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Adaptive chaos: Mild disorder may help contain major disease

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Summary We have qualitatively analyzed different cases of human disorders and displacement activities of animals and hypothesize that some of them are examples of low-dimensional dynamical chaos in biological organisms. We also considered a biological organism in the framework of the control system theory and found that chaotic regime in one subsystem may be compensating for the loss of chaos in another subsystem for the sake of stability of the whole system. According to the hypothesis chaotic behavior of different organs sets in a human body as an alternative to serious diseases or even death. The principle of compensation was applied to different physiological systems with chaotic regimes to explain the adaptive nature of chaos there. Implications of the mechanism of adaptive chaos for sleep diseases, e.g., enuresis, and other potentially life threatening disorders of humans, e.g., RLS, are discussed in connection with the possibility to use these ideas for improved treatment strategies. The main conclusion is that adaptive disorders with chaotic symptoms should not be aggressively treated; if adaptive disorders are overtreated, the whole organism may be thrown into a more regular state, which eventually will lead to a chronic disease or even death.

Background

The fact that brief disturbances in a body can help treat some of the life threatening diseases has been known for centuries. Induced fever spikes, bloodletting, convulsions produced by electrical shocks, and insulin-inspired comas are recognized and widely used not only in folk but also traditional medicine. Electro-convulsive therapy is now considered a safe treatment of severe depression, Parkinson's disease, and obsessive-compulsive disorder even for pregnant women. Episodic outbursts of anger and tears reliving emotional tension, after which the person becomes calm for awhile, may also be examples of how a disorder can treat a disease.

Sleep medicine offers multiple examples of sleep disorders that are usually called parasomnias. A widely spread disorder of enuresis, viz. paroxysmal and involuntary bedwetting, is one such example [1]. Healthy sleep consists of several stages, deep sleep, light sleep, and rapid eye movement

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(REM) sleep, which may be distinguished by the characteristic patterns of brain or cardiac waves coupled to other electrophysiological activities of a subject. It is believed that the deep sleep stages are essential for physical recreation, while the REM stage is important for mental one [2]. In Fig. 1 are represented hypnograms of a healthy child (a) and that of an enuretic one before the treatment (b). Normal sleep patterns have cycles of about 90 min long when stages of deep sleep with low frequencies and large amplitudes of brain waves are followed by brief REM stages with fast brain waves, eye movements and other physiological activities, Fig. 1(a). There may be from 5 to 7 cycles per night with REM stages becoming longer and NREM stages shorter and lighter in the second half of the night. Enuretic sleep patterns are very different: during the first half of the night the REM stage is delayed, while NREM stages are prolonged and very deep; sleep cycles usually normalize after enuretic episodes, Fig. 1(b) [3]. In rare cases enuretic acts reappear several times a night even after forceful awakening.

Broughton [1] explains parasomnias as partial arousal phenomena related to pathological cardiac and mental activities of subjects. With its entire clinical relevance, the arousal theory could not explain whether these symptoms have any functional role or just appear as byproducts of incomplete sleep or wakefulness and why they show strong resistance to treatment [3].

Restless leg syndrome (RLS) is manifested as involuntarily sensations or even jerking of the limbs during sleep and wakefulness [4]. RLS should be distinguished from sleep-related leg conditions, such as nocturnal leg cramps, although symptoms of RLS usually worsen in the evening and at night. No single medication or a combination of medications works predictably for RLS patients. Furthermore, there is evidence from the published case reports that RLS symptoms may be worsened by medications [5—9]. Although an exact pathological mechanism has not been identified yet and no specific causes of RLS are known at the present time, there is, however, evidence that it is a neurological disorder, which might be linked to a brain-to-spinal cord activity [10]. Rhythmic sleep related movements (head rocking and banging, HRB) is another example of parasomnia, which is manifested by a series of 7—15 cycles with short and unequal pauses in between and fluctuating total amounts of movements, depending on the individual's emotional and physical conditions. On the electroencephalograms (EEG) the rhythm of HRB motor activity is characterized by delta waves (large and slow), which are remarkably similar to the waves in delta

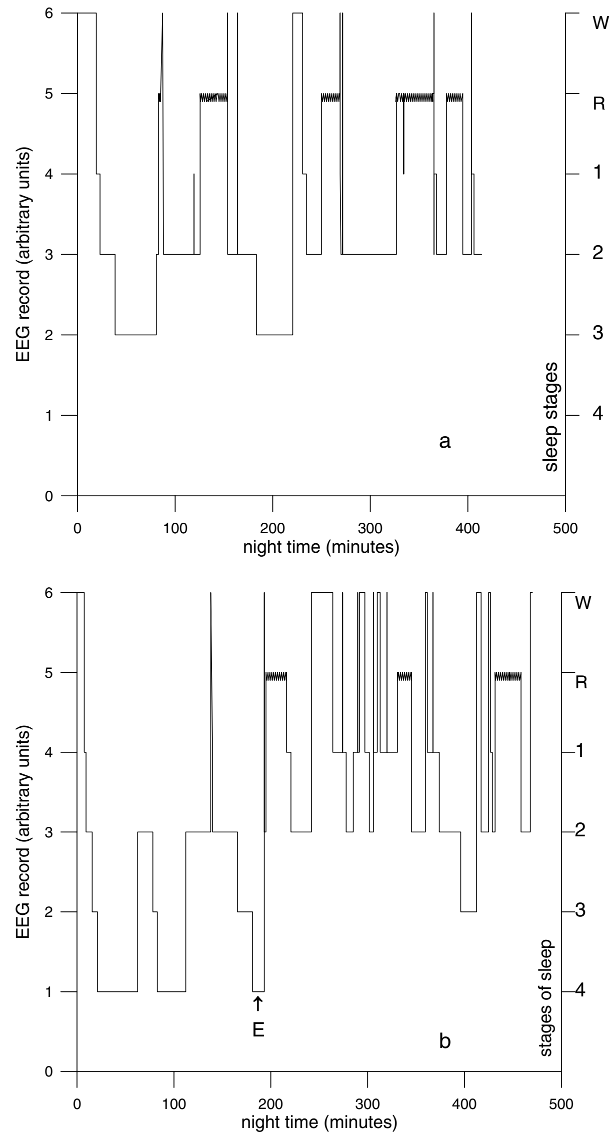

Figure 1 Hypnograms (one-night EEG records) of sleep. Horizontal — night time. Vertical — the sleep stages: W — wakefulness; R — REM stage; 1,2,3,4 — slow wave stages of non-REM sleep (the greater the number, the deeper the sleep): (a) dynamics of the normal sleep of a healthy 8 1/2-year-old child; (b) dynamic of the sleep of an 8-year-old enuretic child on a wet night: during the first half of the night the REM stage is delayed, while non-REM stages are prolong and very deep. Arrow E — time of the spontaneous involuntary urination in sleep. After that the brain switches the non-REM stage to REM stage and the cycling of the sleep stages (sleep architecture) returns to normal.

sleep (stages 3 and 4 in Fig. 1). HRB takes place when the person cannot fall asleep or remains in a transitional stage between wakefulness and sleep and usually stops when the delta rhythm of sleep stabilizes [11—13]. RLS and HRB are examples of a large group of dynamic diseases without known natural causes [14,15], which are not only difficult to treat but when treated may cause even more damage to the patient.

Accepting usefulness of some of the induced or self-produced disorders, practitioners, however, are confronted with a paradoxical uncertainty about their nature, resistance to treatment, and the fact that the disorders may self-cure with age and time. How do we know when convulsions, fevers, or enuresis are helpful and not a result of a broken structure or sign of imminent disease? Thus, it is imperative to have an explanation to why and when a disorder of one organ can help stabilize the whole organism or even cure the disease as oppose to hurting it even more.

Hypothesis of adaptive chaos

Conventional wisdom in physiology and medicine (theory of homeostasis [16]) holds that a healthy organism regulates itself to maintain constant rhythm, while erratic behavior of the organism is symptomatic of unfolding disease because it suppresses natural rhythms. However, interdisciplinary discoveries of the past decade in mathematics and human physiology convinced many practitioners that *chaos in bodily functioning* is not necessarily a bad thing [17,18]. Goldberger et al. [19] convincingly demonstrated that a chaotic cardiac regime is physiologically normal, while a regular periodic regime would be pathological for the heart. They also found scaling (fractal, chaotic) behavior in human gait dynamics [20]. As known, the low-dimensional dynamical chaos is characterized not only by unpredictability of the response due to strong sensitivity to initial conditions but also by structural stability of the nesting system due to existence of an attractor. The latter property makes dynamical chaos extremely useful for controlling purposes. Pecora and Carroll [21] showed how one could effectively synchronize subsystems of a chaotic system by linking them with a common signal. They quoted Freeman who suggested that the brain response should be viewed as a chaotic attractor. Ott et al. [22] showed that chaotic motion possesses great inherent flexibility in reacting on different external or internal demands by using small adjustments. They suggested that presence of chaos in the brain might not only be advantageous but absolutely necessary ingredient for the controlling purposes. Bunde et al. [2] studied the heart rhythm in different sleep stages and found that REM-stages exhibit long-time multifractal correlations, which are absent in NREM sleep. Hence, the healthy sleep patterns that include all stages, c.f. Fig. 1(a), are characterized by the low-dimensional chaos.

On the basis of the above described clinical results, Fig. 1, and analysis of the literature we conclude that human disorders may be examples of *chaotic behavior* of different organs that set in a human body as an alternative to serious diseases or even death. The flexibility of chaotic regimes in heart and brain allows these organs to perform their regulatory functions in wake and sleep. As a result of aging or pathology an organism may lose these functions. Then, we speculate, such inability of heart or brain to self-produce chaos may be *compensated* by chaos provided by another organ of the organism. According to this hypothesis, disorders appear as a response to full or partial loss of chaos by the heart or brain and serve the purpose of reinstating chaotic behavior and control functions of these organs, which is vital for the stability of the whole organism.

Based on the hypothesis of adaptive chaos, parasomnias may be explained as chaotic behaviors of different parts of an organism that reinstate the control function of the brain to produce normal sleep pattern. For example, after the act of enuresis, physiological impulses from the bladder stimulate the brain to switch from NREM to REM stage and the sleep architecture returns to normal, see Fig. 1(b). Thus, in the case of enuresis the organism sets the bladder in a chaotic state in order to compensate for the dysfunction of the brain and the role of bedwetting can be understood as a switch mechanism between different stages of sleep and wakefulness. Behavioral correlations of HRB with delta sleep allow us to conclude that this disorder helps to reinstate the slow delta waves of stages 3 and 4 that is, serves as a sleepmaker. A patient with RLS starts twitching his/her limb because that way the body can ''supply'' chaos to the brain. The hypothesis of adaptive chaos is not only supported by the observations that the healthy sleep patterns are chaotic [2], it can also account for the resistance of parasomnias to treatments by medications.

The adaptive nature of the disorders becomes apparent when a biological organism is divided into interconnected subsystems and analyzed using ideas of the automatic control system theory. It may be expressed in the form of a principle, according to which in order to survive a pathological organism tunes one part of itself (compensatory subsystem, CS) in a high level chaotic regime to *compensate* for the loss of healthy chaos in the main subsystem (MS). Such relations between the subsystems are depicted in Fig. 2 where the whole

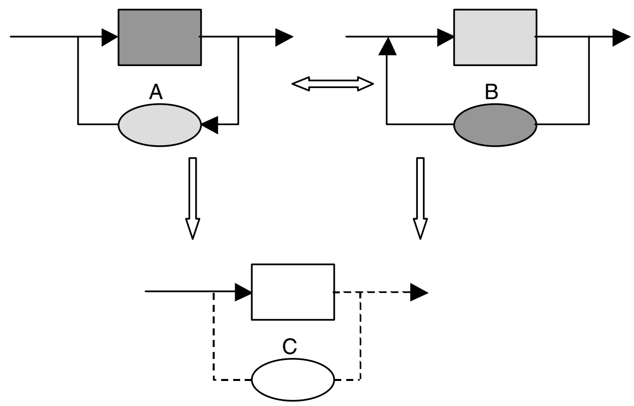

Figure 2 Three possible states of a system: A — stable system with normal levels of chaos in MS and CS (state of health); B — slightly unstable state with a strongly chaotic CS that provides chaos to MS (mildly pathological state, disorder); C — strongly unstable state with conditions of breakdown (disease). Shades of gray designate the level of chaos in a subsystem. ▭ — Main subsystem (MS); ⬭ — Compensatory subsystem (CS).

organism is considered as an open system with nonlinear feedback. The system can exist in three different states: A — stable state where chaotic MS, e.g., healthy heart, controls all non-chaotic subsystems (health), B — slightly unstable state where CS settles in a strongly chaotic regime in order to provide chaos to MS (mild pathology), and C — strongly unstable state with conditions of breakdown (disease).

Animal physiology

The principle of compensation applies to a broader group of phenomena then just human disorders. It may be found working in many open self-regulating physiological and physical systems of the natural world. The behavioral patterns of animals may serve as a case in point. The physiologists of the Pavlovian School in Russia first attempted to understand the reason and goal of seemingly inadequate behaviors in animals. Ukhtomsky [23] observed that in some cases activity of the nervous system of dogs, together with goal directed (positive) effects, can have absolutely senseless (negative) reactions which are resistant to treatment. For example, animals moved away from food when hungry, vomited, scratched themselves without a cause, kept turning around for no apparent reason, etc. He called this group of ultra paradoxical reactions *inadequate reflexes* and explained their existence as ''behind the curtain compensatory dominant''. Kaminsky [24] studied the ''compensatory role of inadequate reflexes'' on monkeys, placing them in stressful situations. Muhametov [25] found sigma rhythms on EEG of animals with inadequate reflexes, which usually appear during light stages of sleep or altered stages of consciousness associated with calmness. That was the first direct evidence that ''inadequate motor reactions help the brain to calm down''. Porshnev [26] collected the most comprehensive material regarding inadequate reflexes and their compensatory role in ontogenetic and evolutional dynamics of animals. Vvedenski [27] studied wide variety of strange, unusual, seemingly absurd body reactions and behaviors, which yet had some role in survival, and called them ''animal hysterias''. Bechtereva et al. [28] focused their research on the functional stability of inadequate reflexes and their amazing resistance to treatment.

The same group of behavioral patterns, termed *displacement activities*, attracted a good deal of attention in the zoology community in the West. Tinbergen [29] and Kortlandt [30] independently studied ''behavior patterns which appear to be out of context with the behavior which closely precedes or follows them'' [31]. Delius [31] studied the displacement activity of black-backed gulls and found it to be a part of their arousal homeostasis. Schino et al. [32] found primate displacement activities to be equivalent to anxiety. Several theories have been put forward to explain a reason for a particular behavioral pattern to appear as the displacement activity [33]. No theory, however, was able to explain the causality of displacement activities and answer the question, why these seemingly disordered behaviors are so stable and yet, may disappear by themselves.

According to the hypothesis of adaptive chaos, displacement activities of animals are examples of chaotic behaviors of different parts of their bodies, which set in as an alternative to death or serious disease of the whole organism. They appear as a response to full or partial loss of chaos by the heart or brain and serve the purpose of reinstating chaotic behavior and control functions of these organs, which are vital for the stability of the whole organism. Functional dependence of pathological organisms on displacement activities and inadequate reflexes explains therapeutic resistance of the latter. Indeed, rejection of the treatment by the organism of an animal comes as a part of its instinct of survival.

Another example of the principle of compensation may be found in the basic human task of balancing. Many investigators recognize now importance of chaos as a control mechanism for the maintenance of balance by the nervous system. Kapitsa [34] studied stability of an inverted pendulum with a vibrating pivot and found that irregular corrective movements of the pivot can restore balance of the pendulum in the position close to vertical. Recently Cabrera and Milton [35] monitored the movements of a stick balanced at the fingertip as an example of the neural control of human balance and found that the chaotic corrective movements of the hand allow balancing the stick. Being analyzed in the framework of the principle of compensation, see Fig. 2, the hand should be considered as the disorderly behaving compensatory subsystem (CS), while the stick is the main subsystem (MS).

Summary

In summary, we have qualitatively analyzed many different cases of pathological symptoms in biological systems that may be explained as manifestations of the chaotic behavior and revealed the adaptive nature of chaos in them. The benefit of chaos in physiological systems is stability of the organism, structural or functional, as opposed to instability or death. A new, seemingly universal feature of the dynamical systems controlled by a chaotic subsystem is discussed. To delineate this feature we proposed the principle of compensation, according to which the loss of controlling function of one subsystem of a defective system may be compensated by chaotic behavior of another subsystem, less important for ''survival'' of the whole system. Briefly speaking, we are wired such that if a central organ fails, a peripheral one comes to rescue. Application of this principle to biological organisms may bring an explanation of their self-treatment: a mild disorder induced in one part of an organism will compensate for the loss of control function of another part of the organism. In other words, in order to stabilize the whole organism, one organ may be actively set into a chaotic state. Such disorder will be stable and resistant to treatment until the control organ restitutes its functionality. Our observations suggest that a wide range of human functional inconsistencies and adaptive disorders (software problems) in fact may be compensating for the structural inconsistencies and diseases (hardware problems). One can say, for instance, that a limb of an RLS patient or a bladder of an enuretic provide a healthy dose of chaos to the heart or brain. Such adaptive disorders stabilize the organism initially, but later on may pose serious health consequences if left untreated.

We hope that the ideas of chaos theory will find a broader way into medicine and practitioners will be using not only ''unpredictability of chaos'' [36] but other, more useful properties of the latter. It is important to recognize the patterns of adaptive chaos for devising therapeutic strategies: adaptive disorders with chaotic symptoms should not be aggressively treated. If adaptive disorders are overtreated, the whole organism may be thrown into a more regular state, which eventually will lead to a chronic disease or even death. Many practitioners would like to know when and which function will ''sacrifice'' itself for the benefit of the whole body. This question will be addressed in a future study.

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