Medical Hypotheses 128 (2019) 64–68

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

A new approach for digestive disease diagnosis: Dynamics of gastrointestinal electrical activity

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A B S T R A C T

Various methods are used for analyzing the status of the human body. In digestive system, myoelectrical activity is recorded from the abdominal surface. Frequency and power of Gastrointestinal (GI) activity is usually assessed using power spectral analysis. However, spectral analysis of GI electrical activity is a nonspecific test, failing to distinguish diseases. Other dimensions of GI electrical waves may help identify diseases more precisely. Studying complex systems is one of the approaches that can be taken for research on body systems. The dynamic variability of a complex system is estimated by nonlinear methods. Previous studies have identified how functional dynamic variability of organs differ in normal and disease conditions. Variation of electroencephalogram, heart rate, and respiratory rate are known examples of system dynamic fluctuation. If we consider the digestive tract as a complex system, the dynamic variation of the waves in the GI system could be analyzed by nonlinear methods to possibly help clinicians assess various conditions of the GI system in healthy subjects and patients.

Introduction

Various approaches can be taken to study the human body. Numerous methods are used for analyzing how the systems and organs of the body function. Researchers are trying to develop non-invasive methods with higher precision than before [1]. In many organs, electrical changes are an indicator of functional alteration [2,3]. Several methods have been designed for recording and analyzing electrical waves generated by various organs of the body [4,5]. Analyzing organ electrical waves helps distinguish health and disease [1,5]. For example, the electroencephalogram (EEG) records the electrical activity of the brain [3]. Another example is electrocardiogram (ECG), which records the electrical activity of the heart, used for identifying and treating heart disease [6,7]. Heart rate intervals, segments, arrhythmias, and variability can be calculated or detected using ECG [8,9]. These methods help clinicians detect abnormalities in the heart [8,9]. However, the electrical activity of other organs, such as the gastrointestinal (GI) system, have not been investigated as extensively as ECG.

GI electrical activity originates from the interstitial cells of Cajal (ICC), scattered in GI syncytium [10]. Electrical changes of the ICC cause GI motility alteration [11]. Dysfunction or loss of ICC causes a variety of GI motility disorders, such as achalasia, diabetic gastropathy, intestinal pseudo-obstruction, ulcerative colitis, and slow transit constipation [11]. Slow waves and spikes of the GI system trigger stomach and intestine contraction [11]. Electrical activity of the GI system can be recorded from the abdomen surface. The type of recording depends on the position of the electrodes over the abdominal skin [12]. Electrogastroenterogram (EGEG) represent stomach, small intestine, and colon motor functions [12]. Among various electrical activity that is recorded from the GI system, electrogastrogram (EGG), which records stomach activity, is the most popular [11,13].

Power spectral analysis of GI electrical activity

Power spectral density, obtained by periodogram, is the most common method used in clinics for evaluating GI myoelectrical and motility changes. This method assesses frequency, amplitude (power), and stability of the GI electrical waves [10].

In this method, wave frequency is measured per minute. The amplitude of waves considered power. The relation between different frequency and power spectrum plotted X-Y diagram. The horizontal axis is the different frequency measured during recording time. The vertical axis is the power of the spectrum. The maximum number of frequency that occurs during recording time is taken as the dominant frequency on the X-axis. The maximum power is called dominant power on the Y-axis (Fig. 1). The dominant frequency of EGG is normally between 2 and 4 cycles per minute (cpm) [10,13]. Various indices extract from power spectral analysis mainly includes dominant frequency and power, fasting-fed power ratio, percentage of normal gastric slow waves, percentage of gastric dysrhythmias, and percentage of power distribution [13]. EGG alteration has been seen in different diseases,

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https://doi.org/10.1016/j.mehy.2019.05.009
Received 11 December 2018; Accepted 12 May 2019

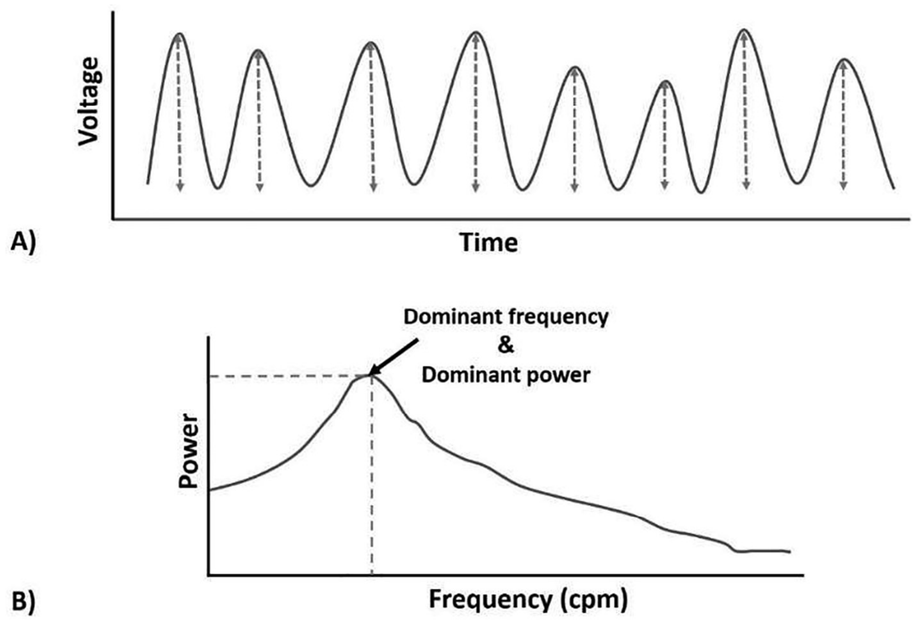

Fig. 1. The principle for computing the dominant frequency and power in a hypothetical wave. A) A diagram of hypothetical recording waves has been demonstrated. Dashed arrow shows the power (amplitude) of each wave. The number of waves occurring each minute are estimated and named "frequency". B) Power spectral analysis for diagram A. Arrow shows the confluence of dominant frequency and power. cpm: cycle per minute.

such as diabetes mellitus, nausea, gastric dysrhythmias, and motion sickness [10].

Bugs of the power spectral analysis of GI activity

Power spectral analysis of GI activity is a nonspecific test [10]. As a result, analyzing the frequency and power of EGG or EGEG failed to diagnose any specific disease, even stomach motor dysfunction [10]. On the other hand, there is no standard protocol on where electrodes should be placed specifically, or the duration and periods of recording. These problems have limited the use of EGG and EGEG in the clinic.

Hypothesis

Due to the mentioned bugs, the power spectral density of EGG and EGEG waves are used infrequently in the bedside. Nonetheless, GI electrical waves may have more information, yet to be noticed, than the spectrum of the rhythm and power. One such neglected area may be the possibility of dynamic alterations of EGG or EGEG waves. Thus, I hypothesized the possibility of identifying GI diseases through the dynamic analysis of EGEG.

Evaluation of the hypothesis

The human body and its organs may be considered as a complex system. With this approach, rules of the complex systems are true in the human body too. One of the important characteristics of complex systems is the communication network between the components [14].

Theoretically, change in any part of a complex system may affect other components through the communication network [14]. There are two main coordinator networks in the human body; the nervous system and the hormonal system. Change in any part of the body can affect other parts through the coordinator networks mentioned above. For example, a communication coordination has been shown among heart rate, brain electrical activity, respiratory pattern, and eye movement [14]. Alteration in this network may shift the activity of other components away from the normal range, thus changing the dynamics of organ activity in healthy and disease conditions [14]. EEG, respiration rate, and heart rate variability are all well-known dynamic fluctuations of the body. We shall explain each briefly.

Variability of EEG signals

The central nervous system (CNS) contains billions of neurons. EEG is the recording of the overall spontaneous electrical activity of the brain. The oscillations of electrical interactions among neural collections generate brain wave variability [15]. The dynamical complexity of neural networks investigated in different physiologic and pathologic conditions such as sleep, coma, anesthesia, epilepsy, seizure detection and prediction, mental states, and psychiatric disease [15,16]. Changes beyond the normal variation of brain-wave dynamics may be signs of CNS disease [15].

Respiratory rate variability

A normal respiratory rhythm demonstrates dynamics of complex systems. Variations in respiratory rhythm are called respiratory rate variability (RRV) [17]. The respiratory rhythm dynamics of healthy subjects shows normal fluctuation along with variety of stimuli in order to maintain homeostasis. However, RRV dynamics have been found to become altered in several circumstances such as some stages of sleep, obstructive sleep apnea, stress, and asthma [18–20]. This alteration seems to be occurring from changes in respiratory control centers of the CNS.

Heart rate variability

Heart rate variability (HRV) demonstrates complex system dynamics obtained from beat-to-beat intervals of the heart [9]. Extreme changes in HRV indicate the probability of morbidity and mortality [9]. Furthermore, HRV is used for the prognosis and diagnosis of various cardiac and non-cardiac diseases. Stroke, Alzheimer, renal failure, leukemia, epilepsy, chronic migraines, obstructive sleep apnea, sepsis, brain trauma, multiple organ failure, myocardial infarction, and diabetic neuropathy are some examples of diseases which could affect HRV significantly [9,21]. It seems that the most important factor causing HRV alteration in diseases, is impairment in the autonomic nervous system (ANS) and heart coordination [9,22,23].

GI as a complex system

The GI tract and its organs is another one of systems that can potentially be explored through complex system dynamics. The GI system has the properties of complex systems, such as numerosity of components, network communication, spontaneous order, self-organization, and adaptation [24].The GI has a syncytium structure similar to the cardiac system. In other words, each cell communicates with other cells using gap junctions. GI electrical activity originates in ICCs and propagates through the GI syncytium [11]. Moreover, the GI tract has a self-neural network which is called the enteric nervous system (ENS). The ENS has more than one hundred million neurons. This plexus has its own communication network. Furthermore, the ENS network is closely coordinated with the ANS [25]. All cellular and neural communications put together may demonstrate the features of complex systems for the GI tract.

Analyses of GI dynamics as a complex system

Power spectral density is a reductionist method which investigates one-to-one communication and relationship between individual characteristics of each component. However, such method do not provide complete information about complex systems and their properties [26,27].

Some previous studies examined the nonlinear analyzes of EGG which estimated entropy and sensitivity to initial conditions for GI motility disorders [12,28]. It should be noted that these evaluations were more about the structure and pattern of EGG, but the dynamic changes of slow waves has not been studied yet.

In order to assess the dynamics of the GI electrical activity as a complex system, holistic methods are preferred.

For analysis of the wave dynamics, the whole of recording considers as a time-series. Maximum peak value of each wave is then identified. Intervals between maximum peaks values are calculated within a time series. This measurement is called peak-to-peak interval (PPI) (Fig. 2). The dynamic variation of PPI is analyzed using nonlinear methods.

Complex systems can be analyzed by various nonlinear holistic methods. Nonlinear measures provide information on the structure or complexity of the data time-series [29]. Various nonlinear analyzing methods show different dimensions of the PPI. It seems that these methods are also applicable to the dynamic analysis of the electrical waves of the GI.

The most common nonlinear analysis are short-term variability, long-term variability, fractal dynamics, entropy, chaos, and so forth.

Briefly, short term and long term variability can be extracted from PPI deviation using Poincaré plot. The Poincaré plot is a graph in which each PPI is plotted against the next PPI. This method separates short-term effective factors from long-term ones [30].

In a complex system, entropy represents the irregularity of the dynamic. Entropy of PPI can be assessed by the degree of irregularity in time-series. More entropy indicates more irregularity of the PPI dynamic [31].

One aspect of dynamic systems is fractal structure. Fractals are self-similarity and scale-free structures which are found in some complex systems. The dynamics of PPI fluctuation can be taken as a fractal structure [32].

The sensitivity of the dynamics of complex systems to their initial condition is assessed by the chaotic approach. In chaotic systems, a small change in initial conditions alters the final dynamic of the system. This characteristic makes chaotic systems unpredictable. Chaos of PPI dynamic is usually estimated by measuring sensitivity to initial conditions [33].

A case study

About one hour EGG was recorded from abdomen surface of a 22 years old healthy male which fastening for 4 h before experiment.

Three electrodes were used for recording. First electrode was placed on the left midclavicular line under last ribs and second one was settled on the middle of the distance between end of the xiphoid and navel. The third (ground) electrode was fixed on the left of the abdomen [12]. The signals were digitized at the sampling rate of 1 kHz and displayed on labchart7 by Powerlab system (model 4/35, ADInstruments, Sydney, Australia). For extract the EGG data, band-pass filter (high cut-off frequency: 0.05 Hz, low cut-off frequency: 0.016 Hz) was used. Therefore all data between 1 and 3 cpm were detected (Fig. 3). Then, EGG data was exported to MATLAB software. In the next step, time-series PPI were calculated using a custom program written in MATLAB software. The peak of each signal was identified and peak-to-peak time intervals were considered. These data can use for linear and nonlinear assessment of PPI dynamics. In the following, the dynamics of PPI fluctuation will be mentioned.

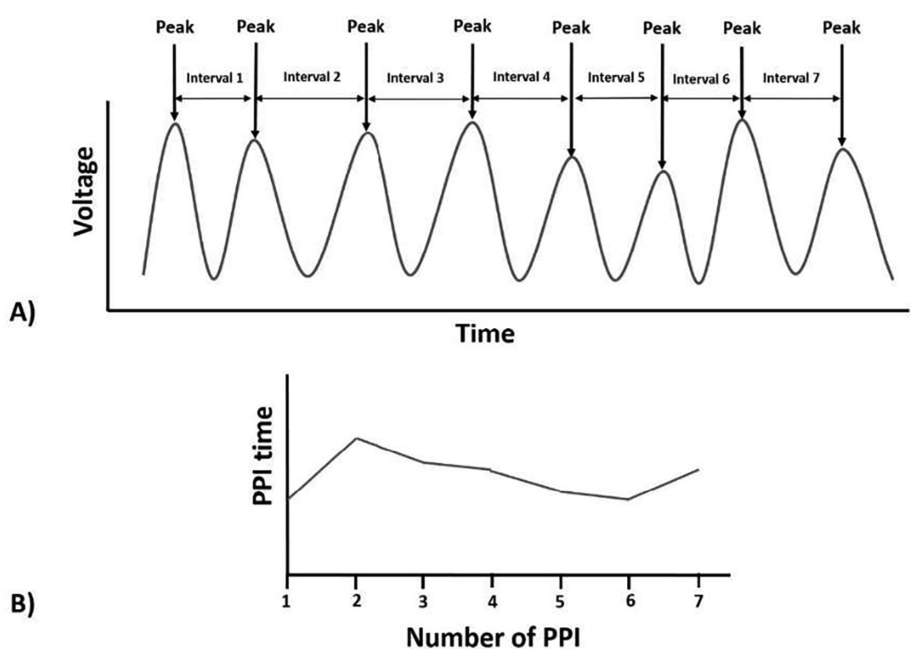

Fig. 2. Peak-to-peak intervals of sample waves. A) Diagram 2A is the same 1A hypothetical waves, but with a dynamical analysis viewpoint. The seven PPIs obtained from the recording time. B) Dynamics of the seven peak-to-peak wave variabilities are shown in 2B.

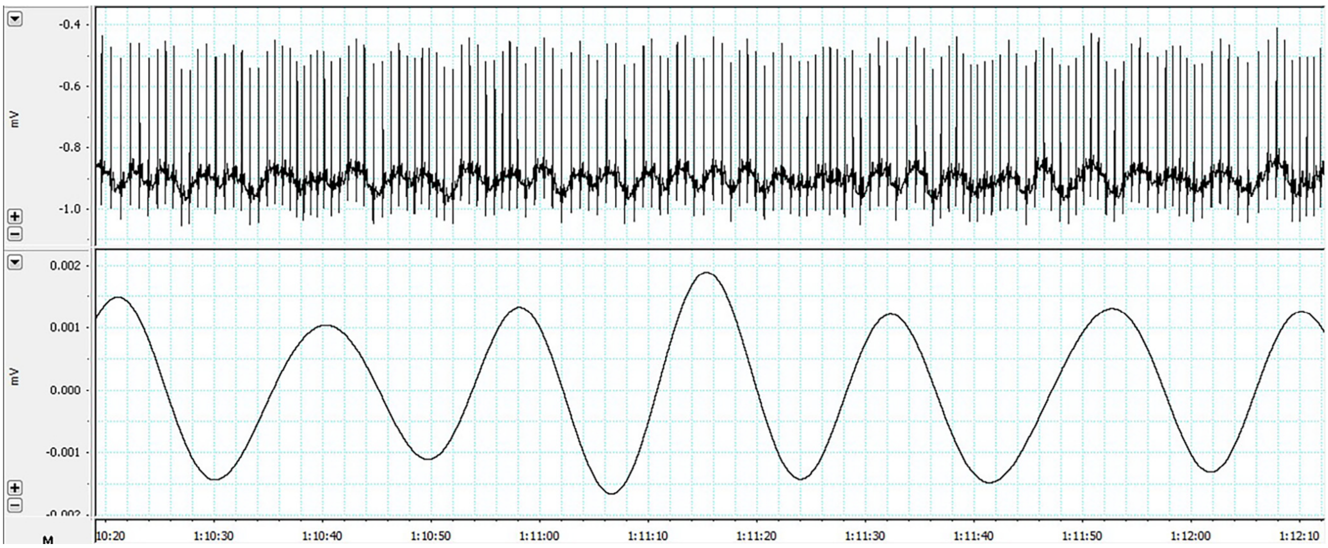

Fig. 3. Sample of raw data (upper panel) and filter data (lower panel, 0.05–0.015 Hz) were recorded from surface of the abdomen by Labchart7. The lower panel indicate the EGG. Note that X axis is time and Y axis is voltage.

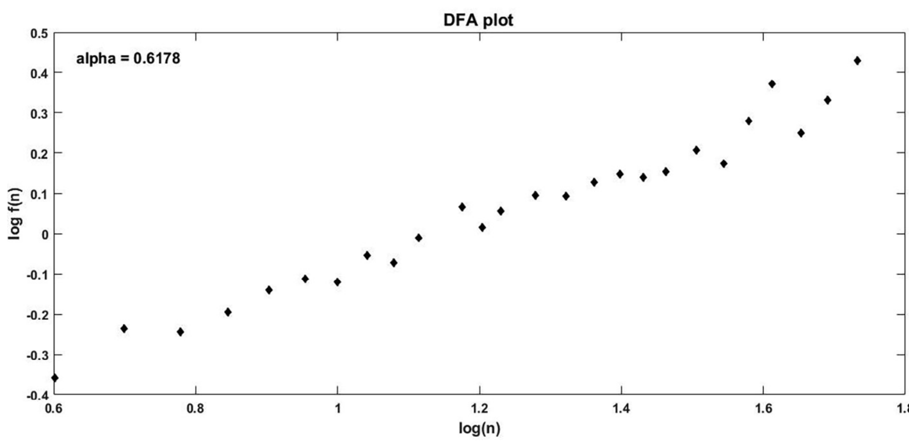

Fig. 4. DFA for representative data set. The data exhibit a linear relationship between log (scale) and log (fluctuations).

Fractal structure was calculated by detrended fluctuation analysis (DFA) through custom program written in MATLAB software. DFA quantifies fractal-like correlation properties of PPIs. In this method, the fluctuation of the integrated and detrended data is measured within observation windows of various sizes and then plotted against window size on a log-log scale. A linear relationship between log (fluctuation) and log (window size) indicates the presence of scaling which serves as a characteristic of a fractal-like time series. The scaling exponent alpha (α) represents the slope of this line [32]. An $\alpha = 0.5$ shows white noise (uncorrelated random data). $0.5 < \alpha \leq 1$ indicates persistent long-range power-law correlations in which a large fluctuation is more likely to be followed by another large fluctuation. An $\alpha = 1$ corresponds to 1/f noise (Pink noise). When $1 < \alpha < 1.5$, correlation exists but cease to be of a power-law form. $\alpha = 1.5$ indicates the integration of white noise (Brown noise) [32].

In present project, α exponent is equal to 0.6178 (Fig. 4). On the basis of this data, it can be concluded that the EGG dynamic shows the fractal-like structure. Moreover, α exponent for EGG dynamic is between 0.5 and 1.0 which demonstrates the correlation between waves.

It should be noted that this result is from a healthy volunteer. For accurate evaluation, the values used for each parameter in the GI system of normal and diseased subjects requires further practical experiments with statistical comparisons among groups.

Consequences of the hypothesis

Since spectral and power analysis of GI electrical activity are both nonspecific tests, nonlinear assessment of PPI dynamics may be help reveal more clues for various GI diseases. Other advantages of this approach include low-cost, non-invasiveness, and safeness for patients and the healthy. Nevertheless, this hypothetical opinion should be tested in practical investigations.

Funding

There is no source of support in the form of grants for this paper.

Acknowledgments

The author is grateful to Dr. G.R. Bayat (Alborz University of Medical Sciences) for providing the laboratory facility and Mrs. M. Mohamadi and Dr. M.R. Raoufy (Tarbiat Modares University) for helping data analysis.

Declaration of Competing Interest

None.

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