Chaos Theory and Behavioral Patterns: A theoretical Approach to Psychosis, Bipolar Disorder and Depression

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Abstract: *Introduction*: In this research, we investigate whether chaotic phenomena (Chaos Theory) regulate human brain physiological and pathological behavioral patterns (BP).

Methods: Modeling the six basic neurotransmitters of Central Nervous System (CNS), that is to say Dopamine (DA), Serotonin (SE), Noradrenalin (NE), γ-aminobutiric acid (GABA), Glutamate (Glu) and Acetylcholine(Ach), a set of six first order differential equations have been developed and studied in phase-space.

Results: The elementary equilibrium points in three (3-DS) and six dimensional (6-DS) phase portrait analysis, include attractors, saddles and repellors. Furthermore, it has been studied the 3-D phase-space of DA, SE and NE.

Conclusions: Attractors indicate a stable equilibrium point which corresponds to the most stable behavioral pattern, while the saddles represent a occasional unstable behavioral pattern and finally the repellors correspond to an unstable dynamic system of a totally disorganized BP.. Among other mechanisms, chaotic phenomena seem to regulate in a particular way the CNS basic neurotransmitters resulting in a huge number of different theoretical BP. The implementation in 3-D phase space provides a different view of Psychosis, Bipolar Disorder and Depression. Further research is needed so as to establish the predictive and therapeutic value of this theoretical approach of Human Behavior.

Keywords: Central Nervous System, chaos, psychosis, bipolar disorder, depression neurotransmitter, behavioral patterns.

1. INTRODUCTION

CNS has been hailed for many years as the main headquarters of all mental and bodily functions. The main distinct characteristics of personality comprises Thinking, Emotions and Behavior. The nature of input stimuli signals are mainly electromagnetic (vision), auditory (hearing) and piezo-bio-electric in case of senses and somato-sensory pathways. Vision signals are analyzed and stored mainly in occipital lobe-primary visual cortex V1 area. Sound signals are processed and stored in specific cells in temporal lobe (auditory cortex, Bodmann areas 41,42 and possibly 22) and finally the rest of input signals are analyzed and processed via Thalamus and stored in sensory and somatosensory cortex. All the previous neuronal areas may communicate to one another and modulate the final outcome in the brain, that is to say, the creation of emotions (positive or negative +,-), thinking power (active or inert) and eventually-through the action of various neurotransmitters-the inner and outer behavioral and cognitive pattern (BCP) of human personality [1].

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Approximately, sixty neurotransmitters exist in CNS but only six of the them play an outstanding role in creation of BCP (DA, SE, NE, GABA, Glu, Ach).

Dopamine (DA), has received extensive research worldwide due to its predominant significance in various physiological and pathological situations, not only in CNS but also in a great variety of specialized tissues and cells. DA receptors are divided into two main categories: first, D1-D5 receptors which activate adenylyl cyclase and secondly the D2-D3-D4 receptors that perform the opposite function than the previous category. In CNS, DA may either follow the rewarding pathway implicated in Addictive Disorders, Bipolar Disorder and Psychosis, or the motor control pathway implicated in Parkinson's Disease, Attention Deficit Hyperactivity Disorder and Restless Leg Syndrome. In peripheral tissues (i.e. kidney, vessels, pituitary gland) may regulate sodium level, vascular tone, hormone secretion etc [2-5].

Serotonin (SE), in CNS (i.e. raphe nuclei) behaves as a multifunctional biochemical molecule demonstrating key roles in behavioral and mood patterns either physiological or pathological. Additionally, in periphery (i.e. enterochromaffin cells) it has a significant impact on cardiovascular, gastrointestinal and circulatory physiology [6-7]. SE receptors are divided into three major types: 1st the 5-

E-ISSN: 2311-1755/16

HT1 type (inhibition of adenylyl cyclase-5subtypes), 2nd the 5-HT2 type (activation of phospholipase C-3subtypes) and 3rd, other 5HT receptors (5-subtypes).

Glutamate (Glu), is an important excitatory neurotransmitter in CNS. Glu acts on ionotropic and metabotropic (G-protein coupled) receptors, whereas-in postsynaptic cell via NMDA or AMPA receptor-activation occurs. Due to its role in synaptic plasticity (i.e. Hippocampus, neo-cortex), it is also involved in cognitive functions such as learning and memory [8].Also, it is implicated via excitotoxicity in chronic diseases such as Epilepsy, Lateral Amyotrophic sclerosis, Huntington's Disease, Alzheimer's Disease etc. Additionally, Glu is the precursor for the synthesis of gamma-aminobutyric acid (GABA).

GABA, is the main inhibitory neurotransmitter in CNS and is implicated in regulating neuronal excitability and muscle tone as well. Drugs that act as allosteric modulators of GABA receptors, increase the amount of GABA, producing anti-anxiety and anti-convulsive effects [9].

Acetylcholine (Ach), in CNS operates as a neuro-modulator and is implicated in arousal, attention, addiction(i.e. nicotinic receptors), learning and motivation. Furthermore, is actively present in neuromuscular junction (i.e. muscarinic receptors), autonomic nervous system and parasympathetic system. Malfunction of cholinergic system in the brain is directly associated with memory deficits in Alzheimer's Disease [10].

Noradrenaline (NA), belongs to catecholamine family that functions in brain and body, either as a neurotransmitter or as a hormone. In the brain, it is produced mainly in locus coeruleus (Pons area), sympathetic ganglia (spinal cord, abdomen) and adrenal glands.Regardless of its source, NA acts on adrenergic receptors located on target cell surface. Generally speaking, NA mobilizes the brain (i.e. arousal, alertness, attention), and bodily functions such as tachycardia, hyperglycemia, hypertension and vasoconstriction. NA receptors belong either to Alpha Family (a1-activation of phospholipase C, a2-inhibition of adenylate cyclase-) and Beta Family (b1,b2,b3-activation of adenylate cyclase-). Current evidence suggest the important role of NA in a variety of health issues such as chronic neuropathetic pain and certain Psychiatric disorders [11-13].

The aforementioned neurotransmitters follow no-linear secretion patterns based on circadian rhythms whereas the SE-enriched suprachiasmatic nucleus operates as the main regulators of this process [14,15]. No-linearity of CNS neurotransmitters secretion has received extensive scientific research worldwide. High performance liquid chromatography is commonly used to determine neurotransmitters concentrations in CNS [16]. While drosophila melanogaster appears to be a reliable genetic model to study neurotransmitter transporters [17]. Additionally, mathematical models have been developed to elucidate neurotransmitters loops in CNS [18,19]. Yet, the interaction among neurotransmitters remain to a significant extent a virgin scientific area to explore. Nowadays, Dynamical System Theory (i.e. Chaos Theory) has emerged as an extraordinary bioengineering "tool", which has found application in a great variety of disciplines, including chemistry, physics, biology, medicine and bioengineering, revealing very often the underlying chaotic, non-linear behavior of the observed systems [20-22]. In the present study, the six basic neurotransmitters (DA, SE, NE, Glu, GABA, Ach) are combined appropriately so as to form a 3 and 6-Dimensional Dynamic System (3-DS, 6-DS respectively) [23], with a view to explore in phase-space domain, possible hidden information derived by mutual interactions among them.

2. METHODS

Based on up to date research, amongst the most neurotransmitters a negative or/and a positive feed back system exists and mostly regulates the final biochemical secretion [24-27]. Thus, we may hypothesize that the six neurotransmitters are related to one another in a particular loop way. Moreover we adopt the next symbolization: DA=X1, SE=X2, NE=X3, Glu=X4, GABA=X5, Ach=X6 and we create a 3-DS (X1,X2.X3) and 6-DS(X1,..X6). We stipulate that the following axiom is valid: Every neurotransmitter's (X1,..X6) secretion through time (T) follows exponential law and may be affected either positively (+) or negatively (-) by the concentrations of the rest of the them. Thus, a positive or a negative feedback exists among X1,..X6.

In more general expression the system 3-DS(X1=X, X2=Y, X3=Z) could be written as:

$$\frac{DX}{DT} = F_X(X,Y,Z)$$
$$\frac{DY}{DT} = F_Y(X,Y,Z) \quad (1)$$
$$\frac{DZ}{DT} = F_Z(X,Y,Z)$$

Where the first part of the equations represent the first Derivatives with respect to time of X,Y,Z and the second part contains non linear Functions ($F_{X,Y,Z}$) of X,Y,Z.

On the basis of local linearization technique applied closely to an equilibrium point, the 3-DS can be converted to:

$$\begin{aligned}\frac{DX}{DT} &= a_{11}X + a_{12}Y + a_{13}Z + b_1\\ \frac{DY}{DT} &= a_{21}X + a_{22}Y + a_{23}Z + b_2\\ \frac{DZ}{DT} &= a_{31}X + a_{32}Y + a_{33}Z + b_3\end{aligned} \quad (2)$$

Where $a_{i,j=1,2,3} \neq 0 \in R$ stand for either the positive or negative quantification feedback; $b_{i=1,2,3} \neq 0 \in R$ correspond to the steady state.

Thus, the 3-DS becomes:

$$\frac{D\vec{X}}{DT} = A \cdot \vec{X} + B \quad (3)$$

With A(3X3) and B(3X1) being the respective arrays of (2).

It is well known that the solutions of (3), exhibit the same stability, instability or asymptotic stability performance like the respective homogeneous system behavior in zero solution:

$$\frac{D\vec{X}}{DT} = A\vec{X} \quad (4)$$

Subsequently, in order to study the homogenous system (4) around the zero solution, it is sufficient to explore the array A for a great variety of $a_{i,j}$ values and determine which of the situations below exist: a) Situation One, here all the eigenvalues (L=(Real)+(Imaginary)·i, where i^2 = -1) of A have negative Real part thus, the zero solution is asymptotically stable; b) Situation Two, if at least one eigenvalue has positive Real part then zero solution is unstable; c) Situation Three, if for all eigenvalues with Real part <=0 and for every eigenvalue with Real part = 0, the dimension of the corresponding subspace is equal to the multiplicity of eigenvalues, then the zero solution is stable.In any other case, the zero solution is unstable. Having identified one of the previous situations, phase-space is easily obtained for the most frequently met equilibrium points. In detail the phase-space of (4) can be found by following the next steps: i) Step One, assumption for exponential solution $\vec{X} = C \cdot e^{L \cdot T}$ where C(3X1) array, L-Real or Complex eigenvalue; ii) Step Two, finding the eigenvalues $L_{1,2,3}$; iii) Step Three, establishment of the analytical solutions X(T),Y(T) and Z(T); iv) Step Four, finding the space function F(X,Y,Z)=0 via elimination of T; v) Step Five, making the phase portrait in 3-D.

3. RESULTS

The array A consists of nine $a_{i,j}$-parameters of positive or negative sign. The positive sign corresponds to a positive feedback, which means that the derivative of X,Y or Z increases under the contribution of $a_{i,j}$. By contrast, the negative $a_{i,j}$-parameters cause the opposite result, that is to say a decrease in the respective derivative. Since every $a_{i,j}$ may have two different signs it is easily deduced that 2^9 different combinations could be formed for the 3-DS, while for the 6-DS the estimated number is 2^36.

From this wide spectrum of $a_{i,j}$-values we focus on those that are related to the most frequently met elementary equilibrium points in a 3X3 first order homogenous 3-DS. On this basis, the following cases can be distinguished: a) Case One, the first eigen value (L_1) is a negative real number, while the second (L_2) and the third (L_3) are complex conjugate numbers with negative real parts. In phase space graph an attractor is formed (Figure **1** part-1) b) Case Two, $L_{1,2,3}$ are negative real numbers and they also give an attractor (Figure **1** part-2) c) Case Three, L_1 is a real positive number whereas $L_{2,3}$ are conjugate complex numbers with negative real parts. Their space function graph results in a saddle-1 (Figure **2** part-1) d) Case Four, L_1 is a real positive number with $L_{2,3}$ being negative real numbers and like the previous Case, a saddle-1 is formed in phase portrait (Figure **2** part-2) e) Case Five, L_1 is a real negative number while $L_{2,3}$ are complex conjugate numbers with positive real parts, while in phase space a saddle-2 is formed (Figure **3** part-1) f) Case Six, L_1 is a real negative number and $L_{2,3}$ are positive real numbers. A saddle-2 is also illustrated in phase portrait (Figure **3** part-2) g) Case Seven, L_1 is a positive real number and $L_{2,3}$ are complex conjugate numbers with positive real parts and in phase space a repellor is illustrated (Figure **4** part-1) h) Case Eight, $L_{1,2,3}$ are positive real numbers and a repellor is formed in phase portrait (Figure **4** part-2). An example of Case Four follows:

$$A = [1,2,1;-1,-1,2;1,1,-1] \Rightarrow |A - L \cdot I| = 0 \Leftrightarrow \phi(L) = (L+4.1)\cdot(L+0.38)\cdot(L-1) = 0$$

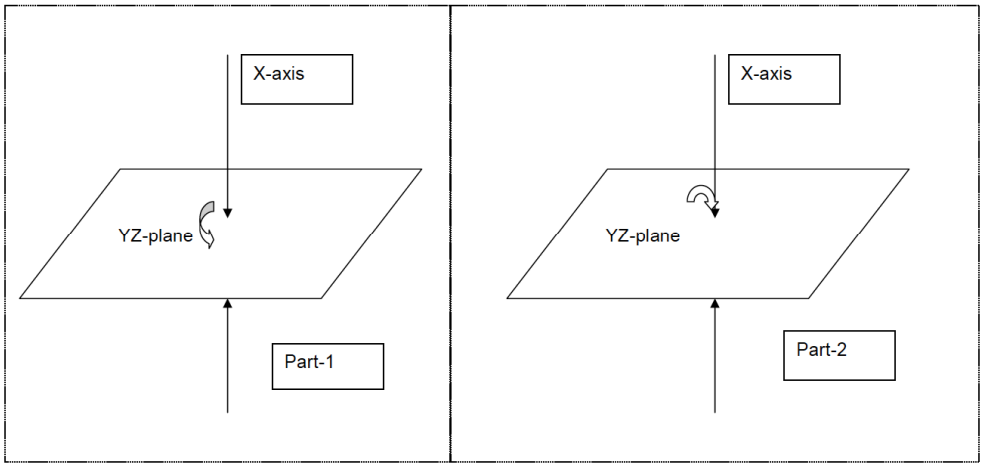

Figure 1: Illustrates in part 1 and 2 the space function graph. In X-axis the direction of the arrows towards YZ-plane shows conversion of X-solution to zero point; in YZ-plane the arrow around zero point or towards it, shows asymptotic conversion of Y,Z-solution.

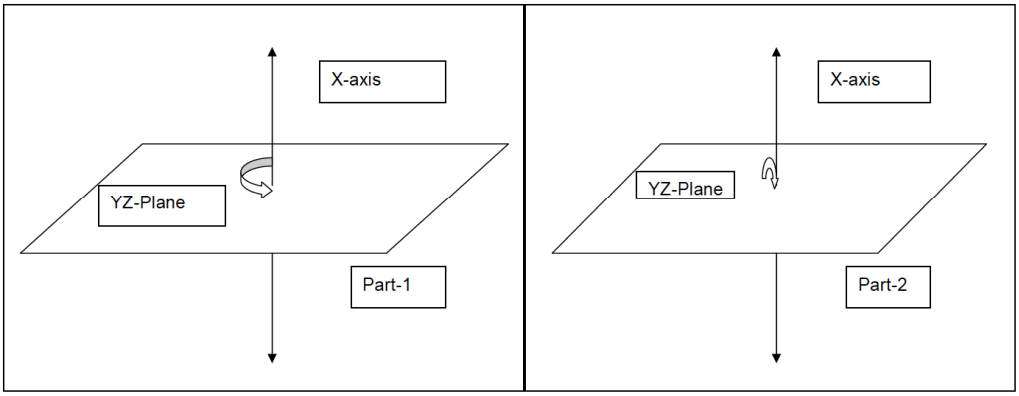

Figure 2: Illustrates in part 1 and 2 the space function graph.In X-axis the direction of the arrows outwards from YZ-plane shows diversion of X-solution to zero point; in YZ-plane the arrow around zero point or towards it, shows asymptotic conversion of Y,Z-solution.

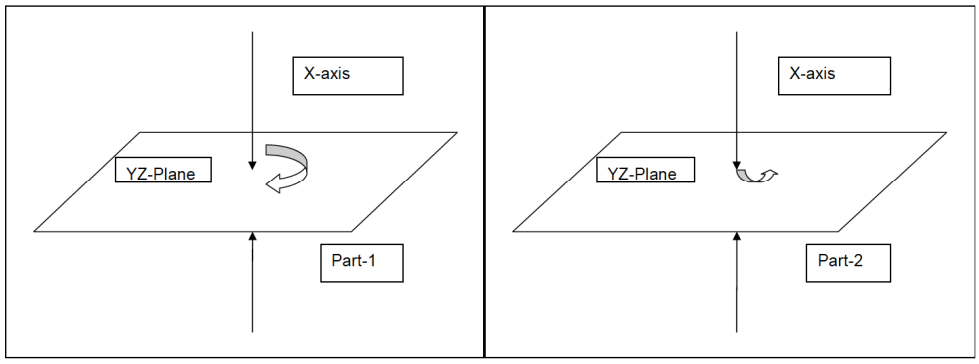

Figure 3: Illustrates in part 1 and 2 the space function graph. In X-axis the direction of the arrows towards YZ-plane shows conversion of X-solution to zero point; in YZ-plane the arrow around and away from zero point or outwards from it, shows diversion of Y,Z-solution.

Thus, the eigen values are L_1=1, L_2=-4.1, L_3=-0.38 and the analytical solution becomes:

$\vec{X} = C_i \cdot e^{L_i \cdot T}, i = 1,2,3$ and $C_i(3x1)$ array of constant parameters is determined by the initial conditions.

4. DISCUSSION

CNS is the most crucial processor unit of human body. Group of Neurons create particular subunits, which modulate every function of human body and

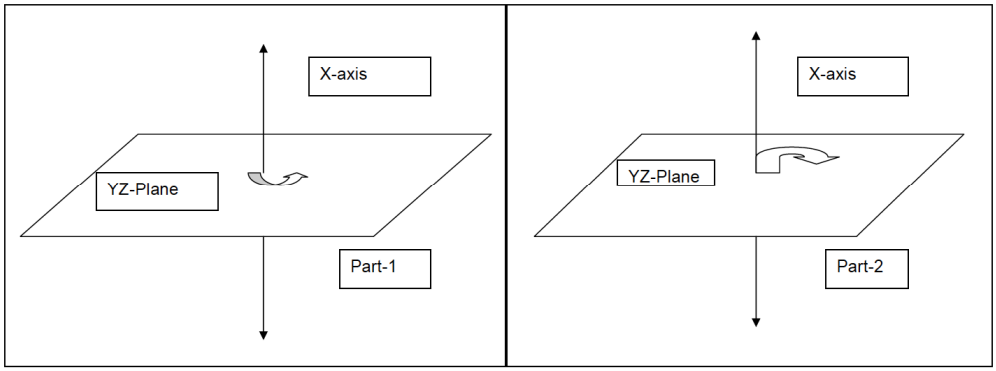

Figure 4: Illustrates in part 1 and 2 the space function graph. In X-axis the direction of the arrows outwards from YZ-plane shows diversion of X-solution to zero point; in YZ-plane the arrow around and away from zero point or outwards from it, shows diversion of Y,Z-solution.

behavior. Human Behavior is nothing more than the reflection of a numerous interwoven biochemical pathways that outstanding passengers follow, the neurotransmitters. Nearly sixty neurotransmitters have been identified so far, yet six of them are considered to be the most important. DA, SE, NE, Glu, GABA and Ach cooperate within a matrix of negative or positive feedback pathways, producing specific BP of an individual, either physiological or pathological. The current study is based on the afore-mentioned assumption and has analyzed the derived 3-DS and 6-DS behavioral dynamic systems. Mathematical results have taken the form of an attractor, a saddle or a repellor.

An attractor represents a stable solution to the system. Thus, as time passes the X,Y and Z parameters (DA, SE, NE respectively), converge simultaneously to the zero solution. But what does this mean for human behavior? From the medical point of view an attractor corresponds to a steady combination of neurotransmitters X, Y and Z which promotes the expression of a healthy-stable BP. In other words, the individual exhibits an organized personality, with rational motivation and goals, stable emotional operation and eventually a viable BP. Figure **5**, delineates the main functions either physiological or pathological of six basic neurotransmitters.

Either saddle-1 or saddle-2 declares that the solution is unstable, so as time goes to “infinity” at least one of X,Y or Z diverges from the zero solution. In other words, one of the neurotransmitters X, Y or Z modifies either its expression or function uncontrollably, while the positive or negative feedback seems to be insufficient to balance the situation. Henceforth, a defective BP is developed. In other words, if the neurotransmitter X=DA diverges over expressed, then situations such as hyperactivity, Mania, Bipolar Disorder and Psychosis may be developed in the short or long run [30,31] (Figure **5**). Correspondingly, if under expressed situations such as lack of motivation, hypo-activity or Parkinson Disease may appear [33] (Figure **5**). Obviously, early medical consultation would be helpful in this situation, in order to prevent the deterioration of individual’s behavior.

A repelor appears when all neurotransmitters X, Y and Z diverge from zero solution. Thus the DA, SE and NE are over or under-expressed rapidly, without mutual interaction among them and finally, a totally disorganized BP takes place. In this case, a pathological personality prevails (Figure **5**) and medical intervention is absolutely necessary Undoubtedly, the repellor’s situation is by far the worse behavior of the system, while the saddle’s situation represents malfunction of the system. It is worth being mentioned that by studying the general version of 6-DS (DA, SE, NE, GABA, Glu and Ach) the outcome follows a 3-DS-like pattern regarding the physiological and pathological expressions (Figure **5**).

Meditating upon the current evidence the following should be highlighted: a) an attractor says that if neurotransmitters X, Y and Z are combined appropriately via an active endogenous feedback system, then a stable BP will be derived, b) a saddle denotes that a flaw BP can be derived if insufficient communication among X,Y and Z prevails; in this case, malfunction of the Behavior may appear, c) a repellor says that when no effective feedback exists among X, Y and Z then a totally disorganized BP is produced.

Over the last decades, Psychiatric Disorders such as Psychosis, Bipolar Disorder, Depression and Addiction have been studied and analyzed extensively

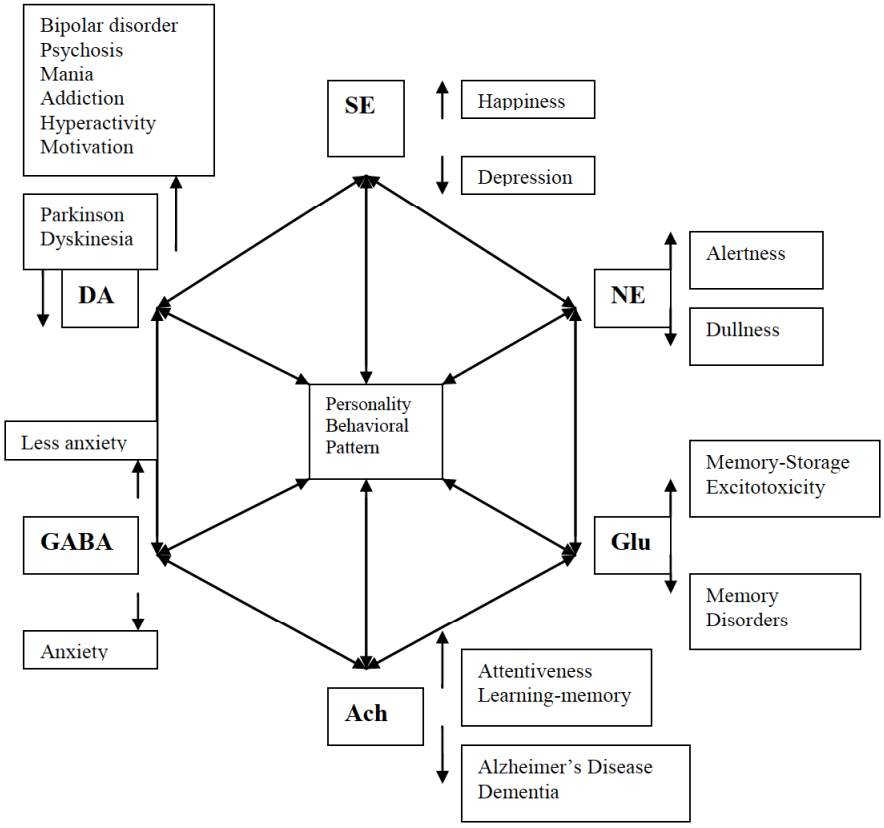

Figure 5: Illustrates the mutually interactive diagram among the six basic CNS neurotransmitters along with their main function or dysfunction.

[29-32]. Psychosis has been linked mainly with DA malfunction, while Depression's main culprit is SE deficiency whereas Bipolar Disorder and Addiction mostly are associated with both DA+SE inappropriate expression and regulation.

Currently, it has been hypothesized and partly verified that the six CNS neurotransmitters communicate one another via negative or positive feedback pathways in such a way that may affect predominantly the personality of an individual [24,28]. Moreover, in this study the results of 3-DS and 6-DS support this hypothesis and have revealed that minor changes of one neurotransmitter may produce a cascade biochemical derailment of another's neurotransmitters pathway. Leading from mild personalities Disorders to serious Psychiatric Diseases.

In conclusion, the present study reveals that CNS neurotransmitters network behaves like an interwoven, complicated mutually interactive system which may be approximated by Dynamic System Theory. Among other mechanisms, Chaos Theory seems to be implicated in Personality Development process. Yet, experimental research is needed towards this direction, so as to establish the biochemical details (i.e. neurotransmitters concentrations values, feedback impact) that regulate the CNS operation. Following this scientific pathway we may be able in the near future to decode Human Behavior under Chaotic perspective, as well. Thus, this new scientific tool may enable us to predict and intervene pharmaceutical at an early stage, providing an effective therapy and a better quality of life for those individuals at threat.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest included in this study.

ACKNOWLEDGEMENTS

The authors would like to express their gratitude to IERION Corporation (www.ierion.com), a global idea enabler which sponsors research and invests in innovative ideas across a broad spectrum of industries including high technology, healthcare, and green energy. This research reveals a different perspective of Human Physiological and Pathological Behavior, which may be a new scientific tool against Psychiatric Disorders. Mr.Domenikos is the Chairman and CEO of IERION and a Harvard University Fellow.

REFERENCES

[1] Hass BW, Miller JD. Bordeline Personality traits and brain activity during emotional perspective taking. Personal Disord 2015; 6(4): 315-20. http://dx.doi.org/10.1037/per0000130

[2] Missale C, Nash R, Robinson SW, *et al*. Dopamine receptors: from structure to function. Physiol Rev 1998; 78(1): 189-225.

[3] Nieoullon A. Dopamine and the regulation of cognition and attention. Prog Neurobiol 2002; 67(1): 53-83. http://dx.doi.org/10.1016/S0301-0082(02)00011-4

[4] Howes OD, Kambeitz J, Kim E, *et al*. The nature of Dopamine dysfunction in Schizophrenia an what this means for treatment. Arch Gen Psychiatry 2012; 69(8): 776-86. http://dx.doi.org/10.1001/archgenpsychiatry.2012.169

[5] Lodge DJ, Grace AA. Abberant himpocampal activity underlies the dopamine dysregulation in an animal model of schizophrenia. J Neurosci 2007; 27(42): 11424-11430. http://dx.doi.org/10.1523/JNEUROSCI.2847-07.2007

[6] Jonnakuty C, Gragnoli C. What do we know about Serotonine? J Cell Physiol 2006; 217(2): 301-6. http://dx.doi.org/10.1002/jcp.21533

[7] Gerson MD. Review article: sérotonine receptors and transporters-roles in normal and abnormal gastrointestinal motility. Aliment Pharmacol Theor 2004; 20 Supp17: 3-14. http://dx.doi.org/10.1111/j.1365-2036.2004.02180.x

[8] Niciu MJ, Kelmendi B, Sanacora G. Overview of glutamatergic neurotransmission in the nervous system. Pharmacol Biochem Behav 2012; 100(4): 656-64. http://dx.doi.org/10.1016/j.pbb.2011.08.008

[9] Abdou AM, Higashiguchi S, Horie K, Kim M, Hatta H, Yokogoshi H. Relaxation and immunity enhancement effects of gamma-aminobutyric acid (GABA) administration in humans. Biofactors 2006; 26(3): 201-8. http://dx.doi.org/10.1002/biof.5520260305

[10] McGleenon BM, Dynan KB, Passmorc AP. Acetylcholinesterase inhibitors in Alzheimer's Disease. Br J Clin Pharmacol 1999; 48(4); 471-480. http://dx.doi.org/10.1046/j.1365-2125.1999.00026.x

[11] Leonard BE. The role of noradrénaline in dépression: a review. J Psychoparmacol 1997; 11(4): 539-47.

[12] Svenson TH. Brain noradrenaline and the mechanisms of action of antidepressant drugs. Acta Psychiatr Scand Suppl 2000; 402: 18-27. http://dx.doi.org/10.1034/j.1600-0447.2000.02604.x

[13] Martins I, de Vries MG, Teixeira-Pinto A, Fadel J, Wilson SP, Westerink BH, Tavares I. Noradrenalin Increases pain facilitation from the brain during inflammatory pain. Neuropharmacology 2013; 71: 299-307. http://dx.doi.org/10.1016/j.neuropharm.2013.04.007

[14] Castaneda TR, de Prado BM, Prieto D, Mora F. Circadian rhythms of Dopamine, glutamate and GABA in the striatum and nucleus accumbens of the awake rat: modulation by light. J Pineal Res 2004; 36(3): 177-85. http://dx.doi.org/10.1046/j.1600-079X.2003.00114.x

[15] Morin LP. Serotonin and the regulation of mammalian circadian rhythmicity. Ann Med 1999; 31(1): 12-13. http://dx.doi.org/10.3109/07853899909019259

[16] Shao XM, Feldman JL. Efficient measurement of endogenous neurotransmitters in small localized regions of central nervous system *in vitro* with HPLC. J Neurosci Methods 2007; 160(2): 256-63. http://dx.doi.org/10.1016/j.jneumeth.2006.09.016

[17] Ciara A Martin, David E Krantz. Drosofila melanogaster as a genetic model system to study neurotransmitter transporters. Neurochem Int 2014; 73: 71-88. http://dx.doi.org/10.1016/j.neuint.2014.03.015

[18] Janet A Best, H Frederik Nijhout and Michael C Reed. Homeostatic mechanisms in Dopamine synthesis and release: A mathematical model. Theoretical Biology and Medical Modelling 2009; 6: 21(doi: 10. 1186/1742-4682-6-21).

[19] Best JA, Nijhout HF, Reed MC. Serotonin synthesis release and reuptake in terminals: a mathematical model. Theoretical Biology and Medical Modelling 2010; 7: 34(doi: 10. 1186/1742-4682-7-34).

[20] Borisuk MT and Tyson JJ. Bifurcation analysis of a model of mitotic control in frog eggs. J Theor Biol 1998; 195: 69-85. http://dx.doi.org/10.1006/jtbi.1998.0781

[21] Tyson JJ, Chen K, Novan B. Network dynamics and cell physiology. Nat Rev Mol Cell Biol 2001; 2: 908-916. http://dx.doi.org/10.1038/35103078

[22] Qu Z, Weiss JN, MacLellan WR. Coordination of cell growth and cell division: a mathematical model. J Cell Sci 2004; 117(18): 4199-4207. http://dx.doi.org/10.1242/jcs.01294

[23] Hirsch MW. The dynamic systems approach to differential equations. Bull Am Math Soc 1984; 11: 1-64. http://dx.doi.org/10.1090/S0273-0979-1984-15236-4

[24] Chen M, Bargh JA. Consequences of automatic evaluation: Immediate behavioral predispositions to approach or avoid the stimulus. Personality and Social Psychology Bulletin 1999; 25: 215-224. http://dx.doi.org/10.1177/0146167299025002007

[25] Nutt DJ. Relationship of neurotransmitters to the symptoms of major depressive disorder. J Clin Psychiatry 2008; 69 Suppl E1: 4-7.

[26] Duk-Su Koh and Bertil Hille. Modulation by neurotransmitters of catheholamine secretion from sympathetic ganglion neurons detected by amperometry. Proc Nat Acad Sci USA Neurobiology 1997; 94(4): 1506-1511.

[27] Mukhamed'yarow MA, Kchunova YO, Telina EN, Zefirov AL. Mechanisms of the facilitation of neurotransmitters secretion in strontium solutions. Behav Physiol 2009; 39(3): 253-9. http://dx.doi.org/10.1007/s11055-009-9123-9

[28] Francis PT. The interplay of neurotransmitters in Alzheimer's Disease. CNS Spectr 2005; 10(11 Suppl); 6-9.

[29] Gregor Hasler. Pathophysiology of Depression: Do we have any solid evidence of interest to clinicians? World Psychiatry 2010; 9(3): 155-161. http://dx.doi.org/10.1002/j.2051-5545.2010.tb00298.x

[30] Donald M. Hilty, Martin H. Leamon, Russel F. Lim, Rosemary H. Kelly and Robert E. Hales. A review of Bipolar Disorder in adults. Psychiatry 2006; 3(9): 43-55.

[31] Broome MR, Woolley JB, Tabraham P, Johns LC, Bramon E, Murray GK *et al*. What causes the onset of psychosis; Schizophr Res 2005: 79(1): 23-34. http://dx.doi.org/10.1016/j.schres.2005.02.007

[32] Jacob T, Sher KJ, Bucholz KK, True WT, Sirevaag EJ, Rohrbaugh J *et al*. An intergrative approach for studying the etiology of alcoholism and other addictions. Twin Res 2001; 4(2): 103-18.

[33] Surmeier DJ, Guzman JN, Sanchez-Padilla J, Goldberg JA. What causes the death of dopaminergic neurons in Parkinson's Disease? Prog Brain Res 2010; 183: 59-77. http://dx.doi.org/10.1016/S0079-6123(10)83004-3

Received on 01-02-2016 Accepted on 18-06-2016 Published on 23-09-2016

DOI: http://dx.doi.org/10.12970/2311-1755.2016.04.01.1