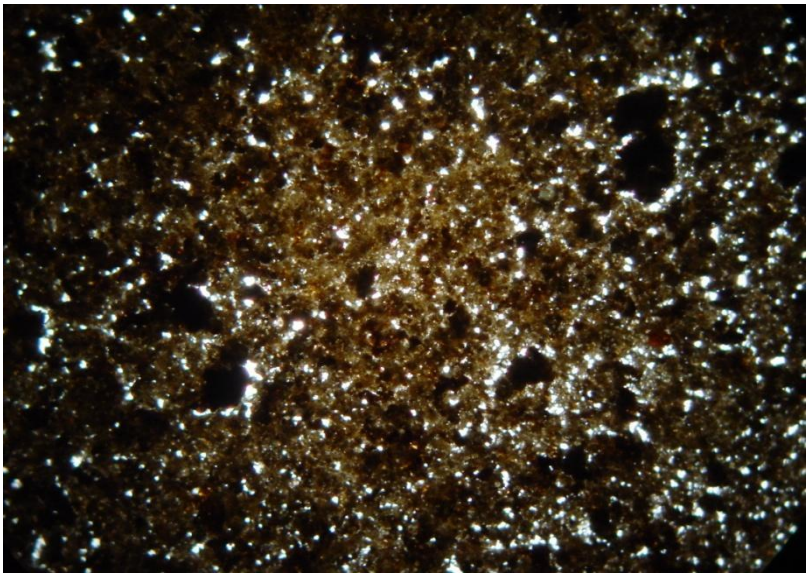

Figure 5. Micro-photography of Melanin, darkest substance known (Solís-Herrera, 2013).

optimally orients the two reactants (substrates) to promote a group transfer reaction from donor X to acceptor Y. Note that ATP is a *Pi -coupling agent* and *not* a fuel. It is not a storehouse of energy set aside for some future need. Melanin is the darkest and more stable substance that man has known (Figures 4 and 5).

ALZHEIMER´S DISEASE AND THE FREE CHEMICAL ENERGY

Many molecular lesions have been detected in Alzheimer´s disease [Querfurth et al., 2010], resulting in oxidative and inflammatory damage, which in turn leads to energy failure and synaptic dysfunction. Brain plaques plenty of β-amyloid peptide (Aβ) is one of many frequent pathological findings in Alzheimer patients. But why are there and the role they play in the development of the disease is still incomprehensible.

Aβ peptides are natural products of metabolism consisting of 36 to 43 aminoacids which originate from proteolysis of the amyloid precursor protein by sequential enzymatic actions of BACE-1, β-secretase and γ-secretase. It is believed to be an imbalance between

production and clearance, and aggregation of peptides causes Aβ to accumulate; and perhaps this would be the factor that triggers the Alzheimer´s disease, what constitutes the base of the amyloid hypothesis. Unfortunately manipulability of such events (production and clearance), which is in any process, a firm scientific validity criterion has failed again and again. The evolution of Alzheimer's disease is not changed even though it has been inclusive, to the disappearance of amyloid plaques. This has been proven by autopsy, but the dementia is not modified in the slightest.

Both the production and the clearance of Aβ peptides are processes that have a very first common requirement: free chemical energy.

It is not easy to understand the presence of amyloid beta in the nervous tissues, as for example the neuronal activation rapidly increases Aβ secretion at the synapse, a process tied to the normal release of vesicle containing neurotransmitters. Therefore AB levels are critical, and you may get them under control very complex and precise, plus dynamic, that is changing, as is usually able to adapt to the constant changes that occur as a result of the interaction between the intricate biochemical processes of neural tissue, which is beyond our grasp because they are the result of four billion years of evolution, and the environment too, which is complex because it also includes the presence of factors such as light intensity, humidity, pressure, temperature, type of feeding, age, sex, etc. e.g. sunlight changes every minute.

It is not possible to know all the mechanisms involved in the regulation of the steady state levels of Aβ. Some of the implied molecules already described in the literature are:

- Neprilizyn, an endopeptidase that degrades Aβ monomers and oligomers [Kanemitsu et al., 2003]. Insulin-degrading enzyme, a metalloendopeptidase, molecule containing sulphihydril group; degrades small peptides such as insulin and monomeric Aβ [Qiu et al., 1998]. Both neprilysin as insulin-degrading enzyme requires the presence of free chemical energy, not only to carry out their work appropriately, as this energy is required from the beginning, during and for the termination of it, but also up to retain the shape of the molecules themselves, then remember that they are immersed in water, which is a compound that tends to dissolve anything that is in it.

- And with free chemical energy I am not referring to ATP. Because on one hand the ATP molecule cannot release energy when is degraded to ADP, on the contrary, energy is absorbed. And granting without accepting that ATP release energy to become ADP, in the best case, it would release as heat. This is unlikely to be a good way to energize some process within the cell, because the specific heat of water is very high, that is the water is able to absorb a lot of heat without being noticed, besides the amount of work that can be accomplished by the release of heat is so limited and randomly in a significant degree given that, for example, according to the enthalpy; the heat is capable of performing more work if the temperature difference is greater between the different compounds involved.

- And as heat energy that degrades ATP to ADP releases, which is totally theoretical, not be practical, because it would be necessary that the ATP molecules almost completely surround the molecules that were to be energized, that is: enzymes, peptides, carbohydrates, amino acids, etc. or otherwise, as in the enzyme adenylate kinase, described above, which completely surrounds the ATP and AMP in the depths of their protein structure, which would allow the heat to be absorbed completely by the enzyme, although we actually thought to degrade ATP to ADP requires energy, so actually that part of adenylate kinase decreases its energy level by giving the energy necessary for degradation, and on the other hand, at the same time, when the AMP is converted to ADP, energy is released, and to be energetically opposed reactions and almost simultaneously, therefore requires the presence of a highly specialized scaffold capable of handling events opposites in many ways, in a very exact manner. And in turn, the molecules that will intervene in some kind of intra cellular reaction also require the presence of free chemical energy consistently, because otherwise the water dissolves them sooner or later, and on the other hand the energy of activation is required in each and every one of intracellular reactions that happen constantly in the intracellular environment.

Melanin releases the chemical energy in the form of increased energy fields that surround the entire cell cytoplasm, including organelles and nucleus (Solís-Herrera, 2013) (Figure 6).

Melanin converts photonic energy into free chemical energy in a way that performs several functions at once.

- The release of free chemical energy is symmetric in all directions, similar to increasing energy spheres.
- The strategic perinuclear location of melanosomes, allowing the free chemical energy to flow in all directions, permeating the entire cytoplasm and the totality of intracellular organelles, including the nucleus, of this free chemical energy.
- The special way in which the melanin released the free chemical energy, as well as how it travels through the interior of the cell, explains why intracellular organelles can perform their highly complex functions without the presence in them of mitochondria, such as the cell nucleus and the rough endoplasmic reticulum.
- Melanin converts the light energy visible and invisible in free chemical energy through the dissociation of the water molecule, which releases hydrogen and diatomic oxygen. But unlike the leaves of the plants, which diss-

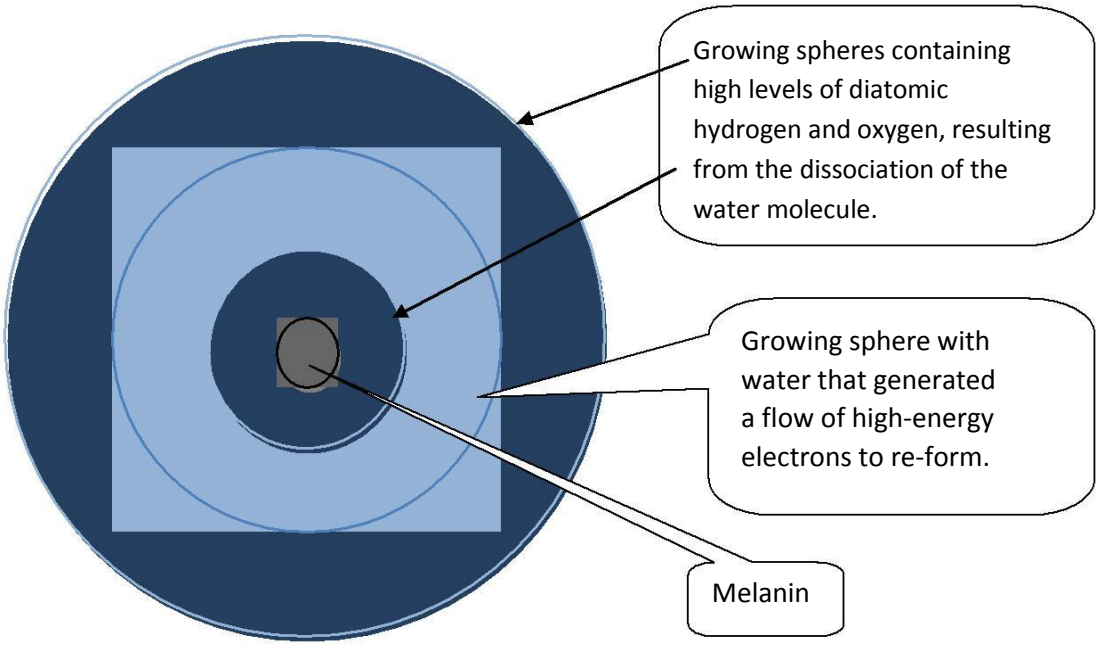

Figure 6. Melanin molecule: an extraordinary transducer.

sociate the water molecule irreversibly, then expel the oxygen to the atmosphere, melanin also has the amazing ability to re-form the water molecule, something unique in nature.

- When the water molecule dissociates diatomic hydrogen and oxygen raising its concentration around the melanin molecule, but this happens in a given time period, not randomly, having a sequence within a precise range. And the opposite reaction, the re-formation of the water molecule, also, what is manifested by decreased levels of diatomic hydrogen and oxygen and the presence of 4 high energy electrons for every two molecules of water re-formed. And this also happens not randomly, instead has a cadence, a rhythm.

- By having different characteristics, the difference between them is something discernible reaction, differentiable appreciable. To cite examples: the hydrogen atom is moving faster but the electron travels at the speed of light. The atomic mass of hydrogen, despite being the smallest atom, is huge compared to the mass of the electron. The charges are opposite. The dissociation and water re-union occur alternately, while not completely symmetrical in a timely manner, if you are fit enough for this alternation constitutes a kind of clock ticking for the cell.

- And the explanation of the amazing harmony that owns the cell requires something to set the pace, something like a conductor. And the perfect candidate is the manner in which melanin released the chemical energy.

- Well, it's the same rhythm or cadence for each and every one of the body's cells, both day and night, and throughout life, as the determining factors are the nature of light and the nature of melanin, and both are remarkably stable. So the unknown regarding the long-sought cellular clock seems resolved.

- We could say that the melanin marks the fundamental rhythm around which the cell organizes all its complex activities, so that the other known rhythms such as breathing and heart rate, come, depend on and are governed by the first.

The molecule of melanin is the quintessential synchronizer (Solís-Herrera, 2013) (Figure 7). The difference between the energy that is released to dissociate the water molecule that is carried by the diatomic hydrogen has substantive differences with the energy that is released to reform the water molecule in the form of high-energy electrons (Solís Herrera, 2013) (Figure 8).

The electromagnetic spectrum is made up of electromagnetic radiation of different wavelengths, frequencies, intensities, combinations, etc. And unlike chlorophyll absorbs only the ends of the visible light, the purple and red; melanin absorbs the entire electromagnetic spectrum of gamma rays to radio waves. And despite all possible combinations that may occur between different wavelengths absorbed by it, the energy emitted by the melanin to dissociate and re-form the water molecule is not modified beyond certain parameters, that is the melanin tempers energy changes, whether rough or not, fading them in the case of excessive light or Intensified them in the case of weak photon energy.

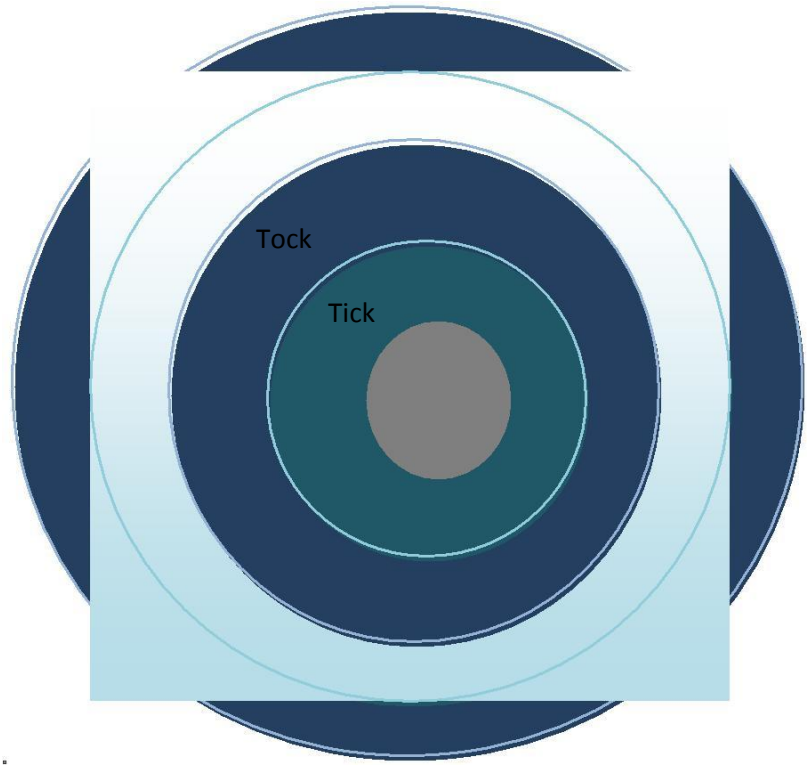

Figure 7. Melanin is the long sought biological clock.

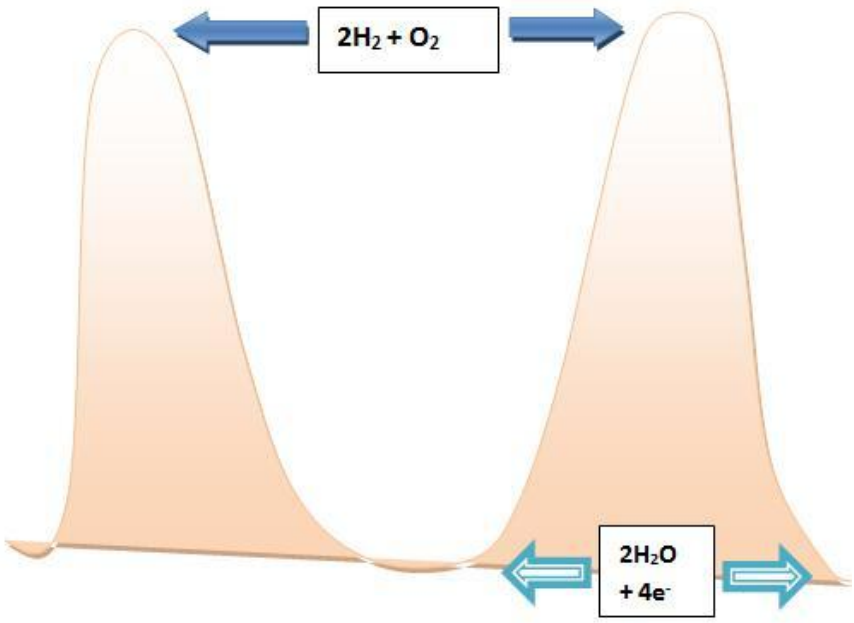

Figure 8. Melanin releases two types of free chemical energy; one is carried by the molecular hydrogen and the other stream in the form of high energy electrons.

Despite considerable variations that occur frequently in the melanin photonic energy absorbed, the rate of dissociation and re-formed from the water molecule is balanced so that the consequent changes in the free

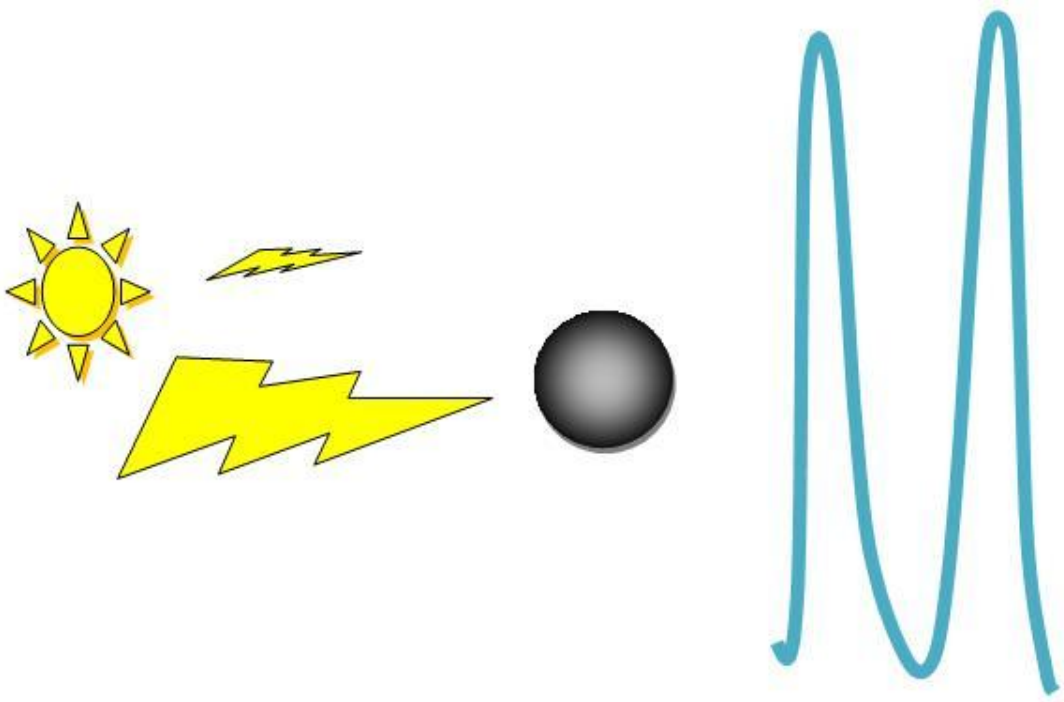

Figure 9. The output of energy from melanin is very stable.

chemical energy does not affect the functioning of the cell beyond certain limits, significantly limiting the irreversible damage might happen with photonic energy peaks (Solís-Herrera, 2013) (Figure 9).

THE SIZE OF THE VENTRICLES AND THE SUBARACHNOID SPACE IS DETERMINED BY THE TURNOVER RATE OF DISSOCIATION AND RE-FORMED FROM THE WATER MOLECULE

The use of cerebral ventricular volume as a measure of AD progression is supported by several studies [Nestor et al., 2008]. Hemispheric atrophy rates, measured by ventricular enlargement, correlates more strongly with changes on cognitive tests than medial temporal lobe atrophy rates. The rate of ventricular volume change is also highly correlated with an increase in senile plaques and neurofibrillary tangles. It may possible to use specific disease-modifying therapies and subsequently assess the biological effect of these treatments.

It is reported that the ventricles are enlarged by 60% more than patients with MCI (Figure 10). Absolute ventricular volumes and ventricular enlargement measured over a six-month interval were greater in subjects with AD and MCI compared to age-matched controls. Ventricular enlargement also demonstrated sensitivity to disease progression by way of discriminating between subjects with stable MCI and those that progressed to AD.

The size of the ventricles explained according to human photosynthesis

The size of the ventricles from which it depends? The feasibility of constructing normative curves of brain and fluid growth as complements to normative head circumference curves is a real possibility. By measuring brain volumes, distinct patterns of brain growth and enlargement can be observed, which are more likely linked to cognitive development and clinical outcome than fluid volumes alone [Mandel et al., 2010].

Although a number of models have been used to study choroid plexus epithelium (CPe) function, analysis in physiological conditions of this polarized epithelium which produces the majority of the cerebrospinal fluid (CSF) and is one of the key barriers between blood and CSF in the brain remains challenging [Swetloff et al., 2006], recall that choroid means grape color by its high melanin content, and if we put aside the intrinsic property of melanin to dissociate and re-form the water molecule, then it makes no sense the presence of a sunscreen deep into the brain. By other side, secretion inhibitors block vesicle formation in the CPe and their expansion. Acetazolamide (AZA) inhibitor of carbonic anhydrase, used in treatment of early or infantile hydrocephalus, is effective in some cases, while its effect on the choroid plexus (CP) remains ill-defined [Allan et al., 2010]. In vivo, the carbonic anhydrase enzyme (CA) catalyses the hydration of CO2 and the dehydration of bicarbonate [Krisnamurthy et al., 2008] as follow:

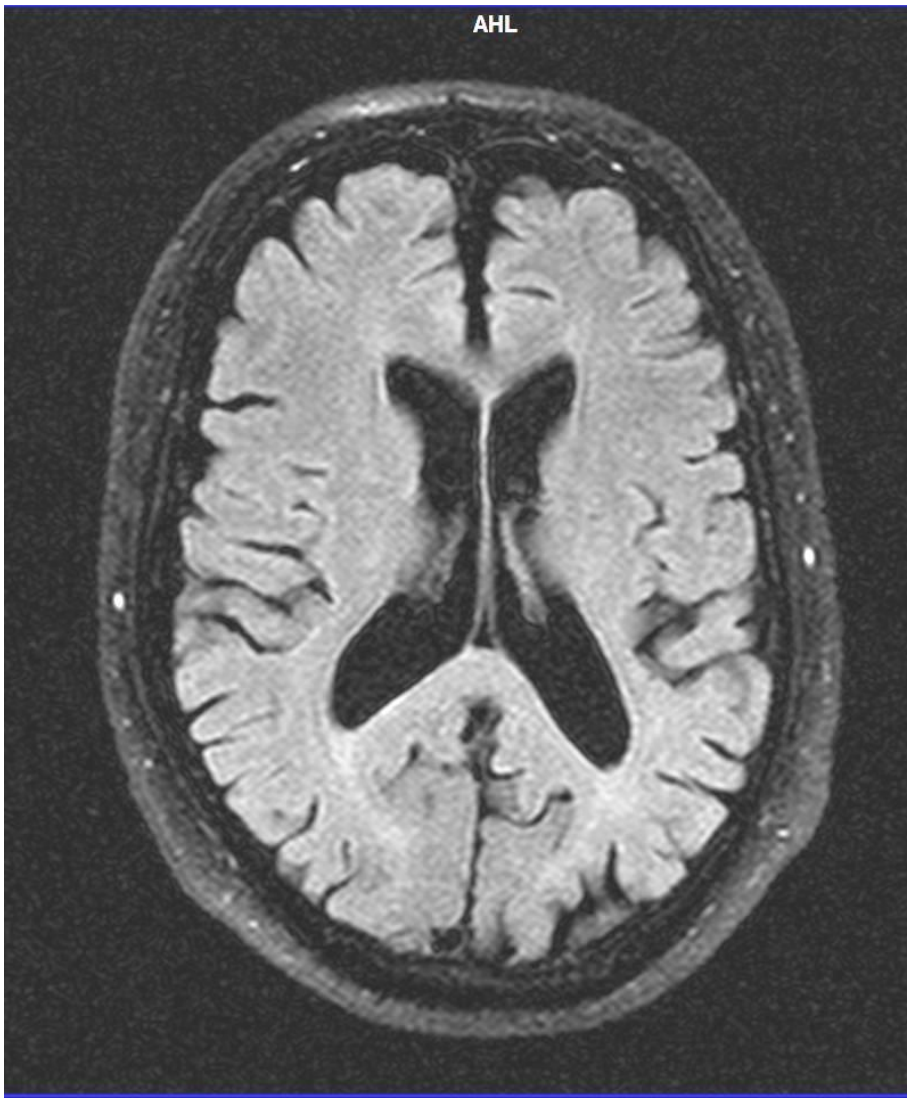

Figure 10. Enlarged ventricles and subarachnoid space in a patient with Alzheimer's diagnosis (Solís-Herrera, 2013).

$CO_2 + O_2 \leftrightarrow HCO3^- + H^+$

Thereby CA catalyzes the reversible hydration of CO_2 to bicarbonate, but also CA can catalyze the hydration of aryl and aliphatic aldehydes and the hydrolysis of a wide variety of esters in vitro [Pocker and Sarkanen, 1978]. Human CA I and CA II (HCA I and HCA II) catalyze the hydrolysis of 1-fluoro-2,4-dinitrobenzene and sulfonyl chlorides [Henkart et al., 1968].

CA is an extremely efficient catalyst: catalytic turnovers for several variants of CA are among the highest known (k_{cat} $CO2 \approx 10^6$ s^{-1}) and the-second order rate constants for these enzymes approach the limit of diffusion control (k_{cat}/k_m $CO2 \approx 10^8$ M^{-1} s^{-1}).

Although carbon dioxide reacts spontaneously with water, at 37°C to produce a proton and bicarbonate, this reactions is not fast enough to accomplish the hydration of CO_2 and the dehydration of HCO_3- that are required for the respiration in living organisms.

The secretion and reabsorption of CSF remains a mystery. The dynamics of the process is based on hypothesis. Explain the behavior of the CSF in various neurological diseases remains a formidable challenge. Small, normal, or slightly enlarged ventricles in pseudo tumor cerebri are consistent with the theory of reduced CSF absorption [Levine, 2000].

Accurate volume determination of the encephalic ventricles is also of importance in several clinical conditions, including Alzheimer's presenile dementia, schizophrenia, and benign intracranial hypertension. However, adequate evaluation of pathological conditions depends on a sufficient amount of morphometric data

from normal subjects. A small but significant correlation was reported between age of subject and ventricular volume, with ventricular size increasing with age [Del Bigio, 1989].

The size of cerebral ventricles in hydrocephalic patients is not exclusively related to CSF dynamics [Cramer et al., 1990], but also depends upon the intrinsic elastic and metabolic properties of the cerebral parenchyma which vary with age.

CEREBROSPINAL FLUID (CSF) GENERALITIES

The cerebrospinal fluid (CSF) is a major part of the extracellular fluid of the CNS, The CSF fills the ventricles of the brain, the spinal canal and the subarachnoid space, in humans has a total volume of approximately 140 ml. The CSF is separated from neuronal tissue by the ependyma, which lines the ventricles and canals, and the pia, which covers the external surface of the brain. The composition of CSF does influence neuronal activity, for instance, in the central chemoreceptors of the medulla oblongata which control respiration by responding to changes in CSF pH.

CSF functions

CSF helps provide mechanical support for the brain, reducing its effective weight, transferring weight shifting pressure to adjacent structures; by more than 60%. CSF also acts as drainage pathway for the brain, by providing a sink, within certain limits; into which products of metabolism or synaptic activity are diluted and subsequently removed.

The CSF also is an important route by which some nutrients reach the CNS, and act as route of communication within the CNS, carrying hormones and transmitters molecules between different areas of the brain. And according to the discovery of human photosynthesis, the CSF water is the energy source of the CNS.

CSF production

The CSF is not an ultrafiltrate of the plasma but is actively secreted by the choroid plexuses [Berg et al., 2002] therefore it is a process which requires constant power supply. It has been clearly demonstrated that the concentrations of some ions in the CSF are very carefully regulated and the regulation also requires energy, and are independent of variations in the plasma concentration of these ions (K^+ and Ca^{++}). The composition of an ultrafiltrate could not be regulated in this manner.

The CSF is constantly produced thereby energy is continuously required, and in humans the total volume is replaced about four times each day, similarly in other bodily fluids such as the aqueous humor, and in turn, the CSF also has variations in secretion and reabsorption depending on the time of day, because both processes depend on the energy of light so well as the aqueous humor, the CSF has variations according to variations in the amount of light that occur during the day and probably according to the seasons.

The total amount of CSF produced in 24 h is about 600 ml, being the majority of this CSF produced by the four choroid plexuses, one in each ventricle of the brain. The rate of CSF secretion is approximately 0.2 ml min^{-1} per g of tissue (Wright 1978). The rate of aqueous turnover is estimated in 2.4 ± 0.6 µl/min. Aqueous humor flows is higher in the morning than at night, and the CSF is probably the same. Aqueous humor is normally about 3.0 µl/min in the morning, 2.4 µl/min in the afternoon, and drops to 1.5 µl/min at night [Goel et al., 2010]. The mechanism that controls this biological rhythm is poorly understood, but at the light of the discovery of the intrinsic property of melanin to split and re-form the water molecule, variations start to make sense, more light, more energy, more flow; less light, less energy and thereby less flow.

The choroid plexuses of the brain ventricles and the choroidal layer of the eye receive between 3 and 4 ml min^{-1} per g of tissue of blood supply (Szmydynger-Chodobska et al., 1994). This is almost 10 times greater than the flow to the cerebral cortex. The capillaries in the choroid plexus and choroidal layer are fenestrated and hence provide little resistance to the movement of small molecules, ions and water.

CONCLUSION

Intracellular metabolic processes carried out in a strictly regulated manner; there are no randomized ways, as each and every one of them has a timing, location, frequency, G, coupling, reactant and products concentrations; etc. regulating through various processes concatenated in a very complex and highly interconnected pathways developed patiently by Nature along four billion years of evolution.

Major metabolic fates of pyruvate and acetyl CoA in mammals [Arias et al., 2011]. According to the definition of that energy is anything that causes a change; we may say in turn that any change requires energy to occur. So any change that is outlined in this scheme requires sufficient free chemical energy available Modified by Berg (2002) (Figure 11).

Alzheimer's disease is multifactorial, the damage is multilevel, and in any system, when failure is widespread, we must first think of energy and in the case of human beings, free chemical energy specifically (Solis-Herrera, 2013) (Figure 12).

Mitochondrial dysfunction is a hallmark of almost all

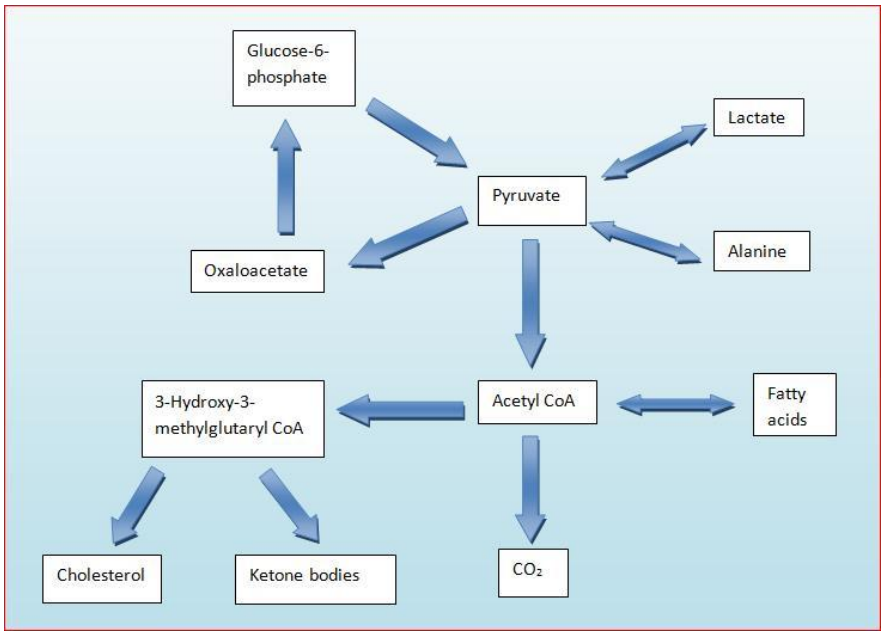

Figure 11. Major metabolic fates of pyruvate and acetyl CoA in mammals.

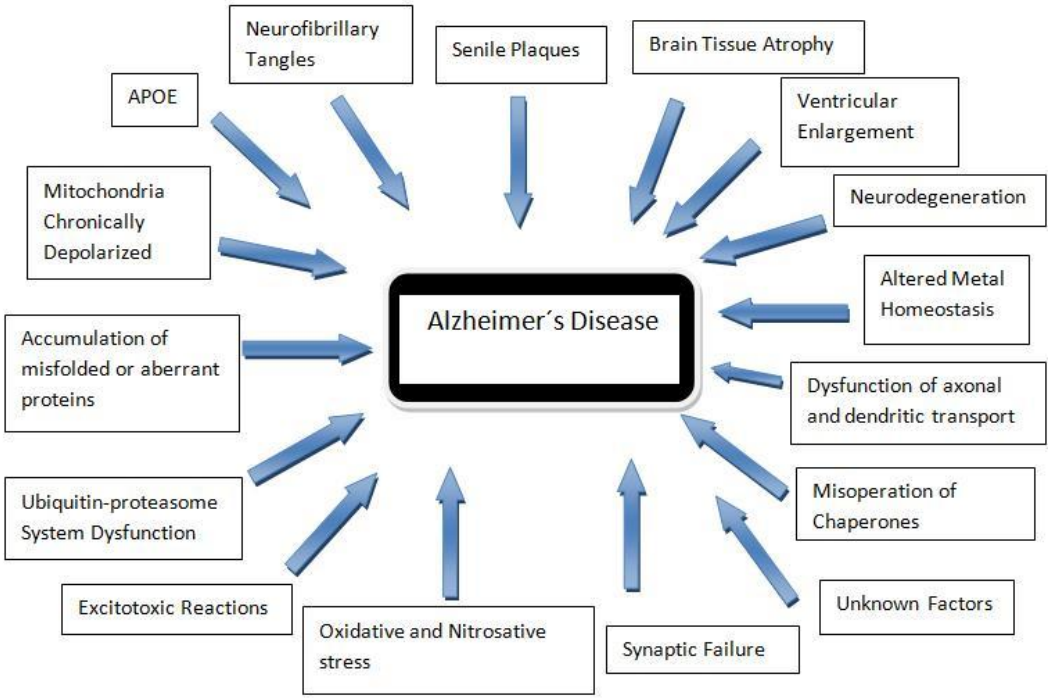

Figure 12. Alzheimer´s Disease is a multifactorial illness.

diseases [Seppet et al., 2009]. But not because the mitochondrion is the energy source of the eukaryotic cell, but because the failure in free chemical energy levels affects the function of all intracellular organelles and mitochondria is no exception.

Intensification of human photosynthesis [Solís, 2013] represents a watershed in the diagnosis and treatment of various neurodegenerative diseases, Alzheimer's disease being the most important for their rapid increase in prevalence and incidence [Ameli et al., 2012].

REFERENCES

Allan D, Hardas Arita S, Bader Lange Miranda L. (2010). Oxidatively Modified Glyceraldehyde-3-3phosphate Dehydrogenase (GAPDH) and Alzheimer Disease: Many Pathways to Neurodegeneration. J Alzheimers Dis 20(2): 369-393

Ameli PA, Madan M, Chiqurupati S, Yu A, Chan SL, Pattisapu JV (2012). Effect of acetazolamide on aquaporin-1 and fluid floe in cultured choroid plexus. Acta Neurochir Suppl 113:59-64

Arias Esparza MC, Solis Arias RI, Solis Herrera Arturo. (2011). The Unexpected Capability of Melanin to Split the Water molecule and the Alzheimer´s disease. Neuroscience & Medicine, 2:217-221

Berg JM, Tymoczko JL, Stryer L. Section 30.1. Metabolism Consist of Highly Interconnected Pathways. Biochemistry, 5th Edition, New York: WH Freeman; 2002.

Brown PD, Davies SL, Speake T, Millar ID (2004). Molecular Mechanisms of cerebrospinal fluid production. Neuroscience 129(4): 957-970.

Cramer GD, Allen DJ, DiDIo LJ, Potvin W, Brinker R (1990). Evaluation of encephalic ventricular volume from the magnetic resonance imaging scans of thirty-eight human subjects. Surg. Radiol. Anat., 12(4):287-90

Del Bigio ER, Age-related MR (1989). changes of cerebral ventricular size. Part II: Normalization of ventricular size following shunting. Acta Neurochir (Wien) 97(3-4):135-8

Fukumoto S (2010). Disorders of Phosphate Metabolism. Rinsho Byori Mar; 58(3): 225-31

Goel Manik, Picciani Renata G, Lee Richard K, Bhattacharya Sanjoy. Aqueous Humor Dynamic, a review. Open Ophthalm J 2010, September 3.

Henkart P, Guidotti G, Edsall JT (1968). J. Biol. Chem., 243:2447

Kanemitsu H, Tomiyama T, Mori H (2003). Human neprilysin is capable of degrading amyloid beta peptide not only in the monomeric form but also the pathological oligomeric form. Neurosci Lett 350:113-6

Krisnamurthy Vijay M, Kaufman George K. Urbach Adam R (2008). Carbonic Anhydrase as a model for biophysical and physical-organic studies of proteins and protein-ligand binding Chem Rev 108(3):946-1051

Levine DN (2000). Ventricular size in pseudotumor cerebri and the theory of impaired CSF absoption. J. Neurol. Sci. 15:177(2):85-94

Mandel JG, Neuberger T Drapaca CS, Webb AG, Schiff SJ (2010). The Dynamics of Brain and Cerebrospinal Fluid Growth in Normal Versus Hydrocephalic Mice. J Neurosurg. Pediatr. 6(1):1-10

Mangialasche Francesca, Solomon Alina, Winblad Bengt, Mecocci Patrizia, Kipivelto Miia (2010). Alzheimer´s disease: clinical trials and drug development. www.thelancet.com/neurology 9

Mikirova Nina, Riordan Hugh D, Kirby R.K., Klykov A, Jackson James A (2004). Monitoring of ATP levels in red blood cells and T cells of healthy and Ill subjects and the effects of age on mitochondrial potential. J Orthomolecular Med., 20:1

Nestor, Sean M. Rupsing, Raul Borrie, Michael (2008). Ventricular enlargement as a posible measure of Alzheimer´s disease progression validated using the Alzheimer´s disease neuroimaging initiative database. Brain 131:2443-2454

Ohnishi M, Razzaque MS (2013). Osteo-renal cross-talk and Phosphate Metabolism by the FGF23-Klotho System. Contrib Nephrol 180: 1-13

Parihar Mordhwaj S, Brewer Gregory J (2007). Mitoenergetic failure in Alzheimer disease. Am. J. Physiol. Cell Physiol., 292: C8-C23,

Pocker Y,Sarkanen S (1978). Adv Enzymol Mol Biol 47:149

Qiu WQ, Walsh DM, Ye Z (1998). Insulin-degrading enzyme regulates extracellular levels of amyloid beta-protein by degradation. J. Biol. Chem., 273:32720-8.

Querfurth, Henry W. LaFerla, Frank M(2010). Alzheimer´s Disease. N Engl. J. Med., 362:329-44

Seppet Enn, Gruno Marju, Peetsalu Ants, Gizatullina Zemfira (2009). Mitochondria and Energetic depression in Cel pathophysiology. Int. J. Mol. Sci., 10: 2252-2353

Solís Herrera Arturo. The Human Photosynthesis. Infinity Publishing 2013

Swetloff A, Greenwood S, Wade AM, Ferretti P (2006) Growth o choroid plexus epithelium vesicles in vitro depends of secretory activity. J. Cell Physiol., 208(3):549-55