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Mini-Review

Chaos: A Complex Noise on Blood Pressure Orchestration

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Abstract

The equilibrium by constancy or just shifts in other intrinsic and extrinsic variables are known as allostatic changes in systemic blood pressure regulation. This short-review intends to introduce the Chaos Theory and "occasional" increases of BP in hypertensives and normotensive individuals. Especially, out of control hypertensives (resistant or refractory) and pseudo resistant individuals of hypertensive crisis or out-of-control hypertension. These changes happen according to a stochastic probabilistic pattern that presumes chaotic and nonlinear modelling of BP-related dynamics as a mathematical approach. Based on the Chaos theory, small changes in the initial condition BP levels can disturb the body's homeostasis by causing extreme BP chaotic shifts. Thus, principles and concepts derived from nonlinear dynamics math should also contemplate the possibility of the Chaos taking part in the out or hard of control blood pressure levels. When evaluating BP levels obtained by any method, physicians might incorporate this concept.

Keywords: Resistant hypertension; Refractory hypertension; Chaos; Hypertensive emergency; Homeostasis; Nonlinearity; Adherence; Pseudo hypertension; BP regulation; Stochastic system; Lorenz's attractor; Determinism

Introduction

Confounders in hypertension

BP technique (brachial) overestimates the prevalence of uncontrolled RHTN in approximately 33% of patients, reinforcing the need of obtaining accurate BP measurements [1-3]. The most recent AHA/ESC statements on RHTN [2, 4-7] require that both the white-coat effect [2,8,9] and nonadherence [10,11] be excluded from the RHTN definition. Also, systemic BP may oscillate to maintain homeostatic needs and the body constancy [12], or just as shifts in other intrinsic and extrinsic (allostatic equilibrium) variables and systems [13,14]. These latter changes happen according to a stochastic probabilistic pattern, which means "randomly determined" [15] that may be analysed statistically but may not be predicted precisely. This approach requires a nonlinear dynamics regressive analysis based on the Chaos Theory [15,16].

Thus, when measuring BP levels variation and cardiovascular variability in hypertensive patients, it is reasonable to exclusion of (false) diagnoses as pseudo-resistance [1, 17], including white-coat [9, 18-20] (WC-RHTN) and masked [21-27] (M-RHTN) hypertension. Thus, Improvements are mandatory and as well as revising some major concepts on "General Systems" [13, 14, 28], BP regulation [29, 30] and "Chaos" theory [13, 14, 28-33] have to be addressed and discussed in these subjects.

To deeply understand these modalities of occasional enhancement in BP, some definitions and theoretical issues on General Systems theory, BP as a chaotic variable and Probabilistic will be revised. Some terminology will be revised (Encyclopaedia Britannica, 1970):

1. Homeostasis: self-regulation processes to maintain stability while adjusting to optimal conditions. Dynamic equilibrium (Homeostasis) by continuous changes;

2. Allostasis: the process by which a state of internal, physiological equilibrium (homeostasis through changes) is maintained by an organism in response to actual or perceived environmental stressors;
3. Stochastic: property described by a random probability distribution. It is often used as synonymous with randomness;
4. Chaos: the study of apparently random or unpredictable behaviors in complex systems governed by deterministic laws. Deterministic chaos suggests a paradox connecting two notions regarded as incompatible: randomness/unpredictability and deterministic processes;
5. Organismic Biology: field interested in how a total creature, organism or population behaves as it interacts with its environment.

The General System Theory and Chaos

Organismic biology evolution

In 1925, Ludwig von Bertalanffy [13, 14], not satisfied with the physical and deterministic approaches to Biology, proposed an organic conception (Organismic Biology) emphasizing the consideration of the organism as a group or system. The biological systems may be the cells, organisms or populations presenting the common characteristic of being composed of many other systems in interaction; these mechanisms were nominated cum plicate (Greek: complicated) systems. Fundamentally, these hard-to-understand subsystems work jointly to produce coherent behaviors (constancy or equilibrium) [12, 34]. This initial concept led to a great number of articles, books and conferences on General System Theory in many areas of the knowledge. Thus, the human organism should be a system of much smaller (subsystems with common characteristics [13]. This most profound intuition concerning real-life "cum plicate" systems historically dates back to Heraclitus (about 540 B.C.) and Claude Bernard (1813-1878) with the concept of Homeostasis. This term was perfected and coined later by Cannon [12]: Homeostasis results from the response to a system perturbation and occurs as a retro alimentation looping called feedback mechanisms, well-known nowadays as positive or negative stimuli [15, 35-37] The concepts above gained space in many other areas of knowledge as a new paradigm, called "General Systemic Thought" [13] and, sometimes, "Cybernetics", somewhat abstract thinking. Returning to human organisms, a nonlinear or chaotic system behavior of almost the totality of the existing systems, including BP control, has grown since the 1960s. The complex nonlinear systems obey Chaos Theory, which studies the foresight and order of the complex (= chaotic) systems, although random [15]. The antique Determinism and complete Predictability are not considered in the chaotic theory because of their nonlinear expression [15, 38, 39]. Later on, chaotic systems and outcomes in Biological Sciences, with well-sustained mathematic equations, were included in the Theory of Chaos. It starts with the principles of negative feedback control and how it regulates blood pressure in humans [13, 38]. Then, it culminates in the population regulation and ecosystem. Finally, the Chaos and the random determinism regulation of such general physiological mechanisms modulate biological systems (including BP) from cell to population levels [13, 28, 30, 40, 41].

"Storms" Shifts in RHTN Follow-Up

Many disturbances contribute to the volemia expansion and autonomous nervous system (ANS) disorders implicated in the RHTN pathophysiology; however, a BP chaotic behavior based on traditional Biology, Mathematics and Physics have not been adequately exploited yet. Of course, some complex concepts are of hard comprehension for biological and health professionals. At this point, we will use the parallelism between the diverse and unstable levels of BP observed in the RHTN syndrome, and the unpredictable and aperiodic changes alternating the weather of "lulls and storms." Characteristically, both initial and small shifts in RHTN subjects start increasing BP and from a beautiful sky, some may start from minor alterations (grey clouds) in the BP system or some "heavy" clouds, respectively. Then, in a few more minutes, slight unpredictable shifts disrupt this well-tuned BP climate equilibrium turning the warm, calm, sunny and blue sky into a windy, unstable, dark and noisy tempest with bolts of lightning and thunder. Although aperiodic, such time conditions tend to come back to be close to its serene starting, but not precisely at the very same first sight. The fundamental issue to address in this (uncontrolled RHTN) tempest is to keep the physiological homeostasis, avoid non-compensatory allostatic changes and chaotic oscillations in the related variables, thus preventing "target-organ damage" in these patients.

PERIODICITY	FINAL DETERMINED BY INITTIAL	PREDICTABILITY (POLYNOMIAL)	TENDENCY TO GO BACK TO THE BEGINNING	CYCLICITY
Aperiodic	"Pre-deterministic"	Imprecise	Yes (Not exactly)	Cyclic

Table 1: Premises that characterize the chaotic behavior (Chaos Theory).

RHTN is often a clinical condition associated with multiple system disorders, ranging from genetic diseases, cellular receptors and endothelial dysfunction to a high salt consumption worldwide. Such unstable, inappropriate, and non-responsive BP levels, besides the complicated pathophysiology, deserve an analytical approach based on the General Systems Theory in health (homeostasis) and disease (allostasis). These harmful and spurious PB oscillations may be due to some failure in the stochastic chaos process of BP regulation and not a part of an allostatic self-restoring process in RHTN individuals. Thus, reviewing some pivotal content on General Systems and deterministic nonlinear (chaotic theory and equations) processes is critical to the better comprehension of outlier and unstable values of BP in these hard-to-control hypertensive patients.

The key to previewing BP values over time is a nonlinear autoregressive integrated (NLARI) process that applies Newton's second law to stochastic self-restoring systems [15, 30, 40, 42-51]. Even though these mathematical cum plicate or cum plex approaches, just the short-time course evolution can be partially foretold using a chaotic method. As in Meteorology, where weather forecasts have accuracy only for the next 5-7 days, predicting BP levels is a hard issue because of the high number of variables involved in a multiple-order polynomial function. On the other hand, the overall peculiarities in the physiopathology of the hard to control hypertension are closely superposed with a chaotic process:

1. small shifts leading to unstable, dramatic and outlier BP patterns;
2. apparent aperiodicity of BP occurrences (not circadian);
3. hard to predict the evolution and medium-long term clinical outcomes;
4. diversity of BP responses (even none) to external stimuli including therapeutics.

Blood Pressure Controlled or Uncontrolled

Poincaré was the first scientist to glimpse the possibility of Chaos, in which a deterministic system exhibits aperiodic behavior that depends sensitively on the initial conditions, thereby rendering long-term predictions [52]. Human organisms work as complex (meaning, chaotic) nonlinear systems as well as almost all the totality of systems known in the Universe [15, 53]. The nature of this characteristic does not exclude Determinism, which makes possible the prediction of BP values over time. However, BP measurements in RHTN patients depend on a constellation of intrinsic and external interfering factors that impede these pressure levels' precise evolution forecast. Unfortunately, modelling the BP interfering factors, multiple exponents (degrees) in a polynomial function equation, works only as a theoretical concept in RHTN.

Analytical techniques derived from chaos theory can help characterize the stability and complexity of blood pressure control, which may provide essential measures for predicting cardiovascular risk. Chaos is located in EEG data, R-R intervals from electrocardiograms, and cellular levels, but only a few studies deal with chaos in sustained hypertension.

Final Reminders

This review reproaches some crucial topics on out or hard to control hypertension and chaotic model [15, 30, 54] (Figure 1)

Following some premises, in 1972, the meteorologist Edward Lorenz gave a talk at the 139th American Association for the Advancement of Sciences meeting entitled "Does the flap of a butterfly's wings in Brazil set off a tornado in Texas?" (Figure 1)

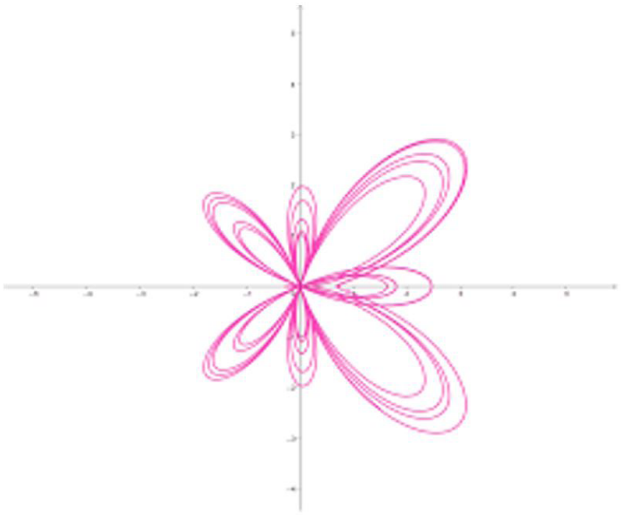

Figure 1: In Chaos theory, the butterfly effect is the sensitive dependence on initial conditions in which a slight change in one state of a deterministic nonlinear system can result in significant differences in a later state. Barile M and Weisstein, EW. "Butterfly Curve." From MathWorld--A Wolfram Web.

Edward Norton Lorenz observed that the butterfly effect derives from minor perturbations such as a distant butterfly flapping its wings earlier. Lorenz initially used a seagull, causing a storm in 1972. A tiny change in initial conditions had created a significantly different outcome. The butterfly effect concept has since been used outside the context of weather Science, including general systems such as blood pressure regulation. However, these effects were not investigated yet as should in true and pseudo hypertensive subjects.

Conclusion

In conclusion, increases in blood pressure may occur even excluding the white-coat, masked hypertension, medical inertia and lack of adherence bias. We presented another form of interpreting the blood pressure (BP) levels in uncontrolled hypertensive subjects as a chaotic, partially deterministic, but unpredictable BP levels syndrome using concepts derived from the field of nonlinear dynamics math: The Chaos Theory [55]. Thus, besides pseudo-hypertension, lack of adherence, circadian variations and other conditions of increasing BP (white-coat, masked, early morning effects or hypertension), chaotic changes can be responsible or co-responsible for out-of-control hypertension.

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