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Research Article

The Impact of TRH-TSH-T3 System on Sexual Offenders Thyroid Function: A Theoretical Chaotic Model

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Abstract

Introduction: The last decades it has been revealed a unique correlation between pathological thyroid function and sex offenders' anti-social behavior. In this research, we investigate the impact of Thyroid Releasing Hormone-TRH, Thyroid Stimulating Hormone-TSH and Triidothironine-T3 system on sexual offenders thyroid function through mathematic modeling (Chaos Theory).

Methods: Modeling TRH-TSH-T3 a set of three first order differential equations have been developed and studied in respective three dimensional phase-space (3-DS). By analyzing the resulting dynamic system, stable and unstable attitudes may be revealed and anticipated.

Results: Linearization technique applied on 3-DS gave way to basic elementary equilibrium points. In three (3-DS) phase portrait analysis the equilibrium points include attractors, saddles and repellors.

Conclusion: Attractors indicate a stable equilibrium point which corresponds to the most stable thyroid function which in turn produces a physiological sex-linked Behavioral Pattern (BP), while the saddles represent a occasional unstable behavioral pattern. That is to say, a potential sex-linked antisocial attitude under certain circumstances and finally the repellors correspond to an unstable dynamic system of a totally pathological sex-linked anti-social behavior. Among other mechanisms, chaotic phenomena seem to regulate in a particular way the biochemical pathway of TRH-TSH-T3, resulting in thyroid malfunction which may trigger sex-offenders attitude. These findings may contribute significantly to the continuous efforts made to anticipate, prevent and possibly cure sex-offenders behavior.

Keywords: Central nervous system; Chaos theory; Sex-offender; Thyroid function; Neurotransmitter; Behavioral patterns; T3; T4; TRH; TSH

Introduction

Central Nervous System (CNS) is considered to be 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 biochemical factors-the inner and outer behavioral and cognitive pattern of human personality [1].

Human personality is characterized mainly by two intrinsic pathways, that is to say the social and anti-social pathway. The second one has received extensive research due to its great impact on human relationships and social infrastructure. Lately, research has revealed that TRH, TSH and T3 Loop algorithm plays a predominant role in the creation of human personality and behavior [2].

Thyrotropin-Releasing-Hormone (TRH) is a releasing hormone produced by hypothalamus in medial neurons of the Para ventricular nucleus [3]. Following secretion, TRH passes the median eminence to the anterior pituitary gland via the hypophyseal portal system and finally stimulates the release of Thyroid Stimulating Hormone (TSH) from thyrotropes cells. Of note, TRH also may detected in other areas of human body such as gastrointestinal tract and pancreatic islets and posses anti-depressant and anti-suicidal properties [4]. In addition, aging-reversing properties have been attributed to TRH due to its total effect on metabolic and hormonal functions [5]. Overall, it seems that TRH exerts its powerful effect on metabolism through secretion of TSH in pituitary gland, which in turn, stimulates the production of T3 in thyroid gland that appears to be the key regulating factor of all oxidative biochemical reactions throughout human organism and a fundamental element in human behavioral phenotype. TRH secretion is mainly regulated by TSH and T3 feedback algorithm.

TSH is produced in a pulsatile manner by the anterior pituitary gland following circadian and ultradian rhythms. The target is the

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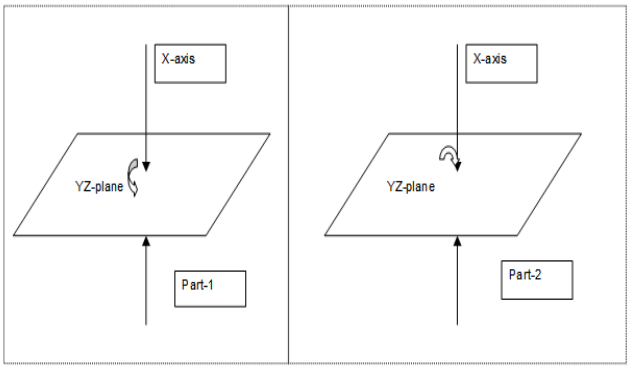

Figure 1: Illustrates in part and 2 the space function graph. In X-axis the direction of the arrows towards YZ-plane shows conversion of X-solution to zero point; in YZ-plane the arrow around zero point or towards it , shows asymptotic conversion of Y,Z-solution.

thyroid gland, so as to secrete the respective thyroids hormones T4 and T3. T4 has only a minor effect on metabolism whereas T3 is the main stimulating metabolic factor [6]. Only 20% of T4 is converted to T3 in Thyroid while the rest 80% conversion takes place in liver. T3 and T4 create a negative feedback loop with TSH regulating at a great extent human metabolism.

T3 and T4 are the cornerstone of metabolic homeostasis and frequently are associated with mood, mental and behavior disturbances. Last decades thyroid abnormalities have been connected with sexual offenders attitudes [7].

The aforementioned biochemical factors follow no-linear secretion patterns based on circadian rhythms whereas the Serotonin-enriched suprachiasmatic nucleus operates as the main regulators of this process [8,9]. 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 [10]. While drosophila melanogaster appears to be a reliable genetic model to study neurotransmitter transporters [11]. Additionally, mathematical models have been developed to elucidate neurotransmitters loops in CNS and peripheral organ targets [12,13]. Yet, the interaction among neurotransmitters and hormones 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 [14-16].

In the present study, the TRH, TSH and T3 are combined appropriately so as to form a 3 Dimensional Dynamic System (3-DS) [17], with a view to explore in phase-space domain, possible hidden information derived by mutual interactions among them, and to elucidate sex-offenders unpredictable behavior.

Methods

Based on up to date research, amongst the most neurotransmitters and hormones a negative or/and a positive feed back system exists and mostly regulates the final biochemical secretion [18-21]. Thus, we may hypothesize that the TRH-TSH-T3 are related to one another in a particular loop way. Moreover we adopt the next symbolization: TRH=X1, TSH=X2, T3=X3. We stipulate that the following axiom is valid: Secretion of biochemical factors X1,X2 and X3 through time (T) follows exponential law and may be affected either positively(+) or/and negatively (-) by the concentrations of the rest of the them. Thus, a positive or a negative feedback exists among X1,X2 and X3.

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

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

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 :

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

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:

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

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:

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

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)

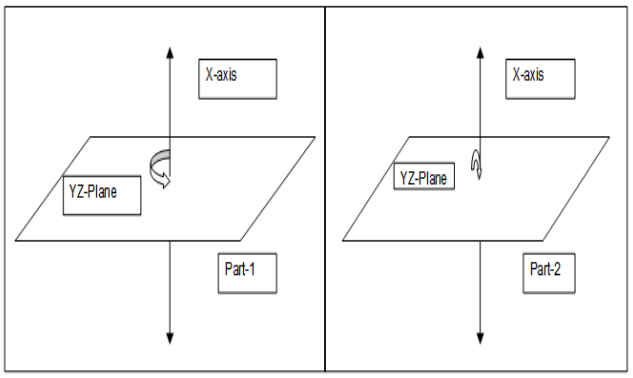

Figure 2: Illustrates in part 1 and 2 the space function graph. In X-axis the direction of the arrows outwards from YZ-plane shows diversion of X-solution to zero point; in YZ-plane the arrow around zero point or towards it , shows asymptotic conversion of Y,Z-solution.

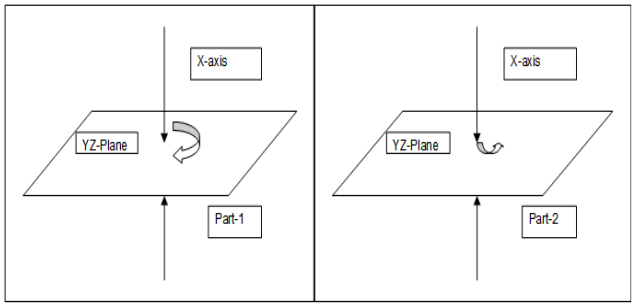

Figure 3: Illustrates in part 1 and 2 the space function graph. In X-axis the direction of the arrows towards YZ-plane shows conversion of X-solution to zero point; in YZ-plane the arrow around and away from zero point or outwards from it, shows diversion of Y,Z-solution.

and Z(T); iv) Step Four, finding the space function F(X,Y,Z)=(ia elimination of T; v) Step Five, making the phase portrait in 3-D .

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 system.

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

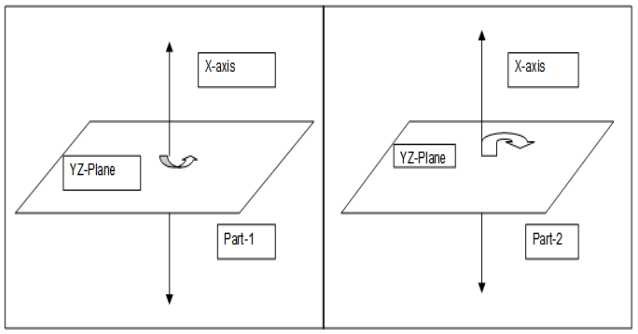

Figure 4: Illustrates in part 1 and 2 the space function graph. In X-axis the direction of the arrows outwards from YZ-plane shows diversion of X-solution to zero point; in YZ-plane the arrow around and away from zero point or outwards from it, shows diversion of Y,Z-solution.

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:

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

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.

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 behavior. Human Behavior is nothing more than the reflection of a numerous interwoven biochemical pathways that outstanding passengers follow, the neurotransmitters. The neurotransmitter Noradrenalin (NE) mostly regulates the TRH release in Hypothalamus. Consequently, TRH acts upon TSH, and finally thyroid hormones T3 and T4 are released into circulation. TRH, TSH and T3 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 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 (TRH, TSH, T3 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 biochemical factors 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 socialized behavior.

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 factors 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 due to T3 hormone malfunction. In other words, if the X=TRH diverges, over expressed, then situations such as sexual hyperactivity, Mania and sexual-linked crimes may be developed in the short or long run. Obviously, early medical consultation would be helpful in this situation, in order to prevent the deterioration of individual's antisocial sexual behavior.

A repelor appears when all factors X, Y and Z diverge from zero solution. Thus the TRH, TSH and T3 are over or under-expressed rapidly, without mutual interaction among them and finally, a totally disorganized BP takes place. In this case, a sexual pathological personality prevails 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.

Meditating upon the current evidence the following should be highlighted: a) an attractor says that if 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 and the sexual offender commits crime.

Currently, it has been hypothesized and partly verified that the CNS biochemical factors communicate one another via negative or positive feedback pathways in such a way that may affect predominantly the personality of an individual. Moreover, in this study the results of 3-DS support this hypothesis and have revealed that minor changes of one factor TRH, TSH or T3 may produce a cascade biochemical derailment of another factor's pathway. Leading an individual to exhibit either a mild sexual disorder or even a serious sex-offender behavior.

Sexual-offenders very often suffer from thyroid abnormalities and especially into the category of violent offenders the proportion is greater [7]. Thyroid disorders may be associated with psychotic episodes, delusions, mania and suicidal thoughts, as well. In most cases, these disorders remain undiagnosed until the person commits a sex-linked crime. Thus, it is essential to have an early test that could screen those individuals at threat and protect both social environment and the individual himself.

In conclusion, the present study reveals that TRH, TSH and T3 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 the formation of personality of sex-offenders. Yet, experimental research is needed towards this direction, so as to establish the biochemical details (i.e.neurotransmitters and hormones concentrations values, feedback impact) that regulate the TRH-TSH-T3 loop operation. Following this scientific pathway we may be able in the near future to decode effectively the sex-offenders' Behavior under Chaotic perspective, as well. Thus, this new scientific tool may enable us to predict and intervene pharmaceutical at an early stage(i.e. TRH,TSH T3, TRH/TSH,TSH/T3,TRH/T3 blood test) providing an effective therapy and a safer social life for all.

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