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Role of Neural Analysis in Epileptic Attacks with Special Reference to Trace Elemental and Immunological Findings

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ABSTRACT

Neural circuits that are involved in feeding behavior show precise coordination with brain centre that modulate energy homeostasis and cognitive function. The effects of food on cognition and emotions can start before act of feeding itself. The recollection of foods through olfactory and visual sensory inputs alerts the emotional status of the brain. The ingestion of foods triggers the release of hormones or peptides. These hormones or peptides can reach centre such as the hypothalamus and the hippocampus and activate signal – transduction pathways. Epileptic attacks or seizures may be regarded as an emergent property of a network where the underlying physiology oscillatory coordination has given way to excessive coordination. It may be significant that the medial temporal cortex, an area where high amplitude oscillation appears to play a role in episodic memory. It is susceptible to seizure. The trace elements such as Cu, Zn, Fe, Ca, Mg, Na and K are found in the traces in our blood .The excess and deficiency cause different body disorders and affect the immunity of human beings. If the immunity is disturbed in our system many diseases affect our CNS. In the present study we have tried to show how the trace elements and other abnormalities are related to neural system.

Keywords: Neuron , Brain ,Excitable cell, Epilepsy and Nervous system.

1. INTRODUCTION

We may giving an idea of a branch of science which is called Neurophysics comes under Biophysics stream. It can be easily understand Biophysics. Biophysics is today the youngest daughter of general Physiology, a sister to Biochemistry and Pharmacology. Subject matter is not very well defined in this stream. Although the basic skeleton of the approach of this stream is very clear. It is a good thought to the engineers and physicist to give a suitable concept of a system, which is twisted and molded to describe the living things. Biochemistry and Biophysics may have an attempt to describe and interpret the chemical as well as physical processes of biological materials in terms of the principles and theories of organic chemistry, physical chemistry and physics. Biophysics is concerned with the unexplained questions about the physics of biological systems. Biophysics has advantages of low complexity and more certainty than the biological subjects. It has main disadvantage of being limited to only specific aspects of the whole living system.

Biophysics for human being can be thought of as providing a description of the whole physical system from the particular point of view of physics.

The scope of biophysics now a day is rather very broad. Hill [1] a Noble prize winner has published a research article in 1910. The use of physical techniques or ideas alone for investigation of biological problems does not make Biophysics. The study of biological function, organization and structure by physical and physiochemical ideas and methods may be put as a subject and then hastens to emphasize.

It has been established that the natural systems are of enormous complexity. It is clearly advisable to subdivide the problem in two phases:

- The first part of the problem is the structure and functioning of such elementary units individually.
- The second part of the problem consists of understanding regarding the orientations of these elements into whole system and how the functioning of the whole system is expressed in terms of these elements.

We would like to introduce a new term 'the cell' here and it has been found that the number of cells in the human body is in general of the order of 10^{15} or 10^{16} . These cells are called neurons and situated in human brain. The number of neurons in the Central Nervous System (CNS) is somewhere in the order of 10^{10} . All of artificial automata made by man have number of parts of the order of 10^3 to 10^6 .

Davied [2] has described in detail for the introductory part of nervous system in terms of nerve cells. Organisms, which are large divided into a number of units called cells. Every cell is progeny of another cell. This statement holds good and constitutes the cell theory. Every cell is bounded by a cell membrane and contains a nucleus in which the genetic material is found. The main part of the living matter of the cell is a highly organized system called cytoplasm, which is concerned with activity of the cell. The cell membrane separates this highly organized system inside from the relative chaos that exists outside the cell.

Every cell requires a continual supply of energy in order to increase and maintain its high degree of organization and in order to respond to and alter its environment. This energy must

be derived ultimately from the environment. This energy is found in the form of chemical energy. It can be extracted by the cell from glucose molecules.

We can describe here the mechanism of the cell in thermo dynamical terms, which is an open system and maintained in a rather improbable steady state by the continual expenditure of energy. It's life is a continual battle against the second law of thermodynamics. The cells of nervous system are called neurons. Their primary function is the handling of information. Within the cells this mainly takes the form of changes in the electric potential across the cell membrane, whereas information is passed between cells largely in the form of chemical messages.

The idea and mechanism tell us about the nervous system is composed of discrete cells. It is known as the theory of neuron development. This is a particular application of the cell theory and it was developed in the nineteenth century.

Neurons have functional regions specialized for different purposes. The places or sites where one neuron contacts another cell called another neuron and transmits or receives some useful or un-useful information are called as synapses. Synaptic transmission is called one way scheme and it works from the pre -synaptic cell to the postsynaptic cell.

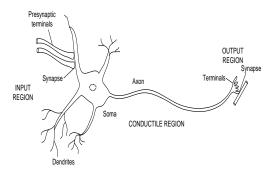


Figure 1: The main region of neuron.

The input region commonly consists of branched processes and it is called dendrites, it may include the surface of the cell body. This cell body is called soma and contains the cell nucleus of the neuron. The postsynaptic responses in the input region may be sufficient to produce excitation in the conductile region of the neuron, whose activity consists of unitary events called nerve impulses or action potentials. The conductile region is a long process and called the axon. The axon terminates in fine branches that make synaptic contact with other cells, such as other neurons or muscle cells. These terminals are pre synaptic and form the output region of the neuron. They secrete a chemical substance, which is called neurotransmitter, where an action potential arrives along the axon. This carries all informations across the synapses to the post-synaptic cell.

If we would like to define a living material, which is a function of the proteins, it must be taken into account and considered. Proteins are composed of chain made up from different combinations of twenty different amino acids, and their properties depend upon the sequence in which these amino acids are arranged. Immunoglobulins are also proteins.

The protein's amino sequences is specified by the nucleotide base sequence in the DNA molecules, which form the genetic material of the cell. Proteins may be considered as the product of evolution.

The shape of many protein molecules changes when they react with smaller molecules or other proteins. Changes of this type underline much protein activity, such as enzymatic hydrolysis, opening of membrane channels, and muscular contraction. The day to day activity of the cell can be described largely in terms of the actions of proteins.

2. CONDUCTION OF IMPULSES BY NERVES AND ROLE OF NERVOUS SYSTEM

Glasser [3] has described the fundamental concepts of Biophysics and given a great knowledge regarding the explanation of neurons to nervous system with all possible difficulties. The rapid co ordinations and response in human brain shows that the CNS must transmit information in an electrical or magnetic forms. The problems of the nervous system are similar to those of transmitting telephone messages over long distances. Either there must be many parallel low frequency channels, or fewer high frequency channels, each modulated by many separate signals. The number of channels has a tendency to increase with the complexity of living organism. The in formations may be transformed by electrical pulses.

Biophysicists have studied both the nervous and endocrine systems. Both the system lend themselves to the application of complex physical technique, and these can be analysed by the type of reasoning common to Physics and Electronics. This is true for the interaction between group of neurons, endocrine glands and also of the neuron-endocrine interactions. Feedback loops exist in which the effect produced alters the behavior of the neurons or endocrine glands producing these effects. Physicists and electrical engineers refer to these types of control mechanisms as negative feedback. Physiologists have called many of them **homeostatic** mechanisms because they tend to keep the state of organism constant.

Human body is a complex suspension of proteins in fluid. Actually the body, being a very special kind of electrolyte with many discontinuities in the form of membranes of different types, generates potentials. This potential difference between points of the body works as a normal function of the living organism.

Milton et al. [4] have studied epilepsy and suggested this disease is a dynamic from the clinical computation- list point of view. A neurologist can approach to a patient with epilepsy is

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to first classify the epilepsy and then try to formulate a treatment plan. Epilepsy may be treated fundamentally as a dynamical disease. Time-dependent phenomena may occur on time scales, which have a range from milliseconds to hours to days and years may too have important consequences both for the occurrence and recurrence of seizures. Treatment strategies must take into account the evolving dynamics of this disease. The fundamental computational challenge in epilepsy is to understand the relationship between the structure of CNS and its dynamics. A cost effective and more effective treatment strategies may be developed by interdisciplinary work.

All the dynamical systems can be easily described by an appropriate mathematical model. Clinicians and Neuro-physiological and Neuro-psychological members are the legally investigators entitled to directly record from the human brain of a patient with epilepsy and measure the responses of the brain to various treatment strategies including electrical stimulation and surgical removal of the epileptic focus.

Scientists who study dynamical systems may think only about this challengeable disease. The discussion begins with the success of computational neuroscience. The description of the generation of the action potential by a single, isolated neuron must be introduced in the process of evolution.

Hodkin-Huxley has developed an equation for the excitable cell. These equations can be easily derived using the basic principles of electricity. Persinger et al. [5] have suggested that all brain functions and their associated experience may be easily studied and determined by physical principles. John [6] suggested that the complexity of brain function can be derived from a small number of basic algorithms.

Graben [7] has introduced Neurophysics and studied the different aspects of brain functions in terms of some specific challenges related to digital computer electronics purposes.

Metaphorically, the brain is compared with a digital computer that runs software algorithms in order to perform cognitive computations. Digital computers consist of circuit boards with chips, transistors, resistors, capacitances, power supplies, and other electronic components wired together. Digital computer mechanisms are non-linear physical systems in nature.

Brain consists of 80% of water contained in cells and also surroundings cells. Physical wetware substrate supports computational dynamics. We can start our work from the physiological facts about neurons, their cell membranes, electrolytes and ions. Biophysical principles of neural computation is parallel to those of computation in electronic circuits may be taken into consideration. Physiological properties may be described by electric equivalent circuits.

Equivalent circuit of the membrane allows for derivation of the action potentials, which are the basic building blocks of neural conductance models. Travelling along the axon, pre synaptic terminals reached at this stage. Hodgkin-Huxley equations have to be supplemented by additional terms describing the dynamics of voltage gated calcium channels. Calcium flowing into the terminal causes the release of transmitter vesicles that pour their content of neurotransmitter into the synaptic cleft of a chemical synapse. Then, at the post synapse, transmitter molecules dock onto receptor molecules, which indirectly open other ion channels. The kinetics of these reactions give rise to the impulse response functions of the postsynaptic membranes. These membranes behave almost passively , a linear differential equation describes the emergence of post-synaptic potentials by the convulsion product of the postsynaptic pulse response with the spike train, i.e., the sequence of action potentials. Post-synaptic potentials propagate along the dendrites and the soma of the neuron and superimpose likely to a resulting signal that eventually arrives at the axon hillock.

Scott [8] has written in his monograph regarding the sodium and potassium ion currents. These currents respond non-linearly to changes of voltage across the membrane. The behavior of these non-linear currents has been described in a simple way. Lytton [9] studied computer modeling in epilepsy in detail with the detail of single neuron. This study has a considerable progress in developing realistic models within anatomically detailed morphology. Neural networks are also moderately realistic simulations. These networks are responsible for the oscillations of brain mechanism. They may be helpful in providing clues to pathophysiology of the disease. All the neurological disorders such as epilepsy, paraplegia, migraine, Alzheimer's disease, muscular dystrophy and other diseases can be better understood with the progress of these networks in neurological science.

The theory of immune network provides the network view that lymphocytes are mutually and dynamically connected by antigen antibody interaction .Not only antigen but also antibody generated by lymphocytes will act as an antigen against the other lymphocytes , thus persuading internal image of antigen .Both antigen and its internal image active the same specific type of lymphocytes .This network view may help in the direction of the immune memory in the network .If it is disturbed by an antigen , the network in an equilibrium will move to the other equilibrium point , We are giving some of the main features of the immune network theory as well as process is controlled by the interaction among antigens . The neural network use electric signals for communication ,while the immune system uses chemical ingredients the neural networks are used for the general pattern recognition ,the immune system is for special pattern recognition .The neural networks form a hierarchical systems , while the immune systems form a network without a center . The neural networks assume homogenous units, while immune systems assume heterogeneous agents. The immune system uses the diversity and self identification .

The mathematical modeling can reduce the gaps between the objects of neuroscience study from the level of chemical concentrations to the neurons and networks.

It is established that the brain's business is information only. Information content may be predicted or inferred at different levels of investigation, from ion concentration up to differential cortical perfusion patterns. We would like to add here that a variety of information theoretical tools for assessing the information content of signals.

The human brain is a complex nervous system with many individual components, neurons, synapses, acting in concert. The brain is said to show emergent properties. These properties can not be explained by considering the properties of the underlying units. We may use a property of such as thermodynamics. Large scale properties emerge from Newtonian approximations of the behavior of individual particles.

In the neural system, the emergent properties are seen in distributed representation. Information is parceled out among many units. The individual unit does not carry individually interpretable information or an individually interpretable processing task.

Neurons have great anatomical and physiological complexity. It remains an open question as to how much of this complexity is used for information processing by the cell and how much is simply a consequence of having to support its life process. Living cells are very complicated. The complexity of the individual neuron makes it an information processing device made up of multiple units. Dendritic sub regions encompassing groups of synapses would serve as processing units. The processing units at this stage are heavy interdependent and dynamically linked. We are unable to separate the units conceptually or informatically. Single neuron is simply computationally a single processing unit. Single neuron may be regarded as a point neuron with only a single and particular state. Neurons differ vastly across different brain areas and across types within an area.

Human body is a complex suspension of proteins in fluid .We can learn by observing their behavior in the presence of an electric field . It is natural to make such kind of experiment on the human body . The body is substantially different from many technological systems. If we have small current in our body then it behaves more or less like the inert circuit elements , which are used by electrical engineers as resistance , captaincies and electrolytes . Our body is made up of special kind of electrolyte with discontinuities in the form of membranes of various types , generates potentials and potential differences between different points of the body as a normal function of the living organism. If we apply some current on the body , tissues are caused to respond actively in such a fashion that is not very simple .On the other hand if current of very large magnitude passed through the body ,shock or death may result . Physiological systems are assumed to be representable as combinations of resistances and capacitors .tissue does not have the property representable as an inductance . This has been established that the appearance of tissue under the microscopic examination often suggests an appropriate circuit diagram .We can identify the tissue electrical properties with peculiarities of cell structure in plausible fashion . When a steady direct current is passed through tissue , the

tissue behaves like a resistance . A proper model for material is an electrolyte , or a suspension of one type of electrolyte in another .

We are using the theory of Hodgkin-Huxley models[10] directly in the present proposed work , which is applied to neurons and a brief idea is given here. If we see an increase of sodium conductance, which leads to a more positive membrane potential, or, to a depolarization, while an increasing conductance either of potassium or of chloride entails a further negativity, or hyper polarization of the membrane potential in case of epileptic attacks . We may achieve these effects with the help of voltage-gated sodium and potassium channels. They can be taken as AN and AK. We can presume that these are into the cell membrane and given by the equivalent circuit , which is given below.

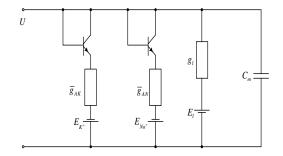


Figure 2: Equivalent circuit for the Hodgkin-Huxley equations.

The first and second mesh represents the voltage-gated potassium and sodium channels. Third mesh is taken from stationary descriptions of leakage potential. The capacitance is now needed for the dynamics of the membrane potential.

Apply Kirchoff's law. Total current through the circuit added upto an injected current I_m

$$I_{AK} + I_{AN} + I_e + I_c = I_m$$
 (1)

We have some other types of currents called partial given below

$$I_{AK} = P_{AK} \overline{g} A K \left(U - E_{K^{+}} \right)$$
⁽²⁾

$$I_{AN} = P_{AN} \overline{g}AN \left(U - E_{Na^+}\right)$$
(3)

$$I_l = g_l \left(U - E_l \right) \tag{4}$$

$$I_c = C_m \frac{dU}{dt}$$
(5)

Now membrane potential U(t) will obey the differential equation as

$$C_{m}\frac{dU}{dt} + P_{AK} \,\overline{g}_{AK}(U - E_{K^{+}}) + P_{AN} \,\overline{g}_{AN}(U - E_{Na^{+}}) + g_{l} \,(U - E_{l}) = I_{m}$$
(6)

Now equation (6) has to be supplemented by the following equations for open probabilities P_{AK} and P_{AN}

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$$\frac{dp_{\kappa}}{dt} = a_{\kappa} \left(1 - P_{\kappa}(t)\right) - \beta_{\kappa} P_{\kappa}(t)$$
(7)

and the rate equation

$$\alpha_{\kappa}(U) = e^{\frac{W_0(C \to 0) + QU}{K_B T}}$$
(8)

For α_{AK} , α_{AN}

Hodgkin and Huxley reported two other relations

$$P_{AK} = n^4, \ P_{AN} = m^3 h$$
 (9)

Now, n, m and h obey three master equations

$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n \tag{10}$$

$$\frac{dm}{dt} = \alpha_m (1-n) - \beta_m m \tag{11}$$

$$\frac{dh}{dt} = \alpha_h (1-n) - \beta_h h \tag{12}$$

Now, equation (6) and (10), (11), (12) are called required Hodgkin-Huxley equations. They constitute a four-dimensional non-linear dynamical system controlled by the parameter I_m .

The emergence of an action potential results from different kinetics of the ion channels. If the cell membrane is slightly depolarized by the current I_m , the opening rate α_n for the sodium channels increases. Further depolarization of the membrane is found.

A spike train travels along the axon and after the several branches reaches to presynaptic terminals, the composition of membrane is totally changed. Voltage-gated calcium channels are seen in addition to the voltage gated potassium and sodium channels.

Now we have

$$I_{AC} = l^5 \,\overline{g}_{AC} \, (U - E_{Ca^{2+}}) \tag{13}$$

where *l* obeys another master equation

$$\frac{dl}{dt} = \alpha_l (1-l) - B_l l$$
(14)

In the absence of an injected current ($I_m = 0$), the presynaptic potential U(t) is introduced in the equation given below

$$C_m \frac{dU}{dt} + I_{AK} + I_{AN} + I_{AC} + I_l = 0$$
 (15)

If the calcium leakage is very low can be neglected. We have an enhancement of the intracellular concentration

$$\frac{d |Ca^{2+}|_{int}}{dt} = \frac{-I_{AC}}{q N_A V}$$
(16)

q = 2e is the charge of calcium ion; N_A = Avogadro number

The accumulation of calcium in the cell plasma gives rise to a cascade of metabolic reactions. Calcium does not act as an electric signal. It acts as an important messenger and chemical reagent enabling or disenabling the functions of enzymes.

3. MECHANISM OF EXCITATION

There are a number of factors involved in active response, which remain obscure because they occur at atomic dimensions.

Tissues will respond to stimuli which are electrical, mechanical, thermal and chemical. The electrical impulses are easy to grade, time, shape and record. We can describe the mechanism of excitation phenomena in terms of characteristics of electrical impulse.

A cell is excited if the current is caused to flow from the inside of the cell outward (i.e., electrons flow from outside inward), and if the current flow is from outside inward, the threshold for a second stimulus is increased. If a pair of electrodes is placed on the surface of a cell (e.g. nerve axon), excitation will appear at the cathode. A tissue may also originate a response at the anode.

4. THEORY OF EXCITATION OF NEURONS

The existing theory of excitation is based on the empirical observations. If we assume that there is a quantity, which is called excitation and increases at a rate which is proportional to the applied voltage to a cell. At the same time, there is also a decrement in excitation, which occurs at a rate which is proportional to the amount of excitation. We can say that a rise in excitation is exponential in nature.

Hill[1] has proposed a theory of excitation. He pointed out one every significant factor in excitation. Threshold may rise at the same time the local excitatory state is building up as a result of passage of an electric current. The threshold for a second stimulus is the difference between the excitatory state and the existing absolute threshold.

Now, if we assume that the absolute threshold begins to increase upon the application of the current and that it does so exponentially, with a time constant λ .

This increase may be associated with the accumulation of K^+ ions in the medium immediately surrounding the cell. A decay of the threshold occurs when the exciting current is

removed. If the local excitatory state before stimulation is V_0 and the excitatory state at time θ is V, the build up is given by the relation

$$V - V_0 = b \ e^{-t/K} \int_{\theta=0}^{\theta=t} I_\theta \ e^{\theta/K} \ d\theta \tag{17}$$

Where *b* is a constant; *K* is the decay constant for the excitatory state; I_{θ} is the current, which is a function of θ .

Similarly, the buildup of threshold which occurs may be expressed by the following relation

$$U - U_0 = \frac{e^{-t/\lambda}}{\lambda} \int_{\theta=0}^{\theta=t} (V - V_0) e^{\theta/\lambda} d\theta$$
(18)

Here, U is the threshold at time θ ; U_0 is the resting threshold; λ is the time constant of threshold decay.

When U and V are equal in nature, the excitation occurs. It has been experimentally verified that a frog's modulated nerve K is about 0.25 m sec and λ is of the order of magnitude of 50 m sec.

The impedance of cells and tissues may be assumed to be a largely function of the capacitive reactance of the cell membranes. It has been already established that the membranes change their characteristics as physiological conditions fluctuate .The measurement of whole body impedance may be considerable interest on clinical point of view. Cole and Curtis [11] have summarized analyses of current distributions in nerve based on the cable theory. According to this theory the nerve consists of a large number of electrical elements connected by a conducting medium inside the cell and outside the cell. Equivalent circuit is given below

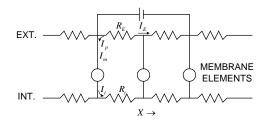


Figure 3: Systematic diagram of the theoretical system involved in cable theory.

If r_1 is the resistance per unit length of the medium bathing the cell, r_2 is the resistance per unit length of the material inside the cell, z_m is the membrane impedance per unit length, i_1 is the current through r_1 , i_2 is the current through r_2 , i_m is the current through z_m , v_1 and v_2 are the potentials of the outside of the resting portion and the inside of the resting portion.

Apply Ohm's law

$$\frac{\partial V_1}{\partial x} = -r_1 i_1 \tag{19}$$

$$\frac{\partial V_2}{\partial x} = -r_2 i_2 \tag{20}$$

and

also

$$V_1 - V_2 = -z_m \, i_m \tag{21}$$

If there is no current flow in this system

$$i_1 + i_2 = 0$$
 and $\frac{\partial i_1}{\partial x} = -\frac{\partial i_2}{\partial x} = i_m$ (22)

$$\frac{\partial^2 V}{\partial x^2} = -(r_1 + r_2) i_n$$
(23)

$$V = V_1 - V_2$$

Membrane current is proportional to the second derivative of the voltage. Now the equivalent circuit of the individual membrane element contains a capacitance C_m in parallel with a resistance r_4 and a battery of potential E in series.

If i_1 is the current in the C_m , i_4 is the current through r_4 and t is the time.

$$\begin{array}{c} i_{3} = -C_{m} \frac{\partial V}{\partial t} \\ i_{4} = \frac{E-V}{r_{4}} \end{array}$$

$$(24)$$

The total current through this element is

$$i_n = i_3 + i_4 = -C_m \frac{\partial U}{\partial t} + \frac{E - V}{r_4}$$
(25)

Now, use equation (23) and substitute the value of i_m from (25) in (23), we get

$$\frac{\partial^2 V}{\partial x^2} = -\frac{r_1 + r_2}{r_4} \left[E - V - r_4 C_m \frac{\partial V}{\partial t} \right]$$
(26)

For convenience, we use two terms such as characteristic length of the cell (λ) and time constant of the membrane (τ_m)

$$X = \sqrt{r_4 / (r_1 + r_2)}$$
(27)

and
$$\tau_m = r_4 C_m$$
 (28)

Now substitute these values in (26), we get

$$\lambda^{2} \frac{\partial^{2} V}{\partial x^{2}} - \tau_{m} \frac{\partial V}{\partial t} - V = -E$$
⁽²⁹⁾

If the cell responds actively, the impulse is propagated at a velocity the cell.

We wish to examine the distribution of currents about the active area, we may use a coordinate system and an equation is given below

$$y = x - Vt \tag{30}$$

$$\frac{\partial V}{\partial x} = \frac{\partial V}{\partial y} \tag{31}$$

$$\frac{\partial^2 V}{\partial x^2} = \frac{\partial^2 V}{\partial y^2}$$
(32)

$$\frac{\partial V}{\partial t} = -V \frac{\partial V}{\partial y}$$
(33)

Substitute these values in (29), we get

$$\lambda^2 \frac{\partial^2 U}{\partial y^2} + V \tau_m \frac{\partial V}{\partial y} - V = -E$$
(34)

$$E = V - \beta \lambda^2 \left[\frac{\partial^2 V}{\partial y^2} + \frac{1}{\lambda_0} \frac{dV}{dy} \right]$$
(35)

where β is defined as the ratio of membrane resistances in activity to that at rest, λ_c is the characteristic length of a non-conducting membrane and is equal to

$$\lambda_0 = \frac{1}{V} (r_1 + r_2) C_m$$
(36)

 $\overline{\lambda}$ is the characteristic length due to membrane conductances, $\lambda_{_0}$ is the property of the membrane capacitance.

The propagation amounts to the spread of a localized short circuit, so that E and r_4 are zero at y = 0, and we obtain their resting values at all other points.

Now if e is the voltage spread from the active area, V is equal to E - e and we get

$$\overline{\lambda}^2 \frac{\partial^2 e}{\partial y^2} + U \tau_m \frac{de}{dy} - e = 0$$
(37)

Except at y = 0, $\overline{\lambda}$ and λ_e are constants so that

$$e = e_0 e^{-(y/\lambda_a)} \tag{38}$$

where λ_a is the space constant, a characteristic length of the membrane outside the active area.

It can be expected that the current flow through the membrane in the inactive region adjacent to an active area would fall off exponentially with distance from the edge of the active areas. The excitatory effect of an active area on adjacent areas would reach to a point at which the membrane current had fallen off threshold value.

It has been experimentally verified that the cable equation hold good at the weak sub threshold stimulus level. If the stronger shock of short duration exist, an excitation will appear with the condition that the cathodic response try to reach a certain level, rather than when a pulse of constant energy flow through the cell.

5. MATERIALS AND METHODS

Blood samples of epileptic patients along with normal healthy control were collected from the Department of Neurology, Safdarjang Hospital, and New Delhi 110016 after the approval of ethical committee of the hospital. 10 ml freshly drawn blood from each patient was collected in clean and dry test tube without any anti-coagulant. The test tube was kept for 45 minutes at room temperature ($22 \pm 2^{\circ}$ C) for the formation of clot. Sera of different patients were separated by centrifugation at 1500 r.p.m. upto 15 minutes and were collected in screw capped test tubes.

The immunological parameters (IgA, IgG, IgM, $C_3 \& C_4$) were quantitated by using singles radial immunodiffusion method of Mancini et al. [12] using commercially available antibody-agar plates. The plates were standardized with purified immunoglobulins.

The atomic absorption spectral estimation of the serum samples from normal persons and epileptic patients were carried out on atomic absorption spectrophotometer Model No. AA-6300 of Shimadzu Japan, at Deptt. Of Environmental study University of Delhi 110007.

6. ROLE OF FOOD AND EFFECTS OF NEUTRITION

Gömez [13] has supplied some information related to brain foods. Effects of nutrients on brain function have also been studied. He has reported in the study with a suspicion that the relative abundances of specific nutrients can affect cognitive processes and emotions. It has been studied the influences of dietary factors on neural function and synaptic plasticity may reveal some of the vital mechanisms. These mechanisms are responsible for the action of diet on brain health and mental function. There are so many gut hormones may enter the brain. These hormones may be produced in the brain itself. These can influence cognitive ability of the brain. Regulators of synaptic plasticity such as brain derived neurotrophic factor can function a metabolic modulators. These are responsible to peripheral signals such as food intake. If we are at the stage of understanding the molecular basis of the effects of food on cognition, we can help the community of research to determine the possibility of increase the resistance of neurons through the adjusting the dietary food habits. These thoughts can promote mental fitness in the human body. Energy homeostasis and cognition is shown in the Figure. 4. Sanjeev Kumar Vinod Kumar and Reena; *Role of Neural Analysis in Epileptic Attacks with Special Reference to Trace Elemental and Immunological Findings*, Journal of Biomedical Engineering and Medical Imaging, Volume 1, Issue 2, pp: 39-50

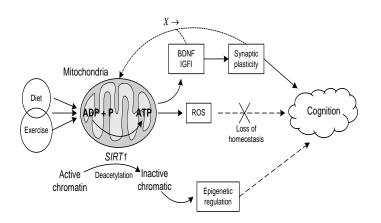


Figure 4: Energy homeostasis and cognition.

It has been established that the diet and exercise can help in affecting the mitochondrial energy production. This production is very important to maintain neuronal excitability and function of synaptic. The arrangement of some definite diets and exercise can have additional effect on synaptic plasticity and cognitive function. Adenosine triphosphate (ATP) is produced by mitochondria. ATP is responsible for the activation of brain-derived neurotrophic factor and insulin like growth factor. This ATP supports synaptic plasticity and cognitive function.

Excess energy production may be caused by very high calorific intake or strenuous-exercise results in the production of reactive oxygen species. If this level goes up the buffering capacity of the cell, synaptic plasticity and cognitive function are compromised. A reduction in the actions of signal transduction may be found.

7. EFFECTS OF FEEDING ON COGNITION

Neural circuits that are involved in feeding behavior show precise coordination with brain centre that modulate energy homeostasis and cognitive function. The effects of food on cognition and emotions can start before act of feeding itself. The recollection of foods through olfactory and visual sensory inputs alerts the emotional status of the brain. The ingestion of foods triggers the release of hormones or peptides. These hormones or peptides can reach centre such as the hypothalamus and the hippocampus and activate signal – transduction pathways. These two can promote synaptic activity and contribute to learning and memory. A schematic diagram of feeding on cognition is shown in Figure. 5.

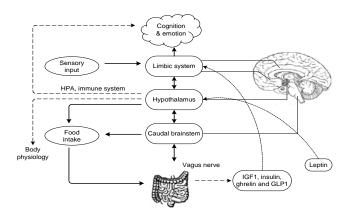


Figure 5: Effects of feeding on cognition.

8. EXPLANATION OF EPILEPTIC JERKS ON NEURAL NETWORKS

It is debatable that the oscillations in the brain are evidence of noise or reflect a vital component of signaling or information processing. The firing of neurons at a particular phase of a cycle would serve to associate the activity of that neuron with others on the same phase. It is easy to define a neural ensemble through which a set of cells could form a distributed representation or perform distributed processing.

The seizure in epilepsy is a specific symptom related to neural activity of abnormal processing in the human brain. Such nerve cells (neurons) are strengthened with the element which we take in the form of food. The trace elements such as Cu, Zn, Fe, Ca, Mg, Na and K are found in the traces in our blood given in Table 1 and regression equations with correlation coefficients of normal and epileptic persons are given in Table 2and Table 3. The excess and deficiency may lead to different body disorders and affect the immunity of human beings. We have measured immunological parameters and given in Table 4. and regression equations with correlation coefficients of normal and epileptic persons are given in Table 5 and Table 6. If the immunity is disturbed in our system many diseases affect our CNS. The abnormal behavior of nerve cells comes into play which is responsible for the epileptic seizures. Computational neuroscience is a helpful tool to present broad picture of the neural activity. A simulation on the basis of elemental supplementation may be proposed and can be demonstrated in future.

S. No.	Element	Type of sample	Mean + S.D.	Disease
1	Copper	Serum	(0.1767 \pm 0.1087) mg/l	Epilepsy
2	Copper	Serum	(0.1329 \pm 0.0380) mg/l	Control
3	Iron	Serum	(1.8483 \pm 1.8079) mg/l	Epilepsy
4	Iron	Serum	(1.1826 \pm 1.7671) mg/l	Control
5	Zinc	Serum	(1.6875 \pm 1.8156) mg/l	Epilepsy
6	Zinc	Serum	(1.0267 \pm 0.6347) mg/l	Control
7	Sodium	Serum	(6.2271 \pm 0.0956) mg/l	Epilepsy
8	Sodium	Serum	(6.1203 \pm 0.0708) mg/l	Control
9	Potassium	Serum	(0.1572 \pm 0.0098) mg/l	Epilepsy
10	Potassium	Serum	(0.1443 \pm 0.0043) mg/l	Control
11	Calcium	Serum	(4.0285 \pm 1.0521) ml/l	Epilepsy
12	Calcium	Serum	(0.0483 \pm 0.0284) ml/l	Controls
13	Magnesium	Serum	(4.7017 \pm 0.9548) mg/l	Epilepsy
14	Magnesium	Serum	(0.1098 \pm 0.0310) mg/l	Control

Table 1 Mean ± Standard deviation of Cu, Fe, Zn, Na, K, Ca and Mg in epileptic patients and normal healthy controls.

Table .2: Regression and correlation coefficient studies on Na, K, Ca, Mg, Zn, Cu and Fe in normal samples

Diagnosis	Regression coefficients	Regression equations	Coefficient of correlation	Coefficient of partial correlation	Multiple correlation coefficient
	$b_{\rm Na.K}$ = 4.1282	Na = 4.1282K + 2.524 K = 0.0156Na + 0.0955	$r_{\rm NaK} = 0.2539$	$r_{\rm CaNa.K} = -0.5293$	$R_{ m Na.KCa}$ = 0.6016
	$b_{\mathrm{K.Na}}$ = 0.0156			$r_{\text{CaK.Na}} = 0.6316$	$R_{\mathrm{K.NaCa}}$ = 0.6616
	<i>b</i> _{Ca.Mg} = -0.0090	Ca = -0.0090Mg+0.04923 Mg = -0.0107Ca + 0.1103	$r_{\rm CaMg} = -0.0098$	$r_{\rm NaK.Ca} = 0.5187$	<i>R</i> _{Ca.KNa} = 0.6894
	$b_{ m Mg.Ca}$ = 0.0107	5		$r_{MgNa.K} = -0.0663$	$R_{ m Mg.NaK}$ = 0.1196
Normal	$b_{\text{Cu.Fe}}$ = 0.0048	Cu = 0.0048Fe + 0.1272 Fe = 10.3828Cu - 0.1974	$r_{\rm CuFe} = 0.2236$	$r_{\rm MgK.Na}$ =-0.0801	$R_{ m Na.MgK}$ = 0.2618
	$b_{ m Fe.Cu}$ = 10.3828			<i>r</i> _{NaK.Mg} =0.2472	$R_{ m K.MgNa}$ = 0.2654
	<i>b</i> _{Cu.Zn} = 0.0109	Cu = 0.0109Zn + 0.1217 Zn = 3.0297Cu + 0.6239	<i>r</i> _{ZnFe} = -0.4814	<i>r</i> _{ZnCu.Fe} = 0.3388	<i>R</i> _{Cu.FeZn} = 0.3988
	<i>b</i> _{Zn.Cu} = 3.0297			$r_{\rm ZnFe.Cu}$ = -0.5447	$R_{ m Fe.CuZn}$ = 0.5761
	<i>b</i> _{Fe.Zn} =-1.3404	Fe = -1.3404Zn + 2.5589 Zn = -0.1729Fe + 1.2320	$r_{\rm CuZn} = 0.1817$	$r_{\text{CuFe.Zn}} = 0.3610$	$R_{\rm Zn.FeCu}$ = 0.5656
	<i>b</i> _{Zn.Fe} =-0.1729				

Diagnosis	Regression coefficients	Regression equations	Coefficient of correlation	Coefficient of partial correlation	Multiple correlation coefficient
	$b_{\rm Na.K} = 0.0888$ $b_{\rm K.Na} = 0.0009$	Na = 0.0888 K + 3.213 K = 0.0009Na + 0.1541	<i>r</i> _{NaK} = 0.0091	$r_{\text{CaNa.K}} = -0.4992$ $r_{\text{CaK.Na}} = -0.7019$	$R_{\rm Na.KCa}$ = 0.4993 $R_{\rm K.NaCa}$ = 0.7019
	$b_{\rm Ca.Mg} = -0.1603$	Ca = -0.1603Mg + 4.7821 Mg = -0.1320Ca + 5.2338	$r_{\rm CaMg} = -0.14$	$r_{\text{NaK.Ca}} = 0.3561$ $r_{\text{MgNa.K}} = -0.5366$	$R_{\rm Ca.KNa}$ = 0.7509 $R_{\rm Mg.NaK}$ = 0.6206
Epilepsy	$b_{\rm Mg.Ca}$ = -0.1320 $b_{\rm Cu.Fe}$ = 0.0254	Cu = 0.0254Fe + 0.1296 Fe = 7.0330Cu + 0.6055	$r_{\rm CuFe} = 0.42$	$r_{\rm MgNa.K} = 0.0000$ $r_{\rm MgK.Na} = -0.4218$	$R_{\rm Mg.NaK} = 0.5367$ $R_{\rm Na.MgK} = 0.5367$
	<i>b</i> _{Fe.Cu} = 7.0330	re – 7.0330cu + 0.0033		<i>r</i> _{NaK.Mg} =-0.2194	$R_{ m K.MgNa}$ = 0.4219
	<i>b</i> _{Cu.Zn} = 0.0357	Cu = 0.0357Zn + 0.1163 Zn = 9.9642Cu - 0.0731	$r_{\rm ZnFe} = 0.33$	$r_{\rm ZnCu.Fe} = 0.5318$	$R_{\mathrm{Cu.FeZn}}$ = 0.6412
	<i>b</i> _{Zn.Cu} = 9.9642			$r_{\rm ZnFe.Cu} = 0.1192$	$R_{ m Fe.CuZn}$ = 0.4366
	$b_{\rm Fe.Zn}$ = 0.2404	Fe = 0.2404Zn + 1.4426 Zn = 0.4785Fe + 0.8030	$r_{CuZn} = 0.59$	$r_{\rm CuFe.Zn} = 0.2922$	$R_{\rm Zn.FeCu}$ = 0.6044
	$b_{\rm Zn.Fe}$ = 0.4785				

Table .3: Regression and correlation coefficient studies on Na, K, Ca, Mg, Zn, Cu and Fe in epilepsy

Table 4: Mean levels and standard deviation of C₃, C₄, IgG, IgM, IgA in epileptic patient and normal healthy control.

S.No.	Immunological Parameter	Types of Samples	Mean ±S.D Unit	Disease/ Control
1	IgG	Serum	(18.18 ± 4.87) gm/l	E
2	IgG	Serum	(17.24 ±3.07) gm/l	С
3	lgM	Serum	(1.38 ± 0.32) gm/l	E
4	lgM	Serum	(7.42 ± 1.64) gm/l	С
5	IgA	Serum	(7.05 ± 1.17) gm/l	E
6	IgA	Serum	(7.83 ± 0.68) gm/l	С
7	C ₃	Serum	(1.53 ± 0.26) gm/l	E
8	C ₃	Serum	(1.58 ± 0.15) gm/l	С
9	C ₄	Serum	(0.26 ± 0.13) gm/l	E
10	C ₄	Serum	(1.28 ± 0.10) gm/l	С

Table 5: Regression and correlation coefficient studies on C₃, C₄, IgG, IgM and IgA in normal blood samples.

S.No	Correlation Coefficients	Regression Coefficients	Regression Equations	Coefficients of Partial Correlation	Multiple Correlation Coefficients
C ₃	$C_3C_4 = -0.0256$	b _{C3C4} = - 0.0394 b _{C4 C3} = - 0.0167	$C_3 = -0.0394 C4 + 1.5966$		
C ₄	$C_4C_3 = -0.0256$		C ₄ = -0.0167 C3 + 0.3087		
IgG	lgG lgM = 0.4814	b _{GM} = 0.9006 b _{MG} = 0.2574	lgG = 0.9006 lgM + 15.0577 lgM = 0.2574 lgG – 2.0109	r _{GM.A} = 0.4201	R _{G.MA} = 0.2386
lgM	IgM IgA = 0.4140	b _{MA} = 1.0214 b _{AM} = 0.1678	IgA = 0.1678 IgM + 2.4291 IgM = 1.0214 IgA - 0.4698	r _{AG.M} = 0.0943	R _{A.GM} = 0.1788
IgA	IgG IgA = 0.2746	b _{GA} = 1.2673 b _{AG} = 0.0595	lgG = 1.2673 lgA + 13.6493 lgA = 0.0595 lgG + 1.8102	r _{MA. G} = 0.3344	R _{M.AG} = 0.3177

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S.No	Correlation Coefficients .	Regression Coefficients	tion	Coefficient of Partial correlation	Multiple Correlation Coefficients
C3	C ₃ C ₄ = 0.5566	b _{C3.C4} = 1.0887	$C_3 = 1.0887 C_4 + 1.2436$		
C4	$C_4C_3 = 0.5566$	b _{C4.C3} = 0.2845	$C_4 = 0.2845 C_3 - 0.1684$		
lgG	lgG lgM= 0.1404	b _{G.M.} = 2.0907 b _{M.G.} = 0.0094	IgG = 2.0907 IgM + 5.2891 IgM = 0.0094 IgG + 1.2146	r _{GM.A} = 0.0609	R _{G•MA} = 0.0778
lgM	IgM IgA= 0.3103	b _{M.A.} = 0.0867 b _{A.M.} = 1. 1104	lgM = 0.0867 lgA + 1.2077 lgA = 1.1104 lgM + 0.5193	r _{AG.M} = 0.2436	R _{A.GM} = 0.1499
lgA	IgG IgA= 0.2728	b _{G.A} = 1.1351 b _{A.G.} = 0.0655	lgG = 1.1351 lgA + 15.8504 lgA = 0.0655 lgG + 0.8658	r _{MA. G} = 0.2855	R _{M.AG} = 0.0996

Table .6: Regression and correlation coefficient studies on C ₃	C ₃ , C ₄ , IgG, IgM and IgA in epileptic blood samples.
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Epileptic attacks or seizures may be regarded as an emergent property of a network where the underlying physiology oscillatory coordination has given way to excessive coordination. It may be significant that the medial temporal cortex, an area where high amplitude oscillation appears to play a role in episodic memory. It is susceptible to seizure. Abnormalities in cognitive coordination would in turn be manifestations of abnormalities in neural coordination associated with either excessive or inadequate involvement of neural subsets in oscillation defined ensembles.

The trace elements such as Cu, Zn, Fe, Ca, Mg, Na and K are found in the traces in our blood .The excess and deficiency cause different body disorders and affect the immunity of human beings. If the immunity is disturbed in our system many diseases affect our CNS. The abnormal behavior of nerve cells comes into play which is responsible for the epileptic seizures. Computational neuroscience is a helpful tool to present broad picture of the neural activity. Chandra[14] has written somewhere else in literature that the interaction between nutrition and immunity focused on protein -energy malnutrition. The absorption, transfer, and distribution of many trace elements are not independent on specific binding and transport of proteins .Thus it is not surprising that changes in the concentration of trace elements exert large impact on immune responses. The process of inflammations increases vascular permeability and allows anti body, complement and other proteins to pass out the circulation and enter the extravaseular space. It may also induce inflammatory cells including lymphocytes to cross the vascular endothelium and accumulate in the tissues. Total net effect is to deploy all the resources of the immune system at the site of injury. Cells antibody and complement leave the blood and go into action where the demand is high. It may be in the affected tissue outside the vessel wall .The effect is to abrogate in CNS, if only temporarily, its isolation from the immune processes of the body. The barrier, which excludes plasma proteins from the brain breaks down, allowing antibody to enter the extra vascular space. The amount of proteins in CSF increases and with it the level of immunoglobulin. Immunocompetent cells enter the CNS. The CNS now becomes capable to generating an immune response [15]. We have proposed the current study in the light of some findings on immunological and trace elemental estimations. We can say that the approach of this study may be use full in the direction of neural network problems of epileptic attacks. Neurons are definitely attached with the brain area and everything is related to our food , which we eat . Suitable diet and other types of food may protect our body from diseases.

9. CONCLUSION

It is very important to understand that seizure can result from many different pathologic mechanisms. It may upset (disturb) the balance between inhibition and excitation. Epilepsy is outcome of the processes, which disturb extracellular ion homeostasis, change energy metabolism, alter receptor function, or alter transmitter uptake. The outcome of synchronous bursting of cortical neurons may superficially appear to have a similar phenotype. Seizure phenotype can be altered by the location and function of neuronal network, recruited into the synchronous bursting than by underlying patho physiologies. Computer scientists have used complex neural network system to model the brain activity. Some of the simulations may use many separate data structures to represent individual brain cells, or neurons .Each neuron can receive information in the form of an electrical pulse from the neurons (of the order 10³ to 10⁴).Scientist are required powerful computer to handling all of the interconnections of neurons.

Neural network models may provide a way to piece things together to understand how epileptic behavior translates from the action of just a few neurons to a behavior affecting the human brain? Human brain contains about 10¹⁰ neurons .Neural network which made earlier treated each neuron as a fixed entity. A neuron can exist only in one of two state such as firing or inactive. Some researchers treated each neuron as a pathway into itself. The route of electrical signal from fibrous dendrites into the cell body and out through the axon to the other neurons. Due to this fact a data chain of the neurons can be build up.

Neural network provide a glimpse into epilepsy that completes information obtainable through clinical or laboratory studies.

A successful seizure prediction requires a combination of further modeling and experimental work in term of measuring the immunological and trace elemental parameters . Multifactorial causes of epilepsy can be understand with the programming of computer models. These models can encapsulate so many conspiring and counteracting causes. We can also extend these complexities to the therapeutic domain. We know that many drugs have multiple binding sites and multiple effects. A new anticonvulsant therapy can be suggested with the help of computer simulation. A further detailed study in the computer modeling related to epileptic attacks can persuade. We have to develop a device that simply alert patients with a

period of high seizure probability. Due to advancement of computer, it is now possible to use super computers to run massive simulations, again with the hope of providing greater verisimilitude by more closely approximating the large numbers of cells in brain areas.

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REFERENCES

[1]. Hill, A. V, Chemical Changes and Mechanical Response in Simulated Muscle. Proc. Roy. Soc. B, 1953 : p . 314-320.

[2]. David, J. A, The Physiology of Excitable Cells, In : Introduction Essentials of Biological and Medical Physics, R. W. Staly, D. T., Williams, R. E., Worden, and Mc Coris ,Editors, Cambridge University Press, New York, Mc Graw Hill., 1998 : p. 3-7.

[3]. Glasser, O, Fundamental Concepts of Biophysics. In : Introduction, in Essentials of Biological and Medical physics, R. C. Stacy D. T. Williams, and Mc Morris, Editors, New York, Mc Graw- Hill, 1955 : p. 263-265.

[4]. Milton, J. G, Medically Interactive Epilepsy. In:Epilepsy as a Dynamic Disease :- Musings by a Clinical Computation, J. Milton, and P. Jung, Editors, Springer, New York, 2003 : p. 1-14.

[5]. Persinger, M. A. and S. A. Koren, A Theory of Neurophysics and Quantum Neuroscience: Implications for Brain Function and the Limits of Consciousness. Intern. J. Neuroscience, 2007. 117 : p. 157-175.

[6]. John, E. R, Representation of Information in the Brain, In: Machinery of the Mind. Boston , E. R. John , Editor , Birkhauser, 1990 : p. 27-56.

[7]. Garben, P. B, Foundations of Neurophysics. In Lectures in Super computational Neuroscience: Dynamics in Complex Brain Networks. P. B. Garben, C. Zhou, M. Thiel, and J. Kurths, Editors, Berlin, Springer, 2008 : p. 4-48.

[8]. Scott, A. C, Non-linear Partial Differential Equations. In : Neurophysics. Wiley Interscience, New York, London,1977: p. 13-64.

[9]. Lytton, W. W, Computer modeling of epilepsy. Nature Review Neuroscience, 2008. 9 : p. 626-637.

[10]. Hodgkin ,A.L.,and Huxley , A.F , A quantitative description of membrane current and its application to conduction and excitation in nerve. J. Physiol. (London), 1952.117:p. 500-544.

[11]. Cole, K. S. and H. J. Curtis, Electric Impedance of the Squid Giant Axon during Activity. J. Gen. Physiol, 1939. 22 : p. 649-670.

[12]. Mancini, G., A. O. Carbonara and J. F. Herman's, Immunochemical Quantitation of Antigens by Single Radical Immunodiffusion. Immunochemistry, 1965. 2 : p. 235.

[13]. Gomez, P. F, Brain Foods : The Effects of Nutrients on Brain Function. Nat. Rev. Neurosci, 2008. 9(7) : p. 568-78.

[14].Chandra, R.K, Trace Elements and Immunity : A Synopsis of current knowledge .The UnitedNationsUniversity// internet news p.1-3

[15]. Tourtellotte, W, On cerebrospinal fluid immunoglobulin – G (IgG) quotients in multiple sclerosis and other disease A review and a new formula to estimate the amount of IgG synthesized per day by the central nervous system. J .Neurol .Sci,1970 .10 279: p.304