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# *Heart rate variability analysis (HRV) under the influence of atropine and propranolol*

Analiza zmienności rytmu serca (HRV) pod wpływem atropiny i propranololu

## INTRODUCTION

Functional reserve sufficiency which is activated under the influence of the correspondent factor provides the necessary level of the organism functioning. As a result of the decline of functional reserve and adaptation possibilities, the organism passes sequentially from satisfactory adaptation to the state of tension of adaptation mechanisms then to unsatisfactory adaptation [1,3,5].

Sensitiveness and reactivity of the autonomous nervous system, its sympathetic and parasympathetic parts can serve as diagnostic and prognostic criteria under the testing factor [1-3,5]. It is the functional loading caused by introduction of the blocker of the cardiac rhythm autonomous control that allows testing the correspondent link of the physiology function of the control system. We have chosen the introduction of atropine and propranolol in different doses as a functional loading during the HRV research.

## MATERIAL AND METHODS

Tests were carried on outbred not narcotized white male rats weighing 180–220 gm (n = 70, 7 rats per group). Animals were kept under ordinary conditions of vivarium with standard ration without any restrictions in food and water. The recording of cardiointervalgram was conducted during the period of 5 min., not invasively, using the photoplethysmographic transformer fixed near the base of the tail and connected to the fast-acting recording device. For that purpose the rats had been immobilized in a universal plexiglass chamber, the form of which fitted the organization of the body. The chamber was covered with a dark dense velvet fabric to avoid unnecessary irritants. That also answered to the "burrow reflex" inherent to the species (the innate propensity to the limited black-out space). The monitoring of the cardiac cycle duration of not narcotized rats was conducted by means of the method introduced by us (Patent of Ukraine № 80520, A61V5/024. The method of non-invasive

identification of the cardiac cycle duration of not narcotized rats M.R. Gzhegotsky, E.V. Storchun, L.V. Panina, O.I. Terletska, S.M. Koval'chuk, R.V.Kmit' (UA) – № a200702659; It is declared on March 13, 2007; published on September 25, 2007. – Bulletin № 15). We carry out the HRV analysis by means of the method introduced by us (Patent of Ukraine № 29596, A61V5/0205, A61V5/024. The functional state estimation method of the experimental animals on the basis of analysis of the heart rate variability M.R. Gzhegotsky, E.V. Storchun, L.V. Panina, S.M. Koval'chuk, O.V. Kless, O.I. Terletska, Yu.S. Petryshyn, O.G. Mysakovets (UA) – № u200702660. It was declared on March 13, 2007; published on January 25, 2008. – Bulletin № 2).

The statistical parameters of the cardio intervals dynamic row were analyzed: Successive Deviation of NN-intervals (SDNN); the square root of sum of differences of successive row of cardio intervals (Root Mean Sum Successive Deviation, RMSSD); the coefficient of variation (CV). The parameters of variation pulsometry are the following: MxDMn, difference between the maximum (Mx) and minimum (Mn) values of the cardio intervals; the mode (Mo); the amplitude of mode (Amo); the stress index (SI) or index of tension of the regulation systems. Using the spectral analysis we characterized such parameters as the total power (TP); the index of centralization (IC). In order to recreate the results received during the tests conducted on the white rats correctly, the HRV analysis was carried out within the following ranges: Low Frequency, LF (0.015 – 0.25) Hz, Mid Frequency, MF (0.25 – 0.75) Hz, High Frequency, HF (0.75 – 3.0) Hz.

The introduction of atropine (blocker of M-cholinergic receptors) was carried out with 0.4 mg/kg dose subcutaneously and 2 mg/kg dose intravenously. Propranolol (blocker of ß-adrenergic receptor) was introduced with the doses of 2 mg/kg intraperitoneally and 5 mg/kg intravenously. The control introduction of NaCl was carried out, and the way of introduction and the solution volume (not exceeding 0.5 ml) was the same as during the introduction of atropine and propranolol. The analysis of the HRV indexes after the injections of NaCl, conducted in a number of different ways, found out their difference (Fig. 1). In the sequel, increasing the dosage of the medicine stipulated the choice of the intravenous way of introduction. The recording of the cardiointervalgram was conducted before the introduction of the correspondent medicine (initial level) and 30 min after it.

The paired comparison of the means was conducted according to Student t-criterion. The differences were considered to be reliable at the significance level $P < 0.05$.

## RESULTS

We registered the growth of the Heart Rate (HR) as a result of atropine introduction in two doses; after the introduction of propranolol in two doses we observed a decline of the HR (Fig. 1). In addition, the use of the blockers mentioned above was accompanied by the opposite changes of such statistical parameters as SDNN, RMSSD, CV (Fig. 1). During atropine and propranolol introduction the growth of the stress-index (SI) appeared to be significant, accordingly with the increase of the doses, comparing with the control introduction. Moreover, AMo grew and Mo declined after the introduction of atropine. With a higher activation of SI and AMo, a decline of the Mo during the blockade of the parasympathetic influence on the cardiac rhythm can confirm the increase of the sympathetic level tone of regulatory mechanisms and can indicate the tension of adaptation.

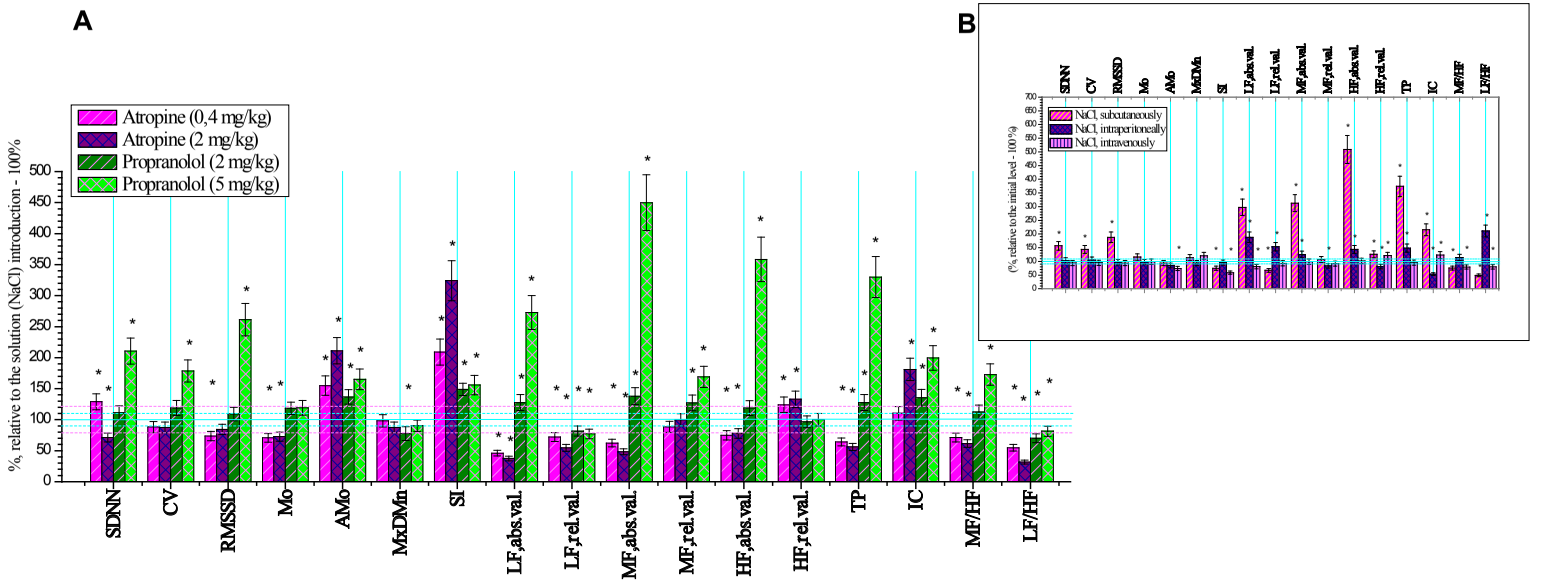


Fig. 1. HRV under the introduction of atropine and propranolol, relative to the solution (NaCl) introduction – 100%; *P < 0.05, compared with solution introduction (A); HRV under the solution introduction, relative to the initial level – 100%; *P < 0.05, compared with initial level (B)

The character of spectral fluctuations also changed in response to the introduction of blockers. In particular, during the use of atropine with the increase of doses, the diminishing of TP could be observed and certain diminishing of absolute values of all its constituents was revealed: HF, MF and LF, in comparison with the control introduction. During the introduction of propranolol we observed an increase of TP, in comparison with the control introduction. It is significant that the increase of TP took place due to the activating of all its constituents (Fig. 1). Interesting changes of the index of centralization (IC) were revealed, namely, a correlation between the autonomous and central contours of the cardiac rhythm regulation. While introducing atropine in a lower dose no possible changes were revealed; however, the increase of the dose of atropine and the introduction of propranolol in two doses resulted in its growth. This index allows to judge the activity of the subcortical cardiovascular center related to activity of higher levels of regulation functions [1].

## DISCUSSION

It is the functional loading caused by introduction of the blocker of the cardiac rhythm autonomous control that allows testing the correspondent link of the physiology function control system. On the basis of the statistical analysis, the measure of vegetative balance shift towards predominance of the sympathetic regulation is analyzed while taking into consideration the diminishing of RMSSD and SDNN indexes [1]. The more stable the rhythm is, the less difference is there between the cardio intervals and the lower RMSSD value. On the contrary, the growth of this index points to the increase of the parasympathetic system activity. During atropine introduction, we observe a decline of this index. On the other hand, propranolol introduction was characterized by the RMSSD increase (Fig. 1).

At this time, it is possible to assess the introduction of separate regulation levels during the adaptation process under the cardiac rhythm spectral constituents' changes [1, 3]. It is significant for the prenosological diagnostics, during the analysis of the regulator systems tension states and their differentiation from overstrain and exhaustion. As it is known, at the initial stages there is activation of the operative regulation mechanisms which later results in the introduction of higher levels of functions regulations into the adaptation process [1]. A possibility of the specific mechanism research which is provided by the functional reserve mobilization on the basis of the HRV analysis is of great importance.

Hence, the integrative index of total spectrum power (TP) is considered to be the absolute level of the regulator system activity [1, 3]. Within the HF fluctuations range the cardio interval periodicity prevails, which is connected with breathing [1, 2, 3, 5]. Afferent inflow changes of the vagi, which play a basic role in the respiratory cycle duration, are significant in the HF genesis. At the same time, as it is known, respiratory periodicity of the cardio rhythm is not only connected with the changes in the parasympathetic part of the autonomous nervous system, but partly depends on the sympathetic activity [1, 3]. MF power is characterized mainly by the sympathetic modulating influence on the cardiovascular system. However, there are data according to which spectral fluctuations within this range are connected with the activity level of both sympathetic and parasympathetic nervous systems [1-3]. Introduction of both links of the autonomous cardiac rhythm regulation into power forming of the HF and MF ranges is confirmed by our research (Fig. 1). The LF changes are connected

with the activity level of the vasomotor center, with the baroreflex sensitiveness, hormonal regulator influences and also with the sensitiveness of the chemoreflex link [1-4]. Within this range we could observe a decline of fluctuations only after atropine introduction.

On the basis of the spectral analysis, sympathetic nervous system activity can be assessed by a degree of the autonomous regulation contour inhibition for which the parasympathetic system is responsible. It is considered that the index of the respiratory waves power (HF) of the cardiac rhythm is sensitive to such changes [1, 3]. During the research we revealed not only the HF decline but also a decline of other spectral constituents in response to atropine introduction (Fig. 1). The correlation between the autonomous and central regulation contours of the cardiac rhythm is represented by the index of centralization (IC) which is calculated on the basis of spectral analysis data [1]. It is noteworthy that according to our research this index was growing with the increase of atropine and propranolol doses.

It is known that the regulator systems are able to mobilize necessary functional reserves that allow preserving the homeostasis and supporting a satisfactory state of adaptation [1]. The features marked by us favour understanding the nature of spectral fluctuations within the investigated ranges, and also favour confirming the important role of the trophotropic mechanisms in the formation of the adaptation potential and in providing great possibilities for the renewable processes, directed on homeostasis preservation. The introduction of the heart work autonomous control blockers can be recommended as the informing criterion of the homeostasis assessment of the autonomous nervous system.

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## SUMMARY

Sensitiveness and reactivity of the autonomous nervous system, its sympathetic and parasympathetic parts, can serve as diagnostic and prognostic criteria under the testing factor. It is the functional loading caused by introduction of the blocker of the cardiac rhythm autonomous control that allows testing the correspondent link of the physiology function control system. We have chosen the introduction of atropine and propranolol in different doses as a functional loading during the

HRV research. The use of the blockers was accompanied by the opposite changes of such statistical parameters, as SDNN, RMSSD, CV. The character of spectral fluctuations also in a contrary manner changed in response to the introduction of blockers.

*Keywords*: heart rate variability, atropine, propranolol, white rats

## STRESZCZENIE

Ocena czułości i reaktywności autonomicznego systemu nerwowego w jego części sympatycznej i parasympatycznej może służyć jako kryterium diagnostyczne i prognostyczne w warunkach prowadzonych testów. Jest to funkcjonalne obciążenie spowodowane przez wprowadzenie blokera autonomicznej kontroli rytmu serca, pozwalające badać odpowiednie fizjologiczne funkcje systemu kontrolnego. W badaniach HRV jako obciążenie funkcjonalne zastosowano różne dawki atropiny i propranololu. Zastosowaniu brokerów towarzyszyły przeciwne zmiany takich parametrów statystycznych, jak SDNN, RMSSD, CV. Charakter wahań spektralnych również zmieniał się przeciwstawnie w odpowiedzi na podanie brokerów.

*Słowa kluczowe:* zmienność rytmu serca, atropina, propranolol, białe szczury