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Review Article

Is Mental Stress Always Chaotic? An Analysis of the Adaptability of Neurovisceral Regulation Through the Complexity of Heart Rate Oscillations

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Abbreviations
EEG: electroencephalography
FC: heart rate
HRV: heart rate variability
SampEn: sample entropy

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ABSTRACT

The biological stress model suggests that the type of adaptive response to stressors depends on the phase of the process. Some of these responses indicate reduced adaptability and decreased chaos in heart rate oscillations. This theoretical review presents experimental findings using sample entropy of heart rate oscillations across the different phases of Selye's predominant biological stress model. Changes in sample entropy occur throughout the phases of this model, with decreases during the alarm and exhaustion phases and increases during the resistance phase. These findings highlight the potential of chaos theory and complex systems analysis to describe dimensions of physiological changes associated with the biopsychosocial-cultural process of stress.

Keywords: Stress, Sample entropy, Heart rate variability

¿Es siempre el estrés mental caótico? Un análisis de la adaptabilidad de la regulación neurovisceral desde la complejidad de las oscilaciones del ritmo cardíaco

RESUMEN

El modelo de estrés biológico refiere que el tipo de respuesta adaptativa a estresores va a depender de la fase del proceso. Algunas de estas respuestas indican disminución de la adaptabilidad y menor caos en las oscilaciones del ritmo cardíaco. En la presente revisión teórica se exponen los hallazgos experimentales que utilizan la entropía muestral de las oscilaciones del ritmo cardíaco, en las diferentes fases del modelo predominante de estrés biológico de Selye. En las fases de este modelo se producen cambios en entropía muestral de las oscilaciones del ritmo cardíaco con disminución en las fases de alarma y fatiga, y aumento en la de resistencia; lo cual revela la posibilidad de utilizar la teoría del caos y de los sistemas complejos para describir dimensiones de los cambios fisiológicos asociados al proceso biopsicosocial-cultural del estrés.

Palabras clave: *Estrés, Entropía muestral, Variabilidad de la frecuencia cardíaca*

INTRODUCTION

Homeostasis is a physical or mental balance that can be altered by harmful stimuli, which induces a state of stress. If this state becomes chronic, a persistent activation of the sympathetic nervous system is maintained, which can trigger physical, psychological, and behavioral abnormalities[1]. Over time, the sensitivity of the sympathetic nervous system to mental stress increases, raising the risk of developing future cardiovascular diseases[2,3]. Furthermore, stress can facilitate the onset of various psychiatric disorders, especially in vulnerable subjects[4].

To date, Selye's biological stress model[5] is the most influential theory for explaining stress and its triggers[6]. Its central concept is the general adaptation syndrome, which describes the stress process in three phases: alarm (alert), resistance (physiological adaptation to restore homeostasis), and, finally, exhaustion[6]. During these phases, three physiological axes —the neural, neuroendocrine, and endocrine— act sequentially[6,7].

- The neural axis is characterized by an increase in muscle tone, body paralysis, a cortical alert reaction, and a massive discharge of the sympathetic system.
- The neuroendocrine axis involves the secretion of adrenaline and noradrenaline by the adrenal medulla and their systemic consequences.
- The endocrine axis is activated by the response of the hypothalamus-pituitary-adrenal cortex axis, which culminates in the production of cortisol.

Repetitive exposure of brain structures to stress hormones, such as those from the hypothalamus-pituitary-adrenal axis, induces neuroplastic modifications mediated by glucocorticoids. These hormones alter the basal activity of the amygdala, hippocampus, and medial prefrontal cortex, which affects cognitive functions such as memory[6,8]. According to this approach, the GAS is the decisive criterion for determining whether stress has occurred. Therefore, any event that does not generate this response cannot be considered a stressor[8].

There is a global consensus that associates stress with chaos and crisis, a view reflected in the definition of acute episodic stress proposed by the American Psychological Association[9]: *"...those people who frequently have acute stress, whose lives are so disordered that they are studies in chaos and crisis"*. This perspective has its epistemological foundations in systems theory and the order of natural and psychosocial phenomena[10]. The epistemology of complexity in social sciences and psychology offers an understanding of the human being as a paradoxical entity, simultaneously ordered and chaotic, regular and irregular, contradictory and fuzzy in their personality and behavior[11]. This is an emerging epistemological perspective that presents itself as an alternative to old reductionist and simplistic paradigms[10]. In the case of stress as a biopsychosocial-cultural phenomenon, it is relevant to explore the contributions of Chaos Theory and Complex Systems[12] in contrast to the predominant biological stress model[5-6]. The analysis of the theoretical behavior of chaotic systems can offer new concepts, as living beings possess biorhythms that, in states of good health, fluctuate in a seemingly random manner[12-14].

The heart is one of the biological systems that has been studied using the tools of chaos theory. This theory states that nonlinear and complex dynamic systems are inherently unpredictable, but they can often be best characterized through graphical representations in the «phase space». In this context, the appearance of regularity in heart function is a sign of alteration, whereas the maintenance of chaotic behavior is an indicator of good function[13-15].

Temporal series obtained from natural systems such as the heart have common characteristics: they are irregular and present a Fourier spectrum with a rich variety of amplitudes; they have global stability by moving within a determined range; and, when plotted on a physical plane, they display complex geometric figures called strange or chaotic attractors[13-16]. In the 90s, Ary Goldberger was one of the pioneers to postulate that the cardiac system was a chaotic system[17]. Chaos, by its nature, leverages the richness of its own structure, which confers benefits to these systems by adopting chaotic regimes with a wide range of possible behaviors[15].

Although heart rate (HR) has traditionally been considered a product of the emotional response to stress[1-3,18], the measurement of heart rate variability (HRV) has also been adopted as a non-invasive and relatively simple method to objectively assess the severity of stress[3,19,20]. HRV is a physiological phenomenon that measures the variation in the time interval between heartbeats (RR interval) and is commonly used as a measure of autonomic nervous system activity[21-24]. In recent years, it has been suggested that HRV has a nonlinear dynamic and a fractal nature[25-27] (**Figure 1**).

Various disease states (such as diabetes, hypertension, heart failure, sleep apnea, and psychiatric and neurological disorders), as well as states of fear, acute stress, anxiety, and fatigue, cause a reduction in the irregularity, complexity, and predictability of heart rate oscillations[15,18,26-30]. In this context, the sample entropy (SampEn) of heart rate oscillations has been proposed as one of the most robust indicators for characterizing the nonlinear dynamics of autonomic cardiac regulation in the identification of anxiety and stress states[18, 28,29,31].

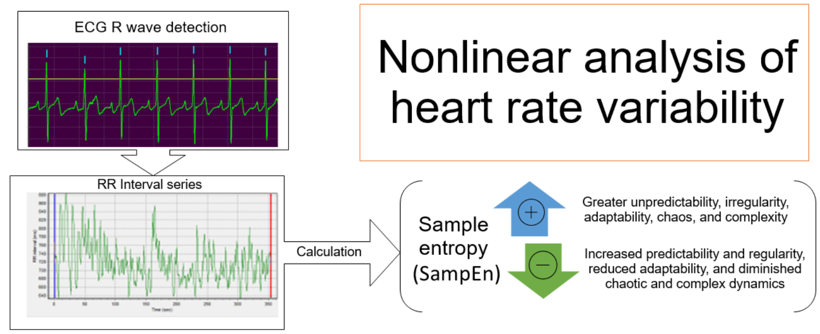

Figure 1. Nonlinear analysis of heart rate variability using sample entropy.

Despite these advances, greater clarity is needed on the points of contact between the experimental findings of the emerging Theory of Complexity and Chaos (which uses sample entropy as a reference parameter) and Selye's predominant biological stress model. Therefore, the present theoretical review aims to present the experimental findings that apply the sample entropy of heart rate oscillations to the different phases of Selye's predominant biological stress model.

CHAOS AND THEORY OF COMPLEXITY ON HEART RATE OSCILLATIONS

The cardiovascular system has been one of the first physiological systems to attract the attention of researchers interested in chaos theory, an area that has been expanding since its relatively recent emergence in the 1960s. In the early 1990s, the first attempts to characterize the cardiac system as a chaotic system in the strictest sense were reported, that is, taking as reference mathematical systems that, through known equations, behave chaotically (unpredictable in the medium and long term) and whose two- or three-dimensional representations form so-called strange attractors[13,14,32].

Nonlinear HRV indices have expanded the description of heart regulation by the autonomic nervous system[33]. In particular, entropy measures have shown great potential for analyzing physiological time series. Therefore, they have been widely used to quantify HRV, based on the hypothesis that reduced entropy values reveal disturbances in underlying physiological mechanisms or disease[28,33,34]. Entropy-based methods have their roots in information theory, conceptualized as measures of the complexity (or “unpredictability”) of a signal. Although originally developed in thermodynamics[35], their applications have expanded to quantify complexity in physiological systems and have been widely used as diagnostic tools in biomedicine[26,36,37].

The underlying concept of entropy is that it quantifies pattern repetitions in a signal, with higher entropy indicating greater randomness and unpredictability (and thus complexity), while lower entropy values imply a more predictable cardiac system (i.e., periodic and not generating much new information)[38]. Common entropy-based methods include approximate entropy (ApEn)[39] and sample entropy (SampEn)[40].

Approximate entropy was introduced by Pincus in 1991 as an entropic measure to quantify the regularity of medical data[39]. Almost a decade later, Richman and Moorman[40] introduced SampEn, a variation of approximate entropy that reduces bias from self-comparisons and is less dependent on data length. SampEn is the negative natural logarithm of the conditional probability that two similar m-point patterns remain similar when extended to m+1 points. SampEn measures the regularity of a time series, with regular series corresponding to low SampEn values and complex series to higher values[40,41].

SampEn serves as a nonlinear indicator of the sympathetic−vagal balance in autonomic heart regulation[42], increasing under conditions of parasympathetic predominance, such as rest in healthy subjects[43] and salutogenic states associated with exercise[44,45], and decreasing under conditions of sympathetic predominance, such as salt sensitivity[46], postural stimulation[42], diabetes[30], and within 30 minutes after alcohol consumption[28]. Additionally, acute mental stress reduces SampEn compared to resting conditions[18].

CHANGES IN SAMPLE ENTROPY OF HEART RATE OSCILLATIONS IN THE DIFFERENT PHASES OF SELYE'S BIOLOGICAL STRESS MODEL

Alarm phase

In the first phase of the general adaptation syndrome, the alarm phase, the hypothalamus responds to a stressor by stimulating the adrenal medulla to secrete adrenaline, which provides immediate energy. This triggers physiological responses such as increased heart rate, vasodilation, and heightened vigilance (also mediated by noradrenaline)[4,7,8,47]. In general, most complexity measures of RR series decrease statistically under stress, making them capable of detecting it[18,28-31]. SampEn is significantly lower during public speaking than at rest[19,48].

This phenomenon appears early in life: during maternal still-face episodes, when infants experienced unresponsiveness from their caregiver, SampEn values of time series were lower than during normal interactions, indicating that the lack of maternal communicative input is associated with variability in infants' behavioral and emotional states[31].

However, this is not always the case: in a sample of 42 university students, mental stress increased SampEn and, therefore, the complexity of sinus node impulse oscillations[49]. This effect seems to depend on the type of response: in subjects whose stress-induced mental load reduces parasympathetic modulation, SampEn decreases; in those with increased vagal activity, it does not[48]. Gender differences are also reported: in a study with 10 men and 10 women exposed to 15 minutes of mental stress, SampEn decreased mainly in men, whereas it increased in women, reflecting biological differences in nonlinear heart rate dynamics[50].

A female-specific stress response has been suggested by Taylor *et al.*[51], who hypothesized that, while men exhibit the conventional fight-or-flight response to stressors, women display a "tend-and-befriend" response, using social coping strategies. This response is driven by estrogen and oxytocin[51]. The study's results revealed cardiac dynamics likely specific to this tend-and-befriend response.

Emotional state, mental health, and workload further influence nonlinear response characteristics. In subjects with anxiety disorders, such as fear of flying, exposure to simulated flights reduces SampEn and, thus, HRV complexity[29]. Blons *et al.*[52] confirmed this in 33 healthy subjects, divided into anxiety responders and non-responders, who participated in three 8-minute periods: rest, cognitive task without stressors (TC-), and cognitive task with stressors (TC+E). SampEn decreased in TC+E for anxiety responders, whereas non-responders maintained elevated entropy achieved during TC-. The authors[52] proposed that increased cardiac entropy during TC, alongside higher cognitive load, reflects a coordinated, flexible, and robust neural network supporting optimal perceptual and cognitive performance.

In summary, acute short-term stress tends to reduce heart rate oscillation variability, making it more predictable and less chaotic, generally decreasing SampEn in the alarm phase. However, this response depends on emotional state, mental health, sex/gender, and cognitive load.

Resistance phase

The resistance phase is activated if stress persists. The adrenal cortex (zona fasciculata) secretes cortisol, the main stress hormone, whose short-term actions are vital for survival[7]. Unlike adrenaline, which provides immediate energy, cortisol maintains blood glucose levels to supply muscles, heart, and brain, replenishing energy reserves. In this phase, the organism must "endure"[8,47].

Neuroendocrine responses to elevated cortisol appear associated with nonlinear dynamics and high complexity of physiological oscillations. One study[53] found that SampEn during peak stress correlated significantly with cortisol awakening response ($r = 0.777$, $p < 0.005$). Hydrocortisone administration in endotoxemia improved HRV and approximate entropy, a complexity measure whose methodological limitations are overcome by SampEn[54,55]. This suggests that prolonged stress with elevated cortisol can increase complexity and variability of heart rate oscillations. However, during childhood, higher cortisol levels and a larger cortisol awakening response were associated with lower parasympathetic HRV patterns, indicating the need for further research[56].

Workload and cognitive demand also affect this phase: SampEn can reflect mental workload in occupational and real-world settings[57,58]. One study[58] showed that SampEn had the highest discriminative power across multiple scales under varying workload conditions, suggesting that long-term heart rate regulation may be influenced by sustained cognitive load, although this is not seen in short-term laboratory tasks[59].

Overall, the resistance phase involves elevated cortisol and, with cognitive or physical workload, increased SampEn and complexity of heart rate oscillations, reflecting enhanced adaptability of autonomic regulatory systems.

Exhaustion phase

The exhaustion phase occurs if stress persists, leading to chronic hormonal alterations with organ and psychiatric consequences. If prolonged further, the organism may become overwhelmed or depleted. Hormonal secretion becomes less effective, and hormones accumulate, negatively impacting health[4,7,8,47].

Heart rate oscillations provide an objective, noninvasive tool to assess autonomic dysfunction in chronic fatigue syndrome, showing significant associations with questionnaire scores and traditional HRV measures[60]. In a driving simulator study[61], subjective fatigue (scored from fully alert to extremely fatigued) was inversely associated with SampEn values, indicating reduced entropy with increasing fatigue (**Figure 2**).

Furthermore, a study conducted on miners[62] before and after an 8-hour workday in extreme conditions of high altitude, cold temperatures, and reduced partial pressure of oxygen, found a decrease in the sample entropy of heart rate oscillations, indicating that it is a suitable indicator of fatigue in this group.

A similar pattern occurs with regard to physical fatigue: in a study, where participants were asked to perform rebar-bending and -fixing tasks for 60 minutes[63], a progressive reduction in HRV SampEn values was observed at 15, 30, and 45 minutes, reaching minimum values at 60 minutes, when compared to the performance of the task. These changes were not found in patients with neurological spinal cord dysfunction, due to associated autonomic nervous system activity disorders[64].

On the other hand, decreases in HRV SampEn are not always observed in association with fatigue, as a study conducted on agricultural workers reported an increase in it after the workday[65]. In the exhaustion phase, where fatigue exists, the sample entropy of heart rate oscillations as a one-dimensional measure is insufficient to characterize the phenomena associated with fatigue-exhaustion. Therefore, it is necessary to complement it with nonlinear measures of brain dynamics using electroencephalography (EEG).

This is described in a study that applied a joint analysis of entropy in EEG and HRV signals in different real-world fatigue states in seventeen subjects participating in a six-month longitudinal study designed to monitor fatigue levels through a daily sampling system[66]. These authors found that the nonlinear analysis of EEG signals allowed for an adequate identification of moments of better alertness, while the sample entropy of HRV allowed for the identification of moments of poorer alertness, suggesting that joint EEG-HRV quantification provides complementary indices for a reliable assessment of human performance.

This highlights the need for further studies to

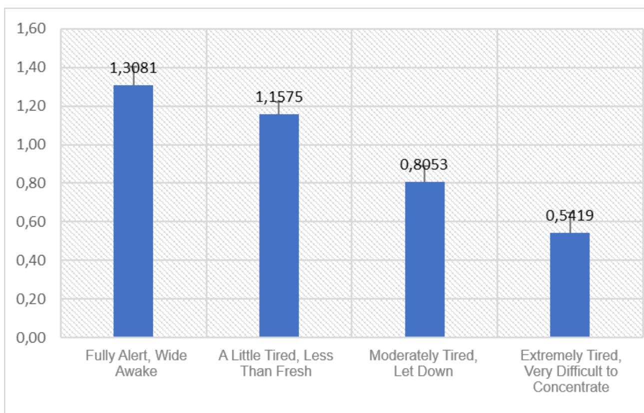

Figure 2. Sample entropy values of RR interval oscillations across key subjective stages of fatigue. Assessment using a simulator revealed that sample entropy values decrease as the subjective perception of fatigue increases.
Source: Prepared by the authors based on data from Table 3 of Wang F, *et al.*, Entropy (Basel), 2018[61].

clarify the physiological interpretation of HRV SampEn and, therefore, its clinical applicability. Despite the limitations of this nonlinear indicator regarding its physiological interpretation, most evidence suggests that in the fatigue and exhaustion phase of the general adaptation syndrome, there is a decrease in sample entropy, complexity, and adaptability of regulatory systems, such as the autonomic nervous system, due to the loss of energetic and metabolic resources associated with this process.

CONCLUSIONS

In the different phases of Selye's biological stress model, changes occur in the sample entropy of heart rate oscillations, which reveal the possibility of using chaos and complex systems theory to describe dimensions of the physiological changes associated with the biopsychosocial-cultural process of stress. In the alarm phase, there is a reduction in entropy and adaptability, dependent on factors such as sex/gender, mental load, and mood and mental health status. In the resistance phase, an increase in entropy is observed, associated with an increase in cortisol levels. Finally, in the fatigue and exhaustion phase, there is a decrease in the entropy, complexity, and adaptability of heart rate regulatory systems.

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