Temporal Evolution of Spatial Regularity in Ventricular Fibrillation Modified by Physical Exercise

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Abstract

This study analyses the modifications produced by physical exercise in cardiac mapping recordings during Ventricular Fibrillation (VF), compared to the ones produced by Glibenclamide. Three groups of rabbits were used. G1: control (sedentary rabbits), G2: trained (rabbits submitted to a running program) and G3: drugged (sedentary rabbits treated with Glibenclamide). VF was induced during each experiment, and two recordings were acquired: maintained perfusion and ischemic damage.

The recordings were analysed in consecutive 4-second segments and Regularity Index (RI) was obtained for every segment and lead. RI quantifies the morphological regularity among local activation waves found in a lead. A map with the RI value in each electrode was computed for each segment. In order to analyse the spatial distribution of RI, Regions Of Interest (ROI) were obtained. Two parameters were calculated: ROI spatial number (ROIsn, a measure of spatial fragmentation), and ROI spatial area (ROIsa, the percentage of area map occupied by ROI).

Control group has shown higher values of ROIsn than trained and drugged groups ($p<0.05$) in both conditions (maintained perfusion or ischemic damage). Regarding ROIsa, control group had the lowest values ($p<0.05$) in maintained perfusion, while these differences where less marked with the presence of ischemic damage. On the contrary, no differences were found between drugged and trained groups in any of the analysed parameters.

The performed ROI analysis has shown that physical exercise and Glibenclamide decrease the fragmentation of VF cardiac response, increasing its spatial uniformity.

1. Introduction

Physical exercise modifies the sympathetic-vagal balance of autonomic nervous system, generating an increase in parasympathetic activity which is manifested in a reduction in heart rate [1, 2], and producing an antiarrhythmic effect by increasing vagal activity [3]. Studies on models of sudden cardiac death have shown that treadmill running improves parasympathetic regulation, increasing cardiac rate variability (HRV) and protecting against the occurrence of VF induced by acute myocardial ischemia [4]. Changes have also been reported in the maximum heart rate (HRmax), although the mechanisms that trigger these changes are not fully established [5].

In addition to these changes induced by the autonomic nervous system, regular exercise also produces intrinsic effects. An increase in the action potential duration of ventricular cardiomyocytes has been observed [6]. Studies in isolated rabbit heart during VF show that there are significant differences between groups of trained and untrained subjects in spectral characteristics and regularity of the fibrillatory signal, showing a more stable cardiac response in the trained subjects [7,8].

One of the objectives in the present work is the analysis of temporal evolution in the morphologic regularity of VF signal for physically trained subjects, both under perfusion and ischemia. So that this goal can be achieved, cartographic epicardical recordings are obtained, showing spatial and temporal information about the ventricular activity during the arrhythmia [9]. In addition, from the computed parameters, regions of interest can be defined [10]. Morphologic regularity is obtained from the regularity index [11,12] which measures the fibrillation organization level according to the similarity in the local activation waves morphology.

Regional dispersion in the refractory period is a key factor in VF evolution, especially under myocardic ischemia situations [13]. Some studies reported that Glibenclamide, a drug blocking the K^+_{ATP} channels, reduces ischemia heterogeneity, having a defibrillatory effect [13,14].

The second aim in this work is to evaluate whether the intrinsic changes produced by physical exercise in a fibrillatory response are related to changes in K^+_{ATP} channels. This is done by comparing results between

trained and sedentary subjects being administered Glibenclamide.

2. Methods

2.1. Data

Cardiac VF electrocardiography recordings were obtained at the cardiac electrophysiology laboratories in University of Valencia using a 256 channel commercial mapping system (MAPTECH). The acquisition was done using a matrix electrode consisting of 240 leads located in the left ventricle of isolated rabbit heart perfused by a Langendorff system [7].

Three groups were analysed: control (G1: no training, N=20), trained (G2, N=11) and drug administered (G3, N=15). Physically trained group was formed by rabbits under controlled exercise in a treadmill. Drug administered group subjects were not physically trained and the used drug was Glibenclamide [5]. In all cases, VF was induced by increasing pacing frequencies with a maximum recording time of 300 seconds at a 1kHz sampling frequency.

Two consecutive recordings were made for each of the subjects. This procedure makes a first recording under Langendorff controlled perfusion for 300 seconds and, right after this, a second recording with a ligation in the circumflex coronary artery. This ligation will produce an ischemia in a region inside the cardiac mapping recording and thus, 300 seconds are recorded under this situation. In some cases, fibrillation was spontaneously finished and thus, all results were analysed for the record duration of the shortest VF period.

2.2. Data processing

The calculation method for the regularity index and regions of interest is detailed in [8]. As a summary, the steps are the following:

- Segmentation: records were processed in 4-second consecutive segments so that the temporal evolution can be studied.
- Pre-processing: the signal quality is checked for each segment, discarding low amplitude or noisy channels.
- RI calculation: RI value is obtained for each segment and channel according to the algorithm proposed in [11,12] but modified to fit the electrophysiological characteristics of this study [8].
- Regions of interest: RI maps are obtained for each of the segments in a record. A threshold was applied to the RI value in each channel and then, mapping electrodes are assigned to a ROI according to vicinity criteria for those above the threshold [8]
- Spatial distribution measures. Two parameters were calculated: 1) The number of ROI for each map (ROIsn) related to the fragmentation in a distribution, and 2) percentage of area occupied by a ROI compared to the total map area (ROIsa) which is related to the distribution homogeneity.
- In order to analyse the statistical significance of temporal variation parameters in all of the three groups, the permutation test was used [15].

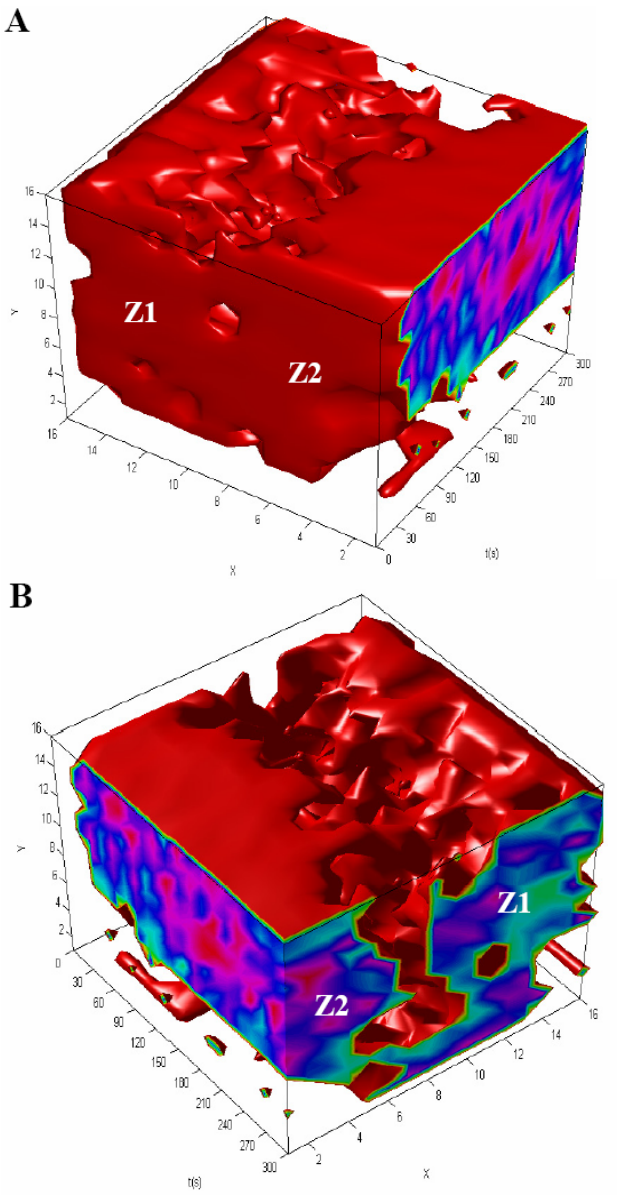

Figure 1. ROI evolution as a function of time under ischemia conditions. A: View starting at the beginning of recording time (t=0). B: View at the end of the record (t=300).

Figure 1 shows the evolution of ROI corresponding to the RI maps for each temporal segment. Two areas can be clearly appreciated, a perfused area (Z2) and an ischemic area (Z1). In early ischemic stages (A), a single ROI is occupying a high percentage in the map. However, the ROI percentage occupation decreases in time and they are also more fragmented (a high number of areas appears).

3. Results

Figure 2 shows the results for the ROI number in each of the groups (ROIsn). Under perfusion, the control group provides the higher significant number of ROI ($p<0.05$), showing higher fragmentation than other groups. For the trained and drugged groups, the behaviour is similar and no significant differences are found. Under ischemia, the control group shows similar behaviour than in the previous analysis but the trained group shows higher values than the drugged group.

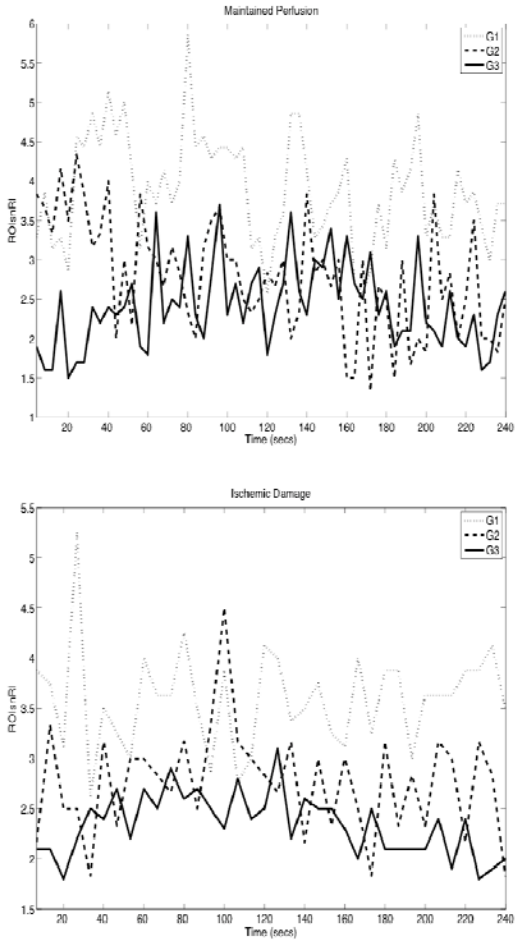

Figure 2. Temporal variation in the ROI number (ROIsn) for perfusion and ischemia conditions. G1: control group; G2: trained group; G3: drugged group.

Concerning ROIsa (figure 3), the control group shows lower percentages compared to the rest of groups, showing lower homogeneity in the spatial distribution of RI. The trained group shows higher values than the drugged group during perfusion, and lower values during ischemia but no significant differences are appreciated.

4. Conclusions

In this work, modifications in the spatial regularity of ventricular fibrillation under perfusion and ischemia, induced by regular physical exercise were studied. In addition, this work analysed if those modifications are related to changes in K^{+}_{ATP} channels by comparing results for physically trained subjects and sedentary subject with Glibenclamide drug administered.

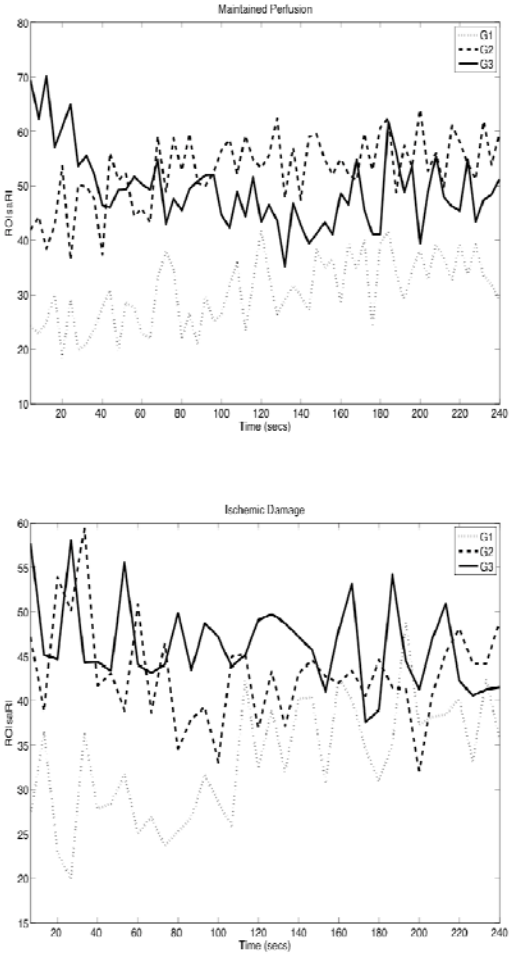

Figure 3. Temporal variation in the percentage of area occupied by ROI (ROIsa) under perfusion and ischemia. G1: control group; G2: trained group; G3: drugged group.

The performed ROI analysis of RI maps has shown that physical exercise and Glibenclamide decrease the

fragmentation of VF cardiac response, increasing its spatial uniformity. These results are obtained both under perfusion and ischemia.

Despite no significant differences are found, the behaviour of the trained group and the drugged group is more different in ischemia. This fact can be an indication that the involved mechanisms are not the same in both cases. A limitation in this study corresponds to the globally maps analysis done during ischemia since no distinction is made between the ischemic area and that being perfused after the artery ligation. A detailed study of sub-areas would probably increase the differences.

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