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Application of cross-recurrent analysis to coupling detection in mathematical model of circulation autonomic control

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ABSTRACT

Study aims to adopt the cross-recurrence analysis for detection of coupling between the loops of sympathetic regulation of cardiovascular system. To test the applicability of the method and to set its parameters it was applied to the mathematical model of cardiovascular system that has a structure similar to the structure of the real system. To investigate whether the cross-recurrence analysis reflects the dynamics of autonomic control the authors conducted four numerical experiments with gradually decreasing activity of sympathetic regulation. No correlation was found between the results of cross-recurrence analysis and the coupling strengths.

Keywords: Cross-recurrence analysis, coupling detection, autonomic control, mathematical modeling, cardiovascular system

1. INTRODUCTION

Detection of coupling between the loops of sympathetic regulation of heart rate and vessels tone has practical importance[1-4] for selection of treatment for hypertonic patients and for evaluation of 5-years mortality risk for the patients after the myocardial infarction.

Current approach too detection of coupling is based on the calculation of total percent of phase synchronization that requires to introduce the instantaneous phases for the investigated signals. Since cardiac signals have wide spectra with a number of pronounced spikes the signals are filtered with rather narrow band-pass filter (0.05-0.15). It leads to a loss of the information.

Cross-recurrence analysis is a prominent tool for detection of coupling in biological systems[5-8] and does not involve the phase analysis. To test this approach we applied it to detection of coupling between the RR intervals (RR) and arterial pressure (AP) signals from the model. We chose to investigate the mathematical model[9] of the cardiovascular system (CVS) over the experimental data because real subjects have different sensitivity to the sympathetic blockers, which makes it impossible to achieve a gradual decrease of the sympathetic activity. Another problem is that experiments with sympathetic blockade are risky for the patients and require the presence of the reanimation team.

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2. MATERIALS AND METHODS

The mathematical model

The model reflects the structure of the real sympathetic regulatory loops of CVS and is able to simulate following processes: sympathetic regulation of heart rate, heart contractility and arterial pressure during the cardiac filling phase. The model also simulates the spontaneous intervals of synchronization between the loops of sympathetic control of heart rate and of AP that were reported in[2]. The detailed description of the model is given in[9] and structure is presented in figure 1.

The model was used to simulate three conditions with progressively weaker autonomic control. It was achieved by lowering the coefficients in sympathetic loops by 40 %, 70 %, and 100%, thus establishing the sympathetic blockade.

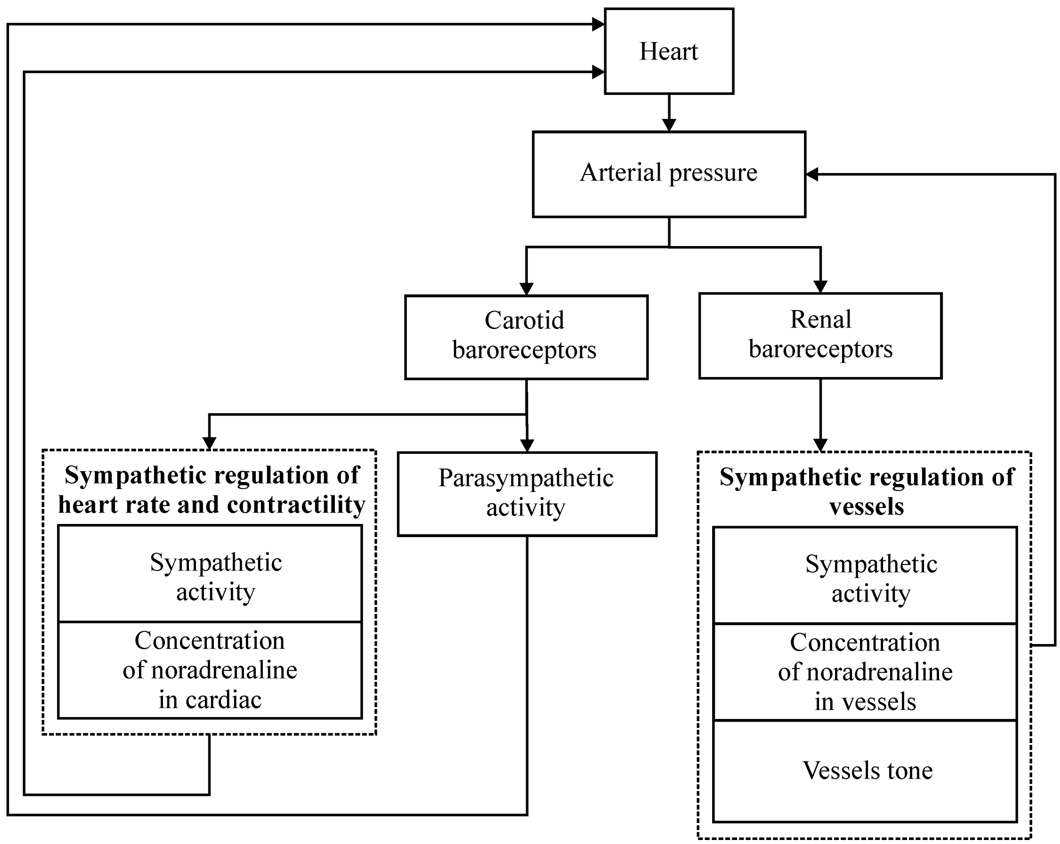

Figure 1. Structure of the mathematical model.

2.1 Cross-recurrence analysis

Cross-recurrence analysis (CRA) is the method of coupling detection based on the analysis of the reconstructed attractors. Taking into account the results from[10] and Takens theorem, we chose the embedding dimension D=13 for the reconstructed attractors of the model RR and AP signals.

We used the delay method to reconstruct the attractor[8]. Time delay was estimated as the absolute maximum of the cross-correlation function. Then we calculated two-dimensional N by N plot, where N is a lengths of the signals in points. Next step is to calculate the distance for each pair of points belonging to the different attractors. We used Euclidian distance.

If the distance between two points, for example RRi and APj, was lesser than set small value ε (0.5 % of the standard deviation), the point on CRA plot with coordinates (i, j) was set to "1". For distant points relevant point on CRA plot was set to 0.

CRA plot is suitable for qualitative analysis of coupling. For quantitative analysis a number of additional indexes needed to be calculated from CRA plot: mean lengths of the diagonal lines (l); maximal length of the diagonal lines (max l); Shannon entropy for the distribution of the diagonal line lengths (E); average lengths of the vertical lines (v); max length of the vertical lines (max v).

2.2 Total percent of phase synchronization

Earlier we introduced the method of coupling detection based on total percent of phase synchronization (*S* index)[2]. The instantaneous phases are calculated for a pair of studied systems using the Hilbert transformation. The instantaneous phases difference is then calculated. The automated algorithm based on linear approximation then detects the horizontal sections on the phase difference. Horizontal sections correspond with the intervals of phase synchronization. A total length of these intervals is calculated, and then its ratio to the overall length of the signals is calculated. Percentage of this ratio is the S index.

3. RESULTS

Table 1 lists the results of application of the CRA and synchronization analysis to detection of coupling in the model. Related CRA plots are represented in figure 2. No assessment of coupling strength could be made from the figure 2. Changes in the patterns and density of points don't seem to correlate with the development of the sympathetic blockade.

From table 1 it is evident that the *S* index decreases with development of the autonomic blockade. This result was expected, since the coupling between loops of sympathetic regulation is strongest when they are fully active and no coupling is possible during the sympathetic blockade. The value of the *S* index doesn't go down to zero, which is likely due to dynamical noises in the model.

Table 1. Results of application of *S* index calculation and cross-recurrence analysis to detection of coupling between the model RR and AP signals.

Index	Full control	60% control	30% control	Blockade
***S* index**	61%	57%	39%	39%
l	0.5	0.5	06	0.5
max *l*	11.0	4.2	10.6	5.4
E	1.2	0.9	1.1	0.9
v	0.6	0.5	0.6	0.6
max *v*	2.4	2.4	2.4	2.6

The results of cross-recurrence analysis don't agree with the dynamics of the *S* index and do not correlate with the gradual decrease in coupling strengths. It is evident that CRA indexes don't reflect the undergoing physiological processes. In regard to parameterization of the method we considered different measures of the distance and different values for ε, but results were not qualitatively different.

The mathematical model qualitatively reproduces the real cardiovascular system. Previous studies also confirmed that model is capable of qualitative simulation of the CVS both in health and disease[9], including the coupling between the loops of sympathetic regulation. These previously obtained results give us the ground to interpolate the simulation data onto the real cardiovascular system.

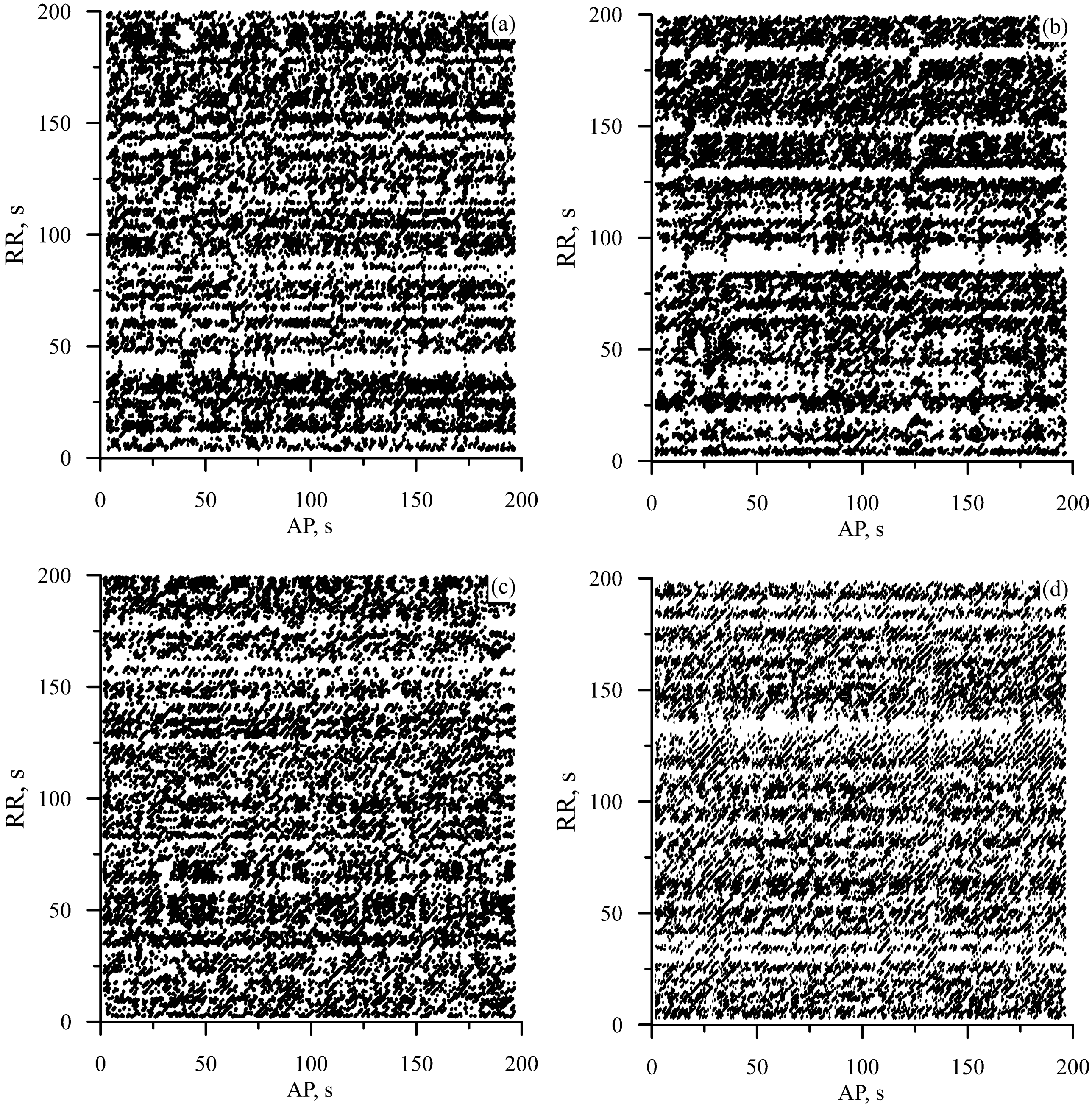

Figure 2. Cross-recurrence plots calculated for the model RR and AP signals during the experiments with fully active sympathetic regulation (a), sympathetic regulation weakened by 40% (b), sympathetic regulation weakened by 60% (c) and under the sympathetic blockade (d).

4. DISCUSSION

Nonlinear dynamics is an important tool both in fundamental studies[11-16] of CVS and medical diagnostics[1-4]. This field is ever advancing and new methods are being applied to the biological data, however, one should be cautious about the interpretations of the results. The biological signals are nonstationary and are subjects to both dynamical and measurement noises. The study of sympathetic regulation is further complicated by the fact that ECG and photopletismographic signals are not direct measurements of sympathetic activity. Proper parameterization is another major problem.

The study aimed to solve the problems of interpretation and parameterization of the cross-recurrence analysis in relation to coupling detection in CVS sympathetic regulation. For this purpose we applied the method to the mathematical model. We chose the model over experimental data because phenylephrine that is used to inflict the state of autonomic blockade has quantitatively different effect on different patients[17]. It not only risky for the subjects but also makes it impossible to decrease the sympathetic activity in gradual steps. Parameters of the sympathetic control also seem to vary among the patients. In[18], it was reported that the synchronization index S can take the values from 30% to 50% in healthy subjects.

The mathematical model has its limitations. We did not intend for it to model any regulatory process with time scales outside of the 0.05-0.5 Hz band. The arterial pressure in the model is a single variable, and hydrodynamics was not considered. Nonetheless, in the previous studies we showed that the model can provide qualitative simulation of the sympathetic coupling in healthy subjects and also the dynamics of the cardiovascular system during the sympathetic blockade[9]. Therefore, we assume that the model is applicable for this study.

5. CONCLUSION

We applied cross-recurrence analysis to the detection of coupling between the loops of sympathetic regulation of cardiovascular system. To set the parameters of the method and to uncover the physiological interpretation of the indexes we applied the method to the signals of the mathematical model. The model was investigated under the conditions of the four-step experiment. Each step was with progressively weaker sympathetic regulation and therefore weaker coupling. Our study showed no correlation between the dynamics of sympathetic control and the indexes obtained from cross-recurrence analysis. Similar results were obtained with wide spectrum of the parameters of the method. Direct application of CRA to the CVS signals and further development of the method is required.

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