Biophysics, Vol. 47, No. 2, 2002, pp. 352–358. Translated from Biofizika, Vol. 47, No. 2, 2002, pp. 369–375.

COMPLEX SYSTEMS BIOPHYSICS

Chaos Theory Analysis of Electrocardiograms Recorded from Humans and Animals with Ventricular Fibrillation

L. V. Mezentseva, S. I. Kashtanov, V. A. Vostrikov, M. A. Zvyagintsev, and I. L. Kosharskaya

Anokhin Research Institute of Normal Physiology, Russian Academy of Medical Sciences, Moscow, 103009 Russia
Sechenov Medical Academy, Moscow, 119435 Russia

Received February 14, 2000; in final form, September 18, 2000

Abstract—Ventricular fibrillation in humans and animals was quantitatively analyzed using the methods of the chaos theory. To test the hypothesis that there are species-specific differences in the level of chaos displayed during ventricular fibrillation, various chaos-theory-derived indices were calculated from electrocardiograms recorded from 5 patients during 32 episodes of sudden ventricular fibrillation and from 17 laboratory animals (dogs, rats, and rabbits) during 235 episodes of experimentally induced ventricular fibrillation. Comparative analysis of the data showed that the indices used to assess the regular and irregular (chaotic) components of the electrocardiographic signal during ventricular fibrillation varied from species to species. The chaotic component was greatest in dogs, smallest in humans, and intermediate in rabbits and rats. The results are consistent with the suggestion of the fractal organization of myocardial structure and function.

Key words: Ventricular fibrillation, chaos theory, correlation dimension, period-splitting index

INTRODUCTION

The view of ventricular fibrillation as chaos in the heart is not new. However, the term "chaotic" formerly used by experimenters and clinicians to qualitatively describe irregular oscillatory components of the electrocardiogram (ECG) and uncoordinated contractions of a dying heart is now used in quantitative analysis of these phenomena in the framework of the nonlinear theory of dynamical systems [1–3]. In previous studies, we assessed the level of chaos in ventricular fibrillation (VF) episodes by calculating the entropy, and showed that this parameter increased with time into fibrillation. Its increase changed to a decrease just before the fibrillation spontaneously ceased [4]. Yet another important characteristic of chaotic processes is the attractor dimension. The degree of disorganization of cardiac electric activity is often described by this quantitative measure of chaos. As shown in our animal studies (rats, rabbits, and dogs), the correlation dimension is also informative in describing the structural and functional organization of myocardium [5]. As assessed by calculating the correlation dimension, the chaotic component is greatest in dogs, intermediate in rabbits, and smallest in rats. In this study, we further elaborated on the dynamic-chaos-theory methods for quantitatively analyzing the irregular components of cardiac activity during ventricular fibrillation. The goal of the study was to calculate various chaos-theory-derived indices for humans and compare them with those obtained for laboratory animals (rats, rabbits, and dogs).

Abbreviations: ECG, electrocardiogram; VF, ventricular fibrillation.

EXPERIMENTAL

Electrocardiograms used in analysis were recorded from 5 patients during 32 episodes of sudden ventricular fibrillation (second standard lead; recording time, 10–20 s) and from 17 laboratory animals (seven Wistar rats weighing 250–300 g, five Chinchilla rabbits weighing 2.1–2.5 kg, and five dogs weighing 8–16 kg) during 235 episodes of experimentally induced ventricular fibrillation (111 in rats, 56 in rabbits, and 48 in dogs). Ventricular fibrillation

was induced in anesthetized animals during the vulnerable period of the cardiac cycle (ascending part of the T wave) by applying a train of 5-ms electric pulses through left ventricular electrodes. The pulse amplitude was gradually increased until it attained the ventricular fibrillation threshold. The electric activity of the heart was recorded before stimulation (sinus rhythm) and during fibrillation with a Lifepack 7 monitor in humans and dogs, and with a mingograph 82 (Siemens) in rats and rabbits.

Raising the stimulus amplitude to the threshold value initiated ventricular fibrillation, which manifested itself in tremendous electrocardiographic variability. Even on visual inspection, it was possible to distinguish between more regular and less regular segments of recording. The patterns ranged from a tachycardia-like process to an erratic series of low-amplitude excitations varying in duration. The electrocardiograms were converted to graphic files with a Turbo HT 800 scanner (Mustek) connected to a computer. The scanner resolution was set to 800 dots per inch. The graphic files were then imported into a dedicated computer program that we developed to digitize the graphic data. The sampling rate was 1000 Hz, which yielded 30 to 50 data points per one wave of fibrillation oscillations. To avoid the effect of the nonstationarity of the process on the results, only short time series (up to 1000 data points) were used in analysis. The accuracy necessary in analysis of the graphical information was achieved by mathematically processing the data using appropriate editing software. Based on this graphics-processing software, a database was established for ventricular fibrillation studies called DBVF, which includes not only the results of current experiments, but also episodes of ventricular fibrillation extracted from archival electrocardiograms stored in our laboratory since the 1960s.*

Segments of electrocardiograms recorded during ventricular fibrillation were analyzed by calculating the following quantitative measures of chaos: the pointwise correlation dimension $PD2i$; the entropy; and the period-splitting index $W = T/t_{mean}$, where T is the mean cycle length during normal sinus rhythm (before the onset of ventricular fibrillation), and t_{mean} is the mean interval between consecutive oscillations during ventricular fibrillation. In addition, for each segment of electrocardiograms recorded during ventricular fibrillation, we determined the ventricular fibrillation (ectopic) rate.

The correlation dimension $D2$ proposed by Grassberger and Procaccia [6] to characterize the chaotic behavior of a nonlinear dynamical system reads

$$C(l, n) = l \exp(D2), \quad (1)$$

where $C(l, n)$ is a cumulative function of differences between all possible pairs of the vectors determining the state of the system, n is the number of differences, and l is the phase space size (length of the observation period). Modifications of this algorithm were later proposed by Farmer *et al.* [7] (pointwise scaling dimension) and by Skinner *et al.* [8] ($PD2i$). By its construction, the Skinner algorithm is well suited for analyzing nonstationary processes. To obtain the vectors required for calculating $C(l, n)$, a sequence of signal values separated by equidistant intervals τ has to be determined for a given segment of the electrocardiogram. Thereafter, moving point by point along the entire time series, one sequentially calculates the differences between the current vector i and vectors j ($j \neq i$), taking the current vector as a fixed reference. Obviously, the dimension calculated in this way is a function of time and can be useful in tracking the chaotic dynamics of the process. We assessed the level of chaos in ventricular fibrillation by calculating $PD2i$ using the Skinner algorithm.

Analyzing how correlation sums depend on the embedding dimension, we found that no nonlinearity-related ambiguity remains in determining the correlation dimension at $n > 500$. Figure 1 shows the correlation integral $C(l, n)$ plotted as a function of n. For $n < 100$, the curve is clearly nonlinear (Fig. 1a). Deviations from linearity are still evident for $n < 200$ (Fig. 1b) and for $n < 300$ Fig. 1c). However, at $n = 1000$, the plot is quite linear (Fig. 1d). If $C(l, n)$ varies linearly with n, the correlation dimension is a valid tool for assessing the irregularity of the electrocardiographic signal. Therefore, only electrocardiogram segments for which $n = 1000$ were used to calculate the correlation dimension.

The degree of disorganization of cardiac electric activity was also assessed by calculating the entropy S

$$S = -k \int f(x, t) \ln f(x, t) dx, \quad (2)$$

where $f(x, t)$ is the probability of a given state of the system at time t, which can be estimated from the

* The DBVF is available from the authors upon request.

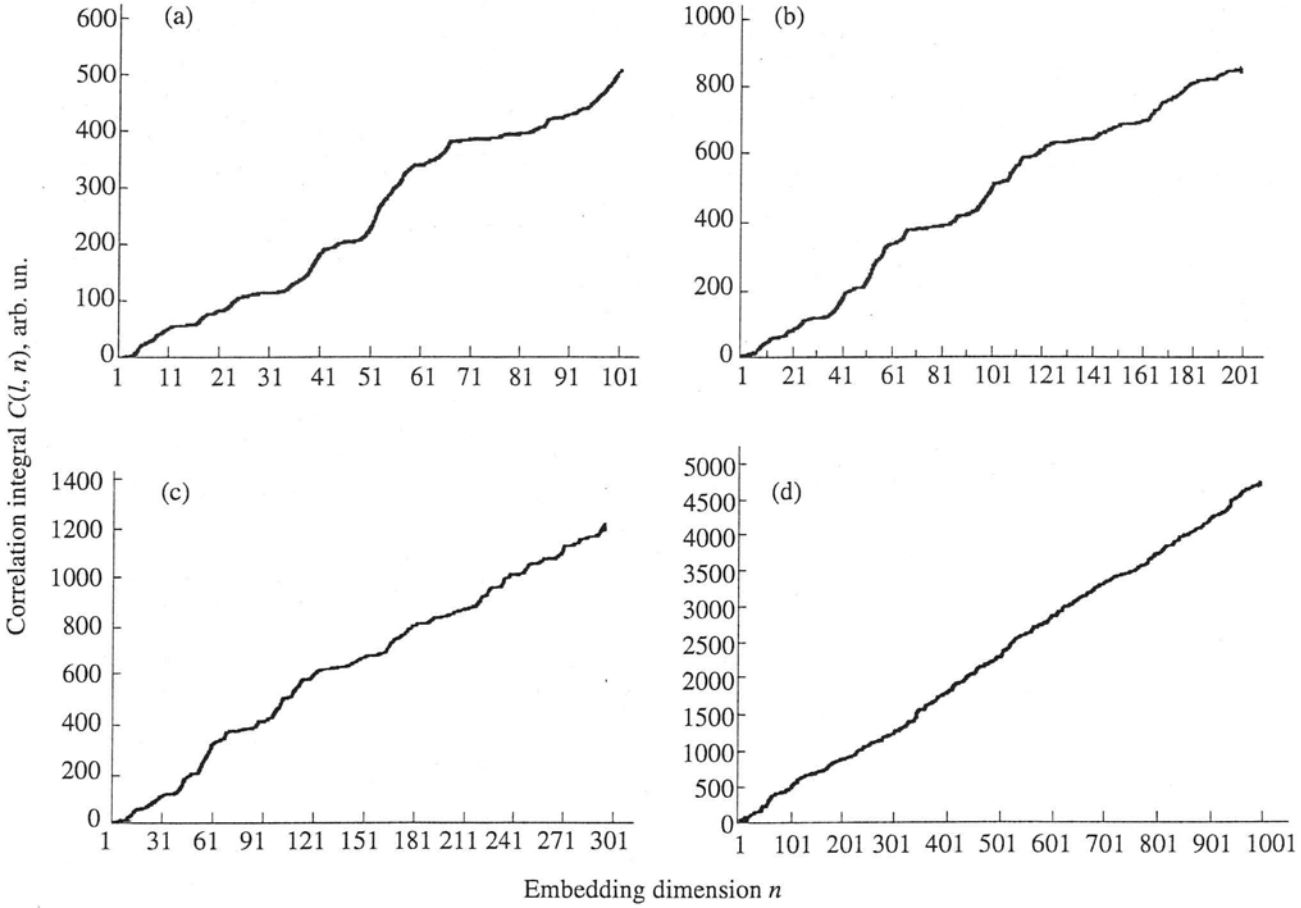

Fig. 1. Correlation integral $C(l, n)$ plotted vs. the embedding dimension n ranging from unity to (a) 100, (b) 200, (c) 300, and (d) 400.

amplitude histogram; and k is the proportionality coefficient, which was set to unity in our calculations.

RESULTS

In humans and laboratory animals, the electric activity of the heart during ventricular fibrillation exhibited generally similar chaotic dynamics. However, in quantitative terms, the degree of disorganization was different in various species. In Fig. 2, fragments of electrocardiograms of a rat (Fig. 2a) and a dog (Fig. 2b) recorded during experimentally induced ventricular fibrillation are shown along with the corresponding histograms of relative beat-to-beat change in amplitude (Figs. 2e, 2f) and scattergrams (Figs. 2c, 2d), which are geometrical descriptors of the chaotic dynamics of the fragments shown. The amplitude and frequency characteristics of ventricular fibrillation vary markedly among different species. Therefore, we attempted to develop a unified technique for comparing the parameters of ventricular fibrillation in different species that would not depend on the electrocardiographic signal intensity. Thus, constructing histograms, we chose to consider relative beat-to-beat changes in amplitudes $(A_{(i+1)} - A_i)/A_{mean}$, rather than their absolute values A_i. As can be seen in Figs. 2c–f, the chaotic component was greater in the dog (eight-bin histogram) than in the rat (five-bin histogram). Visual inspection of their scattergrams leads to the same conclusion, which is further confirmed by calculating various chaos-theory-derived indices. For the dog electrocardiogram shown in Fig. 2b, entropy S was estimated at 1.73; the period-splitting index W, at 3.7; and the pointwise correlation dimension $PD2i$, at 3.1. For the rat electrocardiogram (Fig. 2a), all these parameters were smaller: $S = 1.42$, $W = 2.4$, and $PD2i = 2.5$. The results of other experiments were similar (table). The table shows the quantitative indices of chaos calculated from electrocardiograms recorded from 17 laboratory animals (dogs, rats, and rabbits) during 235 episodes of experimentally

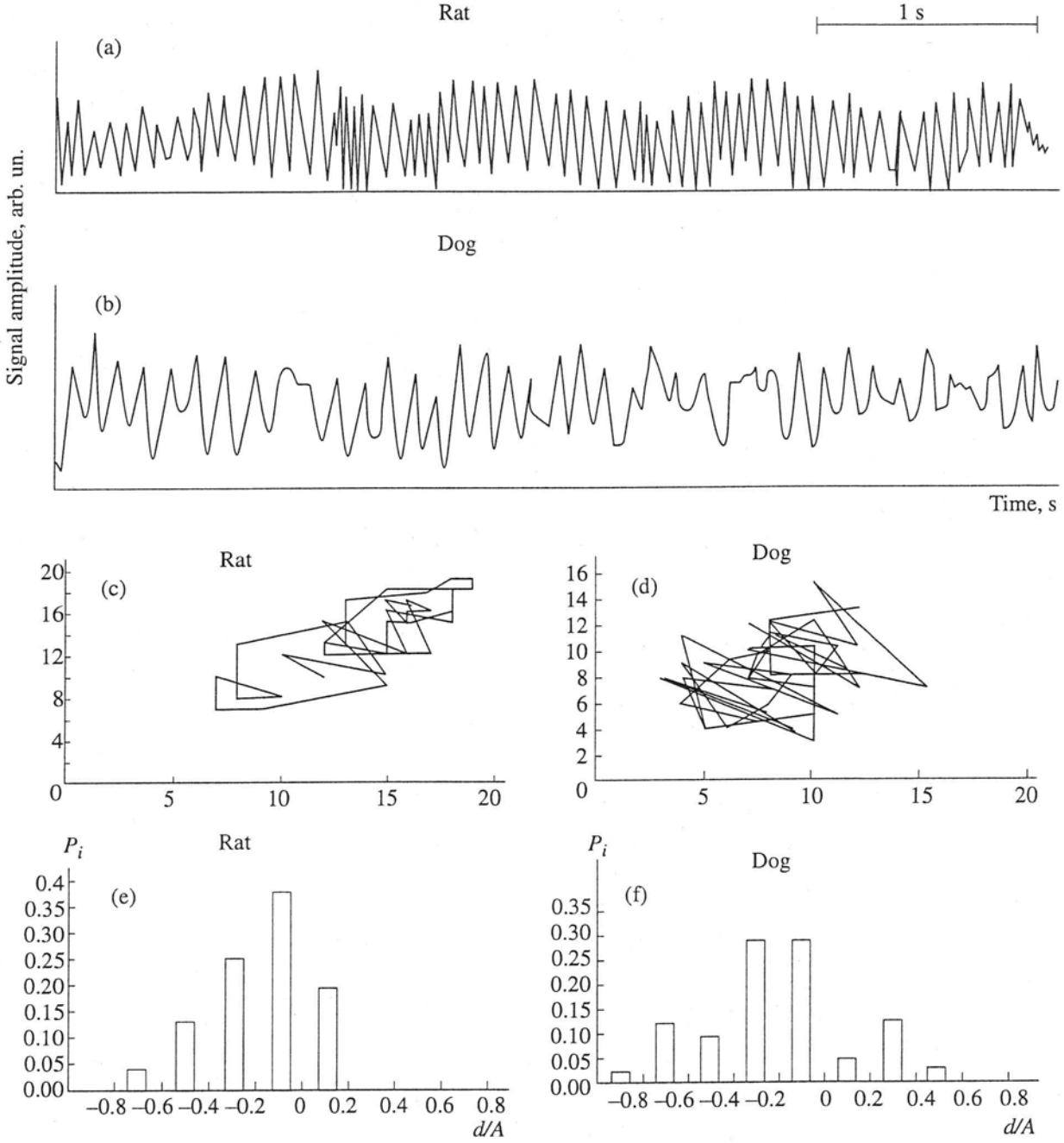

Fig. 2. Comparison of irregular components in electrocardiograms recorded from patients during sudden ventricular fibrillation with those in electrocardiograms recorded from laboratory animals during experimentally induced ventricular fibrillation: (a, c, e) rats and (b, d, f) dogs and humans. Examples of (a, b) raw recordings; (c, d) corresponding scattergrams (arb. un.); and (e, f) probability-distribution histograms of relative beat-to-beat change in amplitude d/A, where $d = A_{(i+1)} - A_i$; and A is the pulse amplitude averaged over the entire segment.

induced ventricular fibrillation and from 5 patients during episodes of sudden ventricular fibrillation.

The entropy of the process, which is a measure of its irregularity, sharply rises as one proceeds from sinus rhythm to ventricular fibrillation, with the higher degree of irregularity corresponding to the greater fractal dimension of chaos. The latter was smaller in humans than in dogs. The differences between these two species in S, W, and $PD2i$ were the largest and statistically significant at $p \leq 0.001$. In rats and rabbits, these indices were usually smaller than in dogs, but greater than in humans. No statistically significant differences were found between rats and rabbits.

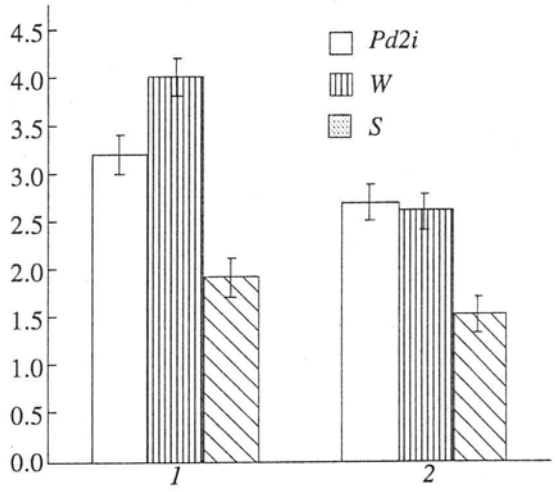

Fig. 3. Pointwise correlation dimension *PD2i*, entropy *S*, and the period-splitting index *W* for (*1*) dogs and (*2*) humans (mean and standard deviation).

In general, ventricular fibrillation contains both regular and irregular (chaotic) components. Therefore, we used the parameters of two types to describe the electrocardiographic signal; the regular component was assessed by determining the ventricular fibrillation rate and the sinus rate in the period preceding ventricular fibrillation (see table).

The fibrillation rate was highest (16.0 Hz) in rats and lowest (6.9 Hz) in humans. During sinus rhythm, the beat interval in rats was found to be nearly half that in humans; likewise, during ventricular fibrillation, the heart rate in rats was roughly twice that in humans. In contrast, although dogs and humans were similar in the normal sinus rate, the ventricular fibrillation rate was nearly 1.5-fold higher in dogs than in humans. This analysis shows that ventricular fibrillation is differently structured in humans and animals. The quantitative characteristics of the regular and irregular (chaotic) components of the electrocardiographic signal during ventricular fibrillation vary from species to species.

To understand the mechanism whereby these differences arise, we took a closer look at the period-splitting index *W*. Previously [5], we found that, during fibrillation, interbeat intervals are quantized to discrete complexes via splitting of the period of the normal sinus rhythm *T*. In general, ventricular fibrillation may be viewed as an erratic series of excitation complexes with variously split periods: 1/2, 1/3, 1/4, 2/3, 3/5...*M*/*N*, where *N* is the number of fibrillation interbeat intervals that fit to *M* interbeat intervals of the normal sinus rhythm. The degree of irregularity in ventricular fibrillation depends on the relative contributions of various *M*/*N* components to the overall structure of the process and on the stability of patterns of their alternation. To quantitatively assess these phenomena, we used the period-splitting index *W*, which is defined as the mean number of interbeat intervals during ventricular fibrillation fitting to one interbeat interval of the normal sinus rhythm. The period-splitting index *W* for humans and laboratory animals is shown in the table. As with entropy and *PD2i*, we found that the largest period-splitting index was in dogs and the smallest one in humans (Fig. 3). By way

Quantitative indices for assessing the regular and irregular (chaotic) components of the electrocardiographic signal during ventricular fibrillation in humans and various animal species

Species	Irregular (chaotic) component			Regular component	
	Entropy	Pointwise correlation dimension	Period-splitting index	Interbeat interval during sinus rhythm before VF, ms	VF rate, Hz
Humans	1.3–1.8	2.1–2.8	2.2–2.9	360–440	6.2–7.6
	1.5 ± 0.3	2.6 ± 0.3	2.7 ± 0.3	393 ± 27	6.9 ± 0.8
Dogs	1.6–2.1	3.0–3.5	3.3–4.5	280–490	8.1–13.2
	1.9 ± 0.3	3.2 ± 0.2	4.0 ± 0.3	362 ± 32	10.6 ± 2.1
Rabbits	1.5–2.2	2.7–3.1	2.1–2.9	250–270	8.4–11.2
	1.7 ± 0.4	2.9 ± 0.21	2.8 ± 0.35	260 ± 15	10.0 ± 1.1
Rats	1.4–2.1	2.5–2.9	2.2–3.7	170–220	10.1–20.1
	1.6 ± 0.4	2.7 ± 0.2	3.0 ± 0.2	190 ± 20	16.0 ± 1.8

Note: Upper line, range; lower line, mean and standard deviation.

that had the same normal sinus rate (Fig. 4). Obviously, the longer the interbeat interval during normal sinus rhythm, the greater the values of the period-splitting index and the pointwise correlation dimension. Interestingly, if the dogs and humans developed ventricular fibrillation from the same normal sinus rate, whatever its value, the period-splitting index and the pointwise correlation dimension were usually higher in dogs than in humans.

DISCUSSION

Asking in the title "Is fibrillation chaos?", Kaplan and Cohen [5] answer that fibrillation seems to be a nonchaotic random signal. They note, however, that such random-looking but nonchaotic behavior can also be generated by a nonlinear deterministic system. Our results lead us to believe that ventricular fibrillation is not a random process. In other words, ventricular fibrillation is more a regular process (pertaining to a deterministic system) than it is a random signal. The evolution from the norm (sinus rhythm) to ventricular fibrillation proceeds via a large spectrum of intermediate split rhythms and can be quantitatively characterized with the period-splitting index. This index is as informative as other quantitative measures of chaos in ventricular fibrillation, such as entropy or the correlation dimension. Our results are consistent with the data of spectral analysis of ventricular fibrillation reported by Goldberger *et al.* [9]. The spectrum obtained in that study contained a dominant frequency component and small-amplitude harmonics at frequencies forming a 1:2:4 or 1:2:3 ratio with the dominant frequency. Presumably, the period-splitting index might be a useful quantitative measure of this behavior. Our results show that it is this index that works best in assessing the degree of disorganization of electric activity of the heart during ventricular fibrillation in humans and various animal species. The species-related differences in the indices of chaos described in this study suggest that there is a link between a nonlinear fractal structure of the conduction system of the heart and the nonlinear modes of behavior of this structure. This hypothesis was put forward by Goldberger *et al.* [9]. They explained the frequency shifts in the power spectrum during ventricular fibrillation by the fractal geometry of the conduction system of the heart. By fractal geometry is meant the hierarchic structure of the His-Purkinje system, with its numerous branching points of fiber

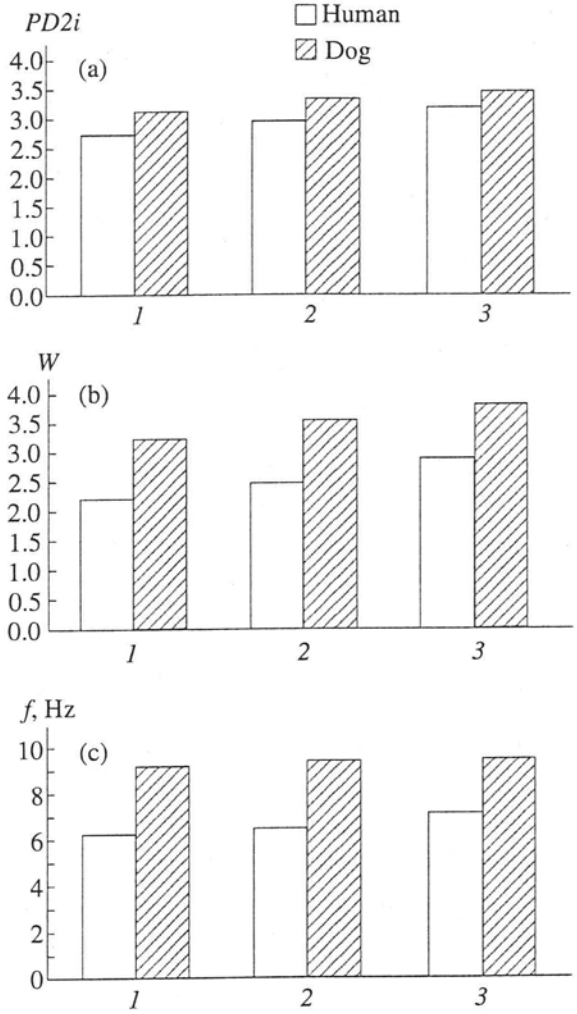

Fig. 4. (a) Pointwise correlation dimension *PD2i*, (b) period-splitting index *W*, and (c) ventricular fibrillation rate *f* (Hz) determined in dogs (hatched bars) and humans (empty bars) that had the same interbeat interval of (*1*) 360, (*2*) 390, and (*3*) 440 ms during sinus rhythm.

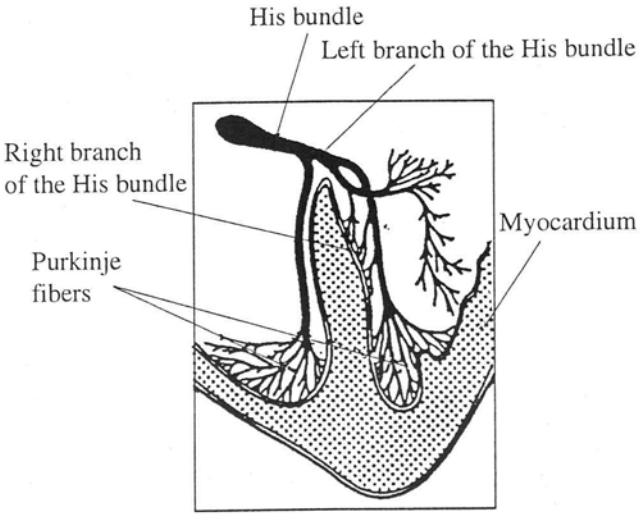

Fig. 5. Fractal geometry of the conduction system of the heart.

frequency shifts in the power spectrum during ventricular fibrillation by the fractal geometry of the conduction system of the heart. By fractal geometry is meant the hierarchic structure of the His–Purkinje system, with its numerous branching points of fiber elements that differ in length and rate of electric impulse conduction (Fig. 5). An impulse arriving at a branching point gives rise to new impulses that propagate at lower hierarchic levels. At each next bifurcation point, the impulse splitting process is repeated. An electric impulse on the heart surface is a superposition of individual impulses $v(t - t(j))$

$$V(t) = \sum_{j=1}^{N} v(t - t(j)). \quad (3)$$

By Goldberger's hypothesis, the normal hierarchic sequence of depolarization events turns to chaotic during ventricular fibrillation; and the parameters of the chaotic dynamics are determined by the particular type of the fractal geometry of the conduction system. The electrophysiological and morphological heterogeneity of animal myocardium [1] is in line with this hypothesis. Our data concerning the degree of disorganization of electric activity of the heart during ventricular fibrillation also indicate that there are considerable differences between species (humans, rats, rabbits, and dogs). Presumably, these differences reflect the species differences in the amount of heterogeneity of myocardium and in the fractal geometry of the conduction system. On the other hand, ventricular fibrillation can be viewed as a series of bifurcations bringing myocardium from the stable state with normal sinus rhythm to an unstable state (ventricular fibrillation), which is a superposition of split-period harmonics [10]. Metaphorically speaking, ventricular fibrillation is a path to chaos going via harmonic oscillations.

REFERENCES

1. Ravelly, F. and Antolini, R., *Biol. Cybern.*, 1992, vol. 67, no. 1, pp. 57–65.
2. Kaplan, D.T. and Cohen, R.J., *Mathematical Approaches to Cardiac Arrhythmias*, N.Y., 1990, pp. 367–374.
3. Kasmacher-Leidinger, H. and Schmid-Schonbein, H., *J. Electrocardiol.*, 1994, vol. 27, no. 4, pp. 287–299.
4. Mezentseva, L.V., Kashtanov, S.I., and Zvyagintseva, M.A., *Biofizika*, 1999, vol. 44, no. 6, pp. 1131–1136.
5. Mezentseva, L.V., Kashtanov, S.I., Zvyagintseva, M.A., Kosharskaya, I.L., and Vostrikov, V.A., *Vestn. Nov. Med. Tekhnol.* (in press).
6. Grassberger, P. and Procaccia, I., *Phys. Rev. Lett.*, 1983, vol. 50, no. 5, pp. 346–349.
7. Farmer, J.D., Ott, E., and Yorke, J.A., *Physica. D*, 1983, 7D, pp. 153–180.
8. Skinner, J.E., Carpeggiani, C., Landisman, C.E., and Fulton, K.W., *Circ. Res.*, 1991, vol. 68, pp. 966–976.
9. Goldberger, A.L., Bhargava, V., West, B.J., and Mandell, A.J., *Biophys. J.*, 1985, vol. 48, pp. 525–528.
10. Smith, J.M. and Cohen, R.J., *Proc. Natl. Acad. Sci. USA*, 1984, vol. 81, no. 1, pp. 233–237.
11. Kobrin, V.I., *Usp. Fiziol. Nauk*, 1993, no. 4, pp. 47–59.