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 mathematical 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].

“Storns” 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.
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 BP 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, 40-51]. 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)
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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**References**

1. Bhatt H, Siddiqui M, Judd E, Oparil S, Calhoun D (2016) Prevalence of pseudoresistant hypertension due to inaccurate blood pressure measurement. J Am Soc Hypertens 10: 493-499.
2. Kaplan NM (1992) Blood pressure measurement and monitoring. Curr Opin Nephrol Hypertens 1: 306-307.
3. Kaplan NM (2016) Predicting home-clinic blood pressure differences. J Am Soc Hypertens 10: 186.
4. Carey RM, Calhoun DA, Bakris GL, Brook RD, Dougherty SL, et al. (2018) Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension 72: e53-e90.
5. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, et al. (2018) 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens 36: 1953-2041.
6. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ (2018) 2017 ACC/AHA/ASCVD/ACP/AAPM/ASPC/ASH/ASPC/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 71: 1269-1324.
7. Kaplan NM (1993) Out-of-office blood pressure measurements. Curr Opin Nephrol Hypertens 2: 923-925.
8. Parati G, Ravogli A, Mancia G (1994) Clinical use of ambulatory blood pressure monitoring: a critical appraisal. J Cardiovasc Risk 1: 108-109.
9. Verdecchia P, Clement D, Fagard R, Palatini P, Parati G (1999) Blood Pressure Monitoring Task force III: Target-organ damage, morbidity and mortality. Blood Press Monit, 1999. 4(6): p. 303-317.
10. de Souza WA, Yugar-Toledo JC, Bergsten-Mendes G, Sabha M, Moreno H (2007) Effect of pharmaceutical care on blood pressure control and health-related quality of life in patients with resistant hypertension. Am J Health Syst Pharm 64: 1955-1961.
11. de Souza WA, Sabha M, Favero FF, Bergsten-Mendes G, Yugar-Toledo JC, et al. (2009) Intensive monitoring of adherence to treatment helps to identify "true" resistant hypertension. J Clin Hypertens (Greenwich) 11: 183-191.
12. Cannon WB (1945) Homeostasis adaptations. Am Med Ateneo Ramon Cajal Mex 3: 1-9.
13. Bertalanffy LV, Hofkirchner W, Rousseau D (1973) General system theory: foundations, development, applications. Revised edition New York: G. Braziller. xxiv, 295 pages: illustrations.
14. Von Bertalanffy L (1969) General System Theory: Foundations, Development. George Braziller, Inc.: New York.
15. Wagner CD, Nafz B, Persson PB (1996) Chaos in blood pressure control. Cardiovasc Res 31: 380-387.
16. Rosser JB (2009) Chaos theory before Lorenz. Nonlinear Dynamics Psychol Life Sci 13: 257-269.
17. Aronow WS (2020) Approaches for the Management of Resistant Hypertension in 2020. Curr Hypertens Rep 22: 3.
18. Modolo R, Barbaro NR, de Fari AP, Sabbatini AR, Paganelli MO, et al. (2014) The white-coat effect is an independent predictor of myocardial ischemia in resistant hypertension. Blood Press 23: 276-280.

19. Siddiqui M, Judd EK, Oparil S, Calhoun DA (2017) White-Coat Effect Is Uncommon in Patients With Refractory Hypertension. Hypertension 70: 645-651.

20. Ghazi L, Cohen LP, Muntner P, Shimbo D, Drawz P (2020) Effects of Intensive Versus Standard Office-Based Hypertension Treatment Strategy on White-Coat Effect and Masked Uncontrolled Hypertension: From the SPRINT ABPM Ancillary Study. Hypertension 78: 1090-1096.

21. Longo D, Dorigatti F, Palatini P (2005) Masked hypertension in adults. Blood Press Monit 10: 307-310.

22. Feitosa ADM, Mota-Gomes MA, Barroso WS, Miranda RD, Barbosa ECD, et al. (2019) Blood pressure cutoffs for white-coat and masked effects in a large population undergoing home blood pressure monitoring. Hypertens Res 42: 1816-1823.

23. Pierdomenico SD, Lapenna D, Bucci A, Tommaso RD, Mascio RD, et al. (2005) Cardiovascular outcome in treated hypertensive patients with responder, masked, false resistant, and true resistant hypertension. Am J Hypertens 18: 1422-1428.

24. Berbari AE, Mancia G (2018) Disorders of Blood Pressure Regulation: Phenotypes, Mechanisms, Therapeutic Options, in Updates in Hypertension and Cardiovascular Protection. Springer International Publishing: Imprint: Springer: Cham. p.1 online resource (XI, 880 pages 131 illustrations, 53 illustrations in color.

25. Siddiqui M, Judd EK, Dudenbostel T, Zhang B, Gupta P, et al. (2019) Masked Uncontrolled Hypertension Is Not Attributable to Medication Nonadherence. Hypertension 74: 652-659.

26. Siddiqui M, Judd EK, Jaeger BC, Bhatt H, Dudenbostel T, et al. (2019) Out-of-Clinic Sympathetic Activity Is Increased in Patients With Masked Uncontrolled Hypertension. Hypertension 73: 132-141.

27. Grassi G, Pisano A, Bolignano D, Seravalle G, D’Arrigo G, et al. (2018) Sympathetic Nerve Traffic Activation in Essential Hypertension and Its Correlates: Systematic Reviews and Meta-Analyses. Hypertension 72: 483-491.

28. Meadows DH, Wright D, (2009) Thinking in systems: a primer, London; Sterling, VA White River Junction. Vermont: Earthscan Chelsea Green Publishing.

29. Mancia G (2013) Resistant Hypertension: Epidemiology, Pathophysiology, Diagnosis and Treatment. Milano: Springer Milan: Imprint: Springer.

30. James GD (2019) The Adaptive Value and Clinical Significance of Allostatic Blood Pressure Variation. Curr Hypertens Rev 15: 93-104.

31. Alwan A, Maclean DR, Riley LM, d’Espaignet ET, Mathers CD, et al. (2010) Monitoring and surveillance of chronic non-communicable diseases: progress and capacity in high-burden countries. Lancet 376: 1861-1868.

32. Wilson T, Holt T, Greenhalgh T (2001) Complexity science: complexity and clinical care. BMJ 323: 685-688.

33. Alderman MH, Budner N, Cohen H, Lamport B, Ooi WL (1988) Prevalence of drug resistant hypertension. Hypertension 11: I171-I175.

34. Coleman TG, Manning RD, Norman RA, Granger HJ, Guyton A (1972) The role of salt in experimental and human hypertension. Am J Med Sci 264: 103-10.

35. Godoy M (2003) Chaos Theory applied to Medicine. Rio Preto Faculty of Medicine (FAMERP). Pp: 179.

36. Guyton AC, Coleman TG, Granger HJ (1072) Circulation: overall regulation. Annu Rev Physiol 34: 13-46.

37. StatPearls. 2021.

38. Gleick J (2008) Chaos: making a new science. 20th anniversary New York, N.Y: Penguin Books. xiii, 360 p.: ill. (Some col.).

39. Persson PB, Wagner CD (1998) From crude cardiovascular signals to chaos. Fundam Clin Pharmacol, 12: 6s-10s.

40. Friston K, Heins C, Ueltzhöffer K, Costa LD, Parr T (2021) Stochastic Chaos and Markov Blankets. Entropy (Basel) 23: 1220

41. Oestreicher C (2007) A history of chaos theory. Dialogues Clin Neurosci 9: 279-289.

42. He Z (2007) A new class of nonlinear integrated models. Far East Journal of Theoretical Statistics 23: 31.

43. He Z (2013) Dynamics and stability of a new class of nonlinear integrated models with resilience mechanisms Far East Journal of Theoretical Statistics 21: 1-32.

44. He Z (2018) Integer-dimensional fractals of nonlinear dynamics, control mechanisms, and physical implications. Sci Rep 8: 10324.

45. He Z (2019) A General Fluctuation Model for Nonlinear Dynamics, Bifurcation, Fractals, and Control Mechanisms. J Telecommun Syst Manage 8: 1.

46. He Z (2019) Cellular and Network Mechanisms for Temporal Signal Propagation in a Cortical Network Model. Front Comput Neurosci, 2019. 13: 57.

47. He Z (2020) The control mechanisms of heart rate dynamics in a new heart rate nonlinear time series model. Sci Rep 10: 4814.

48. Brunton SL, Brunton BW, Proctor JL, Kaiser E, Kutz JN (2017) Chaos as an intermittently forced linear system. Nat Commun 8: 19.

49. Gregório ML, Wazen GLL, Kemp AH, Milan-Mattos JC, Porta A, et al. (2020) Non-linear analysis of the heart rate variability in characterization of manic and euthymic phases of bipolar disorder. J Affect Disord 279: 136-144.

50. Pivatelli FC, Santos MAD, Fernandes GB, Gatti M, de Abreu LC, et al. (2012) Sensitivity, specificity and predictive values of linear and nonlinear indices of heart rate variability in stable angina patients. Int Arch Med 5: 31.

51. Skokos C, Gkolaia I, Flach S (2013) Nonequilibrium chaos of disordered nonlinear waves. Phys Rev Lett 111: 064101.

52. Elbert T, Ray WJ, Kowalik ZJ, Skinner JE, Graf KE, et al. (1994) Chaos and physiology: deterministic chaos in excitable cell assemblies. Physiol Rev 74: 1-47.

53. Wagner CD, Mrowka R, Nafz B, Persson PB (1995) Complexity and “chaos” in blood pressure after baroreceptor denervation of conscious dogs. Am J Physiol 269: H1760-H1766.

54. Wagner CD, Persson PB (1998) Chaos in the cardiovascular system: an update. Cardiovasc Res 40: 257-264.

55. Moreno H (2022) Pseudo and resistant hypertension: A chaotic perspective. J Clin Hypertens (Greenwich).