Neurochaos: Analyzing the Brain and Its Disorders from a Physics Perspective

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Abstract From stock market dynamics to biophysical variability, many investigations for understanding chaotic behaviors in complex systems have been undertaken. Mathematical models have been developed to reproduce the conditions and approximate end results in these systems with theoretical success albeit limited ecological validity. More recently, however, scientists have been pondering the role of chaos in neuroscience, especially in relation to pathophysiological mechanisms. Does chaos theory have a role in the central nervous system? Can it help explain why some individuals' brains go awry? Discussion of these and similar questions with potentially promising avenues of research are suggested in this chapter.

Keywords Neurochaos · Pathophysiological mechanisms · Brain disorders

Introduction to Chaos Theory

The concept of chaos implies a state of confusion, or disorder. Chaos theory is the mathematical approach that aims to explain the state of such systems [29]. These are dynamic systems with apparent random states of irregularities and disarray, in which the states are governed by deterministic laws. In other words, what appears to be random in various systems, biological or otherwise, may not necessarily be stochastic in nature. Furthermore, the underlying patterns that are embedded in these systems are highly sensitive to the perturbations in the initial state of that system. A fractional change in a given non-linear deterministic system can result in significant changes to subsequent states, highlighting a dependence on initial conditions [12]. *Poincaré* summarizes this notion in his essay *Science and Method* writing:

> *It may happen that small differences in the initial conditions produce very great ones in the final phenomena. A small error in the former will produce an enormous error in the latter. Prediction becomes impossible, and we have the fortuitous phenomenon.*

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Ş. Ş. Erçetin et al. (eds.), *Chaos, Complexity and Leadership 2020*,
Springer Proceedings in Complexity, https://doi.org/10.1007/978-3-030-74057-3_3

Time and constant change are the fundamental variables that makeup chaos. The weather, food prices, population numbers, and industrial averages all change with time. With determinism originating from Laplace, Henri Poincaré developed chaos theory specifically to study the evolution of physical systems [31], and in the early 1960s, Edward Lorenz rebirthed the notion. Lorenz, a meteorology professor, wanted to evaluate his hypothesis that using mainframe computers in testing launching satellites and planning weapons would aid in giving error-free weather forecasts [27]. Given that weather is determined by a combination of variables such as pressure, wind velocity, and temperature, Lorenz constructed a series of equations and coded them into special vacuum-tube-based computers. Unlike other programs, Lorenz discovered that his program yielded somewhat different forecasts. He later discovered that the computer printout had rounded decimal values for the data, resulting in a minutely different set from the original data. This tiny alteration in the initial conditions resulted in drastically different results from what Lorenz had expected [14]. Lorenz coined the term "butterfly effect" to refer to the extreme sensitivity to initial conditions and its consequences (i.e., metaphorically the flapping of a butterfly's wings resulting in a tornado elsewhere later in time).

Naturally, the presence of chaos means the absence of order, and this is where chaos can pose a problem. In the scientific world, forecasting future behaviors of a system, be it financial, political, or biological, is of critical importance. Chaotic behaviors can make it near impossible to forecast that particular system's behavior. Deciphering the nature of chaos and the underlying patterns is essential as far as scientific inquiry is concerned [4].

Upon his discovery of chaos and identification of its key mechanisms, Lorenz described the theory as studying random and unpredictable behaviors in systems under deterministic laws [29]. The notion of "deterministic chaos" is well recapitulated by this phenomenon. When graphing his data on several axes, Lorenz noticed that plotting the trajectory of nearby points influenced their separation. The extent of the separation would continue until different regions appeared. Upon iteration, the plotted points would reorganize themselves, resulting in unexpected results which somewhat ironically resembled the shape of a butterfly (Fig. 1). Lorenz called these

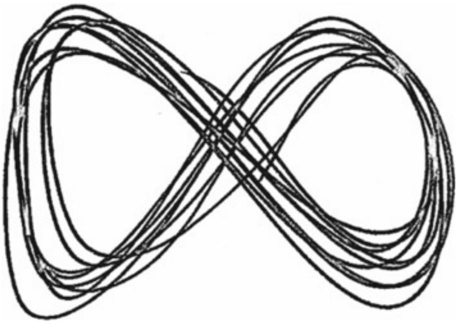

Fig. 1 Lorenz strange attractor

peculiar and complex formations “strange attractors” [40]. Numerous strange attractors would soon be discovered, including the Hénon attractor identified by mathematician Michael Hénon and the Poincaré–Bendixson theorem that posits a strange attractor can appear only in three or more dimensions.

Errors in measurement or numerical computation that change the initial conditions of a system can result in diverse outcomes or altered systems, rendering any long-term predictions useless [21]. Although determinism does not necessarily make a system better; it indicates that future behaviors follow a unique revolution determined by initial conditions with little involvement of stochastic behaviors [3]. As the terms suggests, deterministic chaos is somewhat of a paradox, connecting two scientific notions that were traditionally viewed as incompatible. Nonetheless, it is now understood that deterministic chaos is ubiquitous. Chaotic behavior exists in many natural systems such as heartbeat irregularities, fluid flow, and of course, the climate [19]. Likewise, chaotic behaviors occur spontaneously in some artificial components systems such as road traffic and the stock market. Behaviors in these systems can be examined with sophisticated mathematical models and other techniques such as Poincaré maps or recurrence plots.

Scientists have attempted to solve non-linear equations for several decades now, and from each discipline, valuable contributions have been made. From a meteorologist’s discovery of the first strange attractor in the process of understanding whether unpredictability to a biologist who promoted the study of the quadric map in understanding population dynamics [9] and later, the contributions of engineers, applied mathematicians, and computer scientists that spearheaded problems in their respective fields using non-linear dynamical system approaches. Perhaps the greatest appeal of non-linear dynamics is that it enables interdisciplinary research, incorporating views from different scientific fields such as mathematics and physics [43]. Although the conception of chaos theory was first through observing weather patterns, the theory has become applicable in various disciplines and situations. For example, it has been applied to the field of robotics, where the theory has aided in constructing new technologies [46]; psychology, where the theory is used to guide cognitive analysis of the mind [1]; and most recently in public health, where dynamics of pandemics such as COVID-19 have been investigated [32].

Non-linearity in Neurophysiology

The CNS has often been praised as the primary home of all bodily functions and mental activities. In addition to life sustaining functions and cognitive abilities, the brain is what gives us special traits and skills. Some of the most complex traits of humans that traditional scientific approaches cannot explain in entirety include language, emotions, and mental illness.

The notion of regularity in natural processes is outdated, thus the continued use of linear approaches as the sole method of analysis is insufficient for understanding the brain and other biological systems. Many variables in biological data including neural activity possess non-linear characteristics and temporal variability. In this context, chaos theory attempts to shed new light on cognitive functioning and the processes that lead to dysfunction. Instead of looking at the brain in traditional ways, researchers are now starting to examine the brain as a system of networks. A healthy brain establishes connections and ensures accuracy during the period of information transfer. When functioning properly, the numerous networks support cognitive abilities such as problem-solving, executive function, attention, and language.

For the brain to function effectively, it must adapt to the outside world, even though spontaneous brain activity emerges without external forces. Accordingly, the human brain must be gauged to reformulate its internal connections accurately [12]. In a relatively small network of neurons, each component is considered critical and in some cases discernible functions can be assigned to each. When examining the brain as a whole however, each neuron's contribution may appear insignificant in contrast to the complex operations of its larger networks [7]. Research in this context has focused on activity at both the neuron level and the network level. Chaotic phases, however, are typically properties of large networks which exhibit random-like activity [24, 39].

Applications to Neuroscience

The interdisciplinary feature of non-linear systems theory provides an advantage for researchers interested the relationship between chaos and the brain. Indeed, need to understand the connections and the interactions between macroscopic and microscopic levels of the various activities investigated that involve cellular activity, behavioral patterns, neural assemblies, and other activities that are generated by nerve cells requires sophisticated tools and models to understand their functioning. It is critical that the models and methodologies employed are adapted to handle biological time-series data, both noisy and non-stationary [12].

When investigating chaos in the central nervous system (CNS), there is a need to determine how stochastic patterns can be distinguished from deterministic ones [41]. To this end, ascertaining whether the observed variability in neural activations is characterized by some underlying deterministic order or by true randomness is of critical importance. As Bob [4] points out, variability is an essential ingredient for survival and successful behavior in all living systems. This further implies the need to determine how the effects of noise can be separated or distinguished from those that come from multiple interacting non-linear elements.

The mind-brain relationship is an area of research that also has attracted a lot of attention over the last decade. In an attempt to understand this relationship, studies continue to investigate various trends in cognitive neuroscience and psychology with application of chaos theory and non-linear dynamics showing promise. In this realm, interesting areas of exploration have included determining the explanatory power of chaos theory on altered mental states and the transition between mental states leading to dissociation.

When the field of neuroscience was in its infancy, some researchers believed that the cognitive basis of human behavior was at the individual level of neurons. According to Hubel & Wiesel [16], the single unit approach to brain functioning or the neural doctrine presumed that behavior could be explained by activity of individual cells triggered by a stimulus. Chaos theory, however, doesn't completely support this view. While the neuron is the most basic unit of the brain, complex electromagnetic phenomenology, multiple neurotransmitters, and instability due to autonomous activities can have an overwhelming influence on neural activity. The brain does not function passively in reaction to stimuli and any theory assuming so would be over-simplistic. Rather, the brain is a chaotic system that must be studied as a whole taking into consideration factors such as internal feedback [11]. In this sense, chaos theory offers a more ideal and holistic view.

With the advent of neuroimaging technology, the existence of networks in the brain gained widespread support. The brain's collective dynamics have been investigated from a mathematical physics point-of-view with further support from empirical studies. For example, Haghighi and Markazi [38] investigated mechanisms of seizure generation in epilepsy and found evidence for the contribution of non-linear processes. Further evidence from electroencephalographic (EEG) recordings from the cortex of the brain (similar to electrocardiography data from the heart) have provided support for the hypothesis that brain activity is chaotic and, to an extent, unpredictable [8, 20]. Strange attractors have also been observed in data plotted on phase-space diagrams. These fractal strange attractors in the brain begin to reorganize themselves during cognitive process differentiation [6]. As Hebbian learning suggests, neurons and their connections must be used regularly to keep them alive [28]. Perhaps the unexpected firing of inactive neurons serves as a mechanism for maintaining brain health, making chaos essential for a healthy functioning brain. Furthermore, while background noise in the brain is stable, its electrical activity appears to be chaotic. Chaotic responses and activity allow rapid state transitions necessary for information processing [37]. In the absence of these transitions, cognitive processes such as sensation and perception would be extremely slow. Moreover, the human body is a dynamic and complex system; the body's physiology, including the brain, is similar to that of nature and takes on fractal dimensions. It is safe to say that human beings are creatures of chaos.

The Complexity of Neuroscience and Chaos Theory

The omnipresence of chaos is perhaps one of the many reasons why the search for chaotic patterns has occupied many researchers in the past few decades, including neuroscientists. As Friston [12] explains, future research on neural systems and other higher brain functions will most likely focus on combining traditional reductionist neuroscience with non-linear science. However, applying concepts and tools developed to describe noise-free and low dimensional mathematical models to biological systems such as the brain has not been easy [4]. The question of how neurons in the human brain assemble and give rise to a complex biological machine that outperforms even the most advanced computers continues to motivate research in this area.

The CNS is infamously complex. This complexity emerges from the interaction of different elements and variables resulting in a non-linear dynamical system [13, 36]. The intricate interplay makes it challenging to understand even the healthy brain's functioning fully. Although significant advances have been made in the understanding of genetics and behavior of neural systems over the past decade, a plethora of questions remain unanswered.

Perhaps one of the most significant complexities is the structure and wiring of the human brain. Neurons, approximately 8.6×10^{11} of them in the human brain, emerge from a combination of extracellular signals and transcription gradient factors acting on neocortical cells [33]. These neurons connect with each other forming over one hundred trillion synapses [23]. Furthermore, new evidence for the brain's ability to produce new neurons adds to the already overwhelming complexity of the system [22].

Developing in parallel with these complex connections are chaotic patterns. Using models such as the Huxley and Hodgkin model and the Hindmarsh and Rose model of bursting neurons, researchers attempt to determine the non-linear patterns in higher brain functions [24]. Based on a radical hypothesis, the brain's processing, perception, and storage capabilities may be the end-result of strange attractors. Thus, modifications in the system can result in variation of cognitive outputs. Once again, initial status is critical for the final product of a system. Regulation of excitatory and inhibitory activity in neural circuits is necessary for functional stability [25]. In other words, optimal brain functioning requires a healthy balance between inhibition and excitation processes and failure to maintain this balance may results in various neuropsychiatric conditions [15].

Chaos and Disorder

An important question concerns the processes that characterize neurologic and psychiatric disorders. In this context, the application of chaos theory has been valuable for understanding a variety of pathologies [5, 34]. For example, principles of non-linear dynamics have been used to analyze and interpret EEG recordings in patient populations [8]. Chaos theory has also opened up possibilities for studying the relationship between environmental and genetic factors in various pathologies [4].

Non-linear system research has revealed critical functions and characteristics of both physical and biological systems. Findings in particular have highlighted the appearance of random events across time, resulting in identification of mathematical elements of different systems. Some examples of this phenomenon include the variability of heartbeats, the coding sequences of DNA, and the flow of information across neurons. Identification of these patterns is critical to understanding both

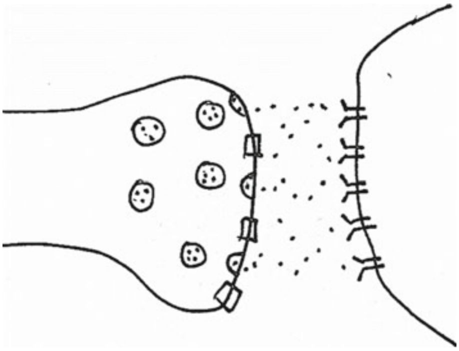

Fig. 2 Neurotransmitter release

normal and pathological processes. With a solid understanding about complex functions and chaotic systems, it may be possible to differentiate between healthy and unhealthy levels of chaos in the brain [42].

In understanding disorders of the brain, neurotransmitters have a critical role. When released, these chemical molecules have the critical task of carrying messages between neurons via synapses (Fig. 2).

Neurotransmitters, namely dopamine, serotonin, glutamate, gamma-aminobutyric acid (GABA), and acetylcholine, are associated with different disorders of the CNS [18]. These neurotransmitters are responsible for behavioral, psychological and cognitive patterns of activity. Because dopamine has been implicated in a vast number of diseases, it has been one of the most widely researched neurotransmitters. Dopamine receptors are divided into two main categories. This first category consists of D1 and D5 receptors. These receptors are responsible for the activation of adenylyl cyclase enzymes. The second category of dopamine receptors is the D2, D3, and D4 receptors. Their primary function is to inhibit the adenylyl cyclase enzymes [42]. Given this complex interaction, it is not surprising that dopamine is associated with pathways linked to addiction disorders, psychosis, and bipolar disorder. Other conditions related to dopamine include Parkinson's disease [45], restless leg syndrome [44], and attention-deficit hyperactivity disorder [35].

Serotonin, another well-studied neurotransmitter, usually behaves as a multifunctional biochemical particle. This is demonstrated by its distinguishing role in behavioral and mood patterns. Serotonin imbalances are associated with epileptic seizures [2], migraine [17], and major depressive disorder [10] just to name a few examples.

GABA is defined as one of the primary inhibitory neurotransmitters. It is responsible for regulating excitement levels and muscle tones. Its receptors are usually associated with drugs that act as modulators. A surplus of GABA in the CNS is usually associated with anxiety reduction and anti-convulsion. Abnormally low levels of GABA are usually associated with anxiety disorders and convulsive disorders such as epilepsy [42].

Acetylcholine has a modulatory role in the CNS. It is present in the neuromuscular junction, the parasympathetic system, and the autonomic nervous system and has been associated with issues of learning, motivation, attention, arousal, and addiction. Problems in the production and regulation of acetylcholine have also been linked to memory impairments, a hallmark of Alzheimer's disease [42].

Noradrenaline is a neurotransmitter in the catecholamine family. As such, it can be identified as both a hormone and a neurotransmitter. Noradrenaline is produced from different sources, including the sympathetic ganglia and is responsible for the mobilization of functions such as alertness, arousal, and attention. Based on the current evidence, noradrenaline plays a vital role in pathologies. Some of the health issues associated with this neurotransmitter include different psychiatric disorders and neuropathic pain [42].

The disorders mentioned above are associated with a malfunction in the production and/or regulation of different neurotransmitters. For instance, movement disorders such as Parkinson's disease are attributed to issues with dopamine and serotonin production [30, 42] and epilepsy, can be attributed to dysregulation of dopamine and GABA production. In addition to neurochemical factors, atypical electrical activity observed in epilepsy has also been shown to be consistent with chaotic systems [34].

Needless to say, the interaction of neurotransmitters through various receptors is notably complex, even in the normal brain. This vulnerability however, is not specific to neurotransmitters or just to healthy brains. Disruption in the fluid dynamics of the brain or electrical activity can play a role in mental illnesses. Moreover, application of chaos theory and non-linear analyses have proven to be a valuable approach for understanding psychiatric conditions including psychosis, bipolar disorder, depression, and schizophrenia [26, 42]. In concordance with chaos theory, a small imbalance or oscillation in the brain can result in a system that functions unpredictably. Based on the evidence to date, it appears that this may very well be the case in neuropsychiatric conditions.

Summary

Neural activity, like other biological processes, is inherently non-linear. The application of chaos theory and non-linear system approaches to physiological processes has contributed to the field of neuroscience over the last few decades. While many questions still remain, theoretical and empirical evidence continues to grow rapidly. An interdisciplinary approach including physics, mathematics, neuroscience, and related fields will be beneficial for furthering our understanding of chaotic mechanisms in biological systems. Research on both healthy and disordered populations is needed to delineate the nature and function of chaos in the brain and to develop new models of neuropathology.

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