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Modeling of epilepsy based on chaotic artificial neural network

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ABSTRACT

Epilepsy is a long-term chronic neurological disorder that is characterized by seizures. One type of epilepsy is simple partial seizures that are localized to one area on one side of the brain, especially in the temporal lobe, but some may spread from there. GABA (gamma-aminobutyric acid) is an inhibitory neurotransmitter that is widely distributed in the neurons of the cortex. Scientists recently discovered the basic role of neurotransmitters in epilepsy. Synaptic reorganizations at GABAergic and glutamatergic synapses not only enable seizure occurrence, they also modify the normal information processing performed by these networks. Based on some physiological facts about epilepsy and chaos, a behavioral model is presented in this paper. This model represents the problem of undesired seizure, and also tries to suggest different valuable predictions about possible causes of epilepsy disorder. The proposed model suggests that there is a possible interaction between the role of excitatory and inhibitory neurotransmitters and epilepsy. The result of these studies might be helpful to discern epilepsy in a different way and give some guidance to predict the occurrence of seizures in patients.

1. Introduction

Epilepsy is a relatively widespread disease from which about 1% of people in the world are suffering [1–4]. Roughly 50% of adults with active epilepsy have at least one other medical condition including depression, anxiety, dementia, migraine, heart disease, peptic ulcers,... [5–17]. This disease is characterized by episodes of spontaneous seizures. This abnormal behavior is the result of defective or excessive activity of nerves which are located on cortical or other tissues in the brain. Causes of epilepsy differ depending on the age of the patient [18], and are unknown for about half of epileptic patients [19]. Genetic mutations [20–23], changes in structure of the brain and head injuries [24–27], autism spectrum disorder [28–30], infections [31,32], strokes [33,34] and tumors [35–37], are some of them. The exact cause is yet not certain [19]. Therefore, understanding the mechanism of this disease is of great importance. Computational modeling plays an important role in gaining an insight into this disease.

There is growing evidence that research on brain functions and their modeling benefit by combining classic neuroscience with nonlinear dynamics [38–41]. There are also some strong claims about chaotic behavior in many biological systems, especially in the human brain [42–44]. The dynamics in brain signals called electroencephalograms (EEGs) appear to have random features, but there are some hidden patterns in the signals [44,45]. Moreover, these signals are very sensitive to any changes in the brain's parameters [46]. Such behavior makes these systems similar in some aspects to chaotic systems [43,47]. The brain, like a chaotic system, does not reach equilibrium after a transient time, but it is always going back and forth between different states. In the research of Freeman et al. [48], the information in the odor sensory part of the brain indicates the existence of a pattern that could be discriminated whenever there was a change in the odor environment. Further dissection of the experimental data led to the conclusion that the activity of the olfactory bulb is chaotic and may switch to any desired perceptual state at any time [49]. These states are considered equivalent to attractors in dynamical systems. The authors claimed that some of the activities in mammalian brain dynamics are governed by strange attractors, or in simpler words, show chaotic behavior.

However, sometimes the neural activity in the brain can change from chaotic to periodic. These changes are mostly due to an abnormality or disorder, like some changes in EEG caused by attention deficit disorder [50] or an epileptic seizure [51]. When the brain's behavior starts to change, either because of a disease or other reasons, a bifurcation occurs. Bifurcation is a sudden change in the dynamics of a system when a parameter of the system

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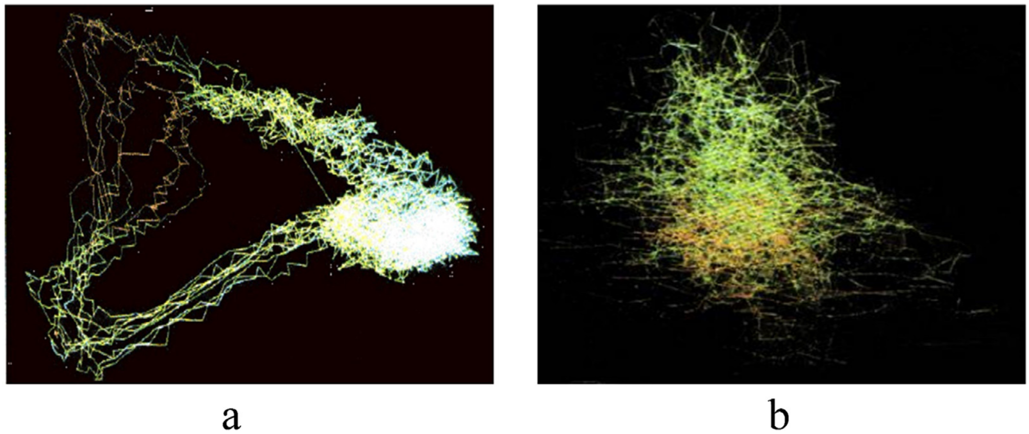

Fig. 1. (**a**). Phase space view of the EEG taken from a rat during seizure. (**b**). Phase space view of the EEG taken from a healthy and awake, but resting motionless rat [49].

changes [52]. When a brain working in a normal state (chaotic mode) suddenly undergoes seizure (periodic mode), a bifurcation occurs [53,54]. A trace of an EEG signal of a rat is shown in Fig. 1, which is a comparison with the EEG signal of a healthy and awake rat (Fig. 1(b)) with the EEG of epileptic rat during the seizure (Fig. 1(a)). Fig. 1a illustrates a rather periodic behavior and provides an example of the claim in Ref. [48].

Sometimes when a dynamical system is in its chaotic mode, it bifurcates to a periodic behavior by changing the control parameter. A further change in the parameter restores the chaos. This is called a periodic window in the midst of chaos. In a similar way, the healthy brain has a chaotic activity but epileptic seizure associated with excessive harmonic synchronization of large neuronal populations leads to a hypersynchronous state causing the brain to undergo a bifurcation that switches it from chaotic (normal) to periodic (abnormal).

In previous studies, different epileptic models were proposed in which various scientific views of epilepsy were presented. For instance, Takeshito et al. [55] modified Wilson's neuron model [56] to model the epileptic seizure dynamics by transition between multistable states. They claim that changes in field potential amplitude and frequency during the course of a seizure may be explained by noise-induced transitions among multistable states. Larter et al. [57], developed a lattice model with a type of coupled ordinary differential equations by modifying the Morris–Lecar neuron model [58]. Larter's model describes mechanisms for lack of inhibition and an alteration in conduction time, both of which seem necessary for the development of a realistic seizure model. On the other hand, some researchers argued that models could be developed from Poincare maps. They used the electroencephalographic (EEG) recordings to find the time interval between spikes as a characteristic variable and plotted the time delay interpeak interval (IPI) to study seizure. After that, a one-dimensional map was developed by fitting a polynomial function to the return map obtained by the data [59,60].

In this study, we base our main model on an artificial network since it is similar to the real brain structure. On the other hand, the dynamical and chaotic features of brain behavior are of great importance [61,62]. Therefore, the novelty of this model lies in the fact that it is not only a simple artificial neural network, but it also depicts the chaotic features of the disease.

The rest of the paper is as follows: Section 2 contains a brief review of the biological and physiological mechanisms associated with epilepsy and seizure. Section 3 introduces the proposed model for different behaviors of the brain in a natural versus seizure state. After that, Section 4 illustrates the results and discusses the model. Finally, Section 5 gives conclusions.

2. The physiological background

Epilepsy emerges from the improper dynamics of neural networks [63]. A neural network is formed by several types of cells in the nerve systems that are interact with each other through different mechanisms such as synapses [64]. Its activities are greatly dependent on the extra cellular environment, while any modification in its structure can induce epilepsy [65]. There are many known types of epilepsy, but partial onset epileptic seizures (also called focal or local seizures) is the most common form of epilepsy [66–71]. It can be distinguished from the others by some unique seizure features (e.g. seizure initiation is from a particular portion of brain tissue (seizure focus or foci) [72,73] and propagates to the other parts but is limited to a specific part of the brain especially the temporal lobe, which is most likely to be resistant to seizure treatment drugs [74–79]). The temporal lobe is the fourth major lobe of the cerebral cortex in the mammalian brain. This complex part of the brain deals with many 'higher function', behaviors and abilities, including hearing, speech, memory, emotions, learning. All these higher functions will be affected if the temporal lobe does not function well [80,81]. The temporal lobe also plays an essential role in the excitation/inhibition balance of information processing [82]. In patients with epilepsy, temporal lobe dysfunction decreases the inhibitory power of the brain or increases the excitatory function of brain [83–87]. It has been reported that some neurotransmitters called GABA (gamma-aminobutyric acid) and glutamate have a significant influence on cortex function [88]. GABA is an inhibitory and glutamate is an excitatory neurotransmitter that is widely distributed in the neurons of the cortex [89]. Synaptic reorganizations at GABAergic and glutamatergic synapses not only enable seizure occurrences, they also modify the normal information processing performed by these networks [90–92]. In the following section, we propose a novel model of temporal lobe epilepsy by using different neurotransmitters as the main bifurcation parameters.

3. The proposed model

In this section, we introduce a novel nonlinear neural network [93–96] to model the switching behavior of the brain in epileptic patients (Fig. 3). This model is a network representing different parts in the brain that are interconnected in order to depict the interaction that occurs during seizures. A multilayer perceptron (MLP) artificial neural network (ANN) is used in this model. The main network consists of several sub-networks which were developed by Baghdadi et al. in Ref. [50]. This sub-network or the basic function of the main network is a single layer nonlinear network