

## PHYSIOLOGY

### CORRELATION BETWEEN ATRIAL AND VENTRICULAR CONTRACTILITY

#### A POSSIBLE USE OF THE ATRIA TO CONTROL THE ARTIFICIAL HEART

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The possibility of using the atrial myocardium to control artificial ventricles is examined. Correlation was studied between the tension of the atrial wall and the tension and pressure in the ventricles during random variation of the cardiac rhythm was studied. Tension in the wall of the corresponding part of the heart was recorded by means of arch strain gauges and the intraventricular pressure by means of an electromanometer during catheterization of the chambers of the ventricles. The cardiac rhythm varied from 2.0 to 4.0 sec<sup>-1</sup>. Correlation was demonstrated in the atria between the tension and interspike interval (coefficient of correlation  $0.62 \pm 0.05$ ). Close correlation was detected between tension in the atrial wall and the intraventricular pressure. The coefficient of correlation in this case varied from  $0.713 \pm 0.09$  to  $0.874 \pm 0.02$  depending on the mean duration of the interspike interval. Information on atrial contractions can be used to control an artificial heart.

KEY WORDS: control of the artificial heart; cardiac rhythm; isometric atrial contraction; intraventricular pressure; rhythmic-ionotropic correlation.

An important problem during the creation of an artificial heart is that of its control. Adequate control of the cardiac frequency is its principal aspect. Generally, it is necessary to regulate not only the heart rate but also the cardiac output, the rate of rise of pressure, and other parameters of mechanical activity of the artificial heart. It is natural to use the surviving atria, which preserve their innervation and their sensitivity to humoral agents [5] to control the artificial ventricles. For this purpose various types of mechanical tension or deformation formed in the atrium, on the basis of which the control system carries out regulation of the activity of the artificial ventricle, can be used for this purpose. Such a system must have definite advantages over control systems based on the original information of the state of the internal milieu ( $pO_2$ ,  $pCO_2$ , pH, etc.), for closer correlations are used between activity of the atria and ventricles.

To put this proposed approach into effect, the first step must be to ensure that correlation exists between the contractile activity of the atria and ventricles during normal functioning of the heart, at different values of the heart rate or in the presence of a randomly varying rhythm. Preference was awarded to the "random regime" for it corresponds to a greater degree to the natural conditions of function [1, 2].

#### EXPERIMENTAL METHOD

Experiments were carried out on mongrel dogs of both sexes weighing 5-8 g on which thoracotomy had been performed under thiopental anesthesia and the heart, free from pericardium, was exteriorized into the wound. Tension in the wall of the atria and ventricles was recorded by means of arch strain gauges, sutured to the corresponding regions. The rigidity of construction was 20 g/mm, ensuring a sufficiently close approximation to isometric conditions. The intraventricular pressure was recorded by an electromanometric system

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TABLE 1. Mean Values of Coefficients of Correlation ( $\bar{R}$ ) and Dispersion ( $\eta$ ) Functions (with errors of means) of "Interspike Interval-Tension" and Characteristics of Nonlinearity  $n$  and  $y$  at Different Mean Values of Interspike Intervals ( $T$ ) in Left (A) and Right (B) Hemispheres

	$\bar{T}, \text{msec}$	$\tau$	-1	0	+1
A	$350 \pm 20$	$\bar{R}$	$0,113 \pm 0,05$	$0,620 \pm 0,05$	$-0,257 \pm 0,07$
		$\eta$	$0,239 \pm 0,04$	$0,675 \pm 0,05$	$0,330 \pm 0,07$
		$n$	$0,21$	$0,22$	$0,21$
	$270 \pm 15$	$y$	$0,18$	$0,10$	$0,4$
		$\bar{R}$	$0,260 \pm 0,02$	$0,608 \pm 0,04$	$-0,266 \pm 0,01$
		$\eta$	$0,301 \pm 0,06$	$0,638 \pm 0,02$	$0,337 \pm 0,01$
B	$350 \pm 20$	$n$	$0,2$	$0,19$	$0,21$
		$y$	$0,25$	$0,09$	$0,4$
	$270 \pm 15$	$\bar{R}$	$0,100 \pm 0,05$	$0,699 \pm 0,02$	$-0,395 \pm 0,05$
		$\eta$	$0,265 \pm 0,05$	$0,731 \pm 0,03$	$0,462 \pm 0,06$
		$n$	$0,3$	$0,21$	$0,24$
		$y$	$0,37$	$0,09$	$0,27$

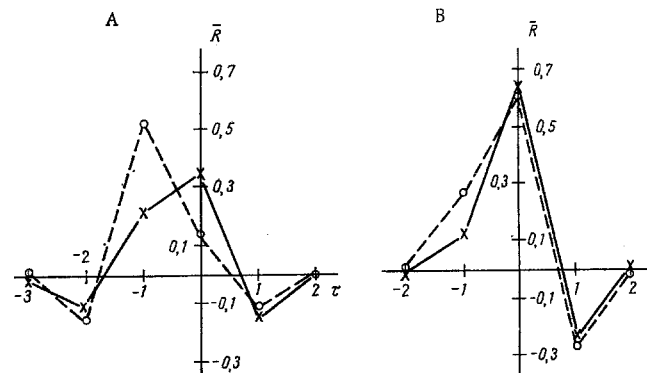


Fig. 1. Average correlation function between interspike interval and tension in left ventricle (A) and left atrium (B). Ordinate, coefficient of correlation ( $\bar{R}$ ); abscissa, No. of shift ( $\tau$ ). Crosses indicate mean interspike interval 350 msec; circles indicate mean interspike interval of 270 msec.

for cardiac catheterization. Electrical stimulation was applied in the form of square pulses (5 V, 5 msec). The electrodes were located on the right ventricle. A specially designed stimulator, providing both a constant rhythm and a random sequence of pulses (a gaussian stochastic process with autocorrelation coefficient at the first shift of not more than 0.07) with coefficient of variation (var  $T$ ) regulatable between 4 and 22%. The frequency range used was 2.0, 3.0, and 4.0  $\text{sec}^{-1}$ . After the first processing the experimental results were calculated on the BÉSM-4 computer. The mean values, dispersion, coefficient of variation, and cross-correlation functions between series were calculated. To determine the class of the system and the possibility of using correlation analysis in order to study the relationship between the variables, a test for nonlinearity was used [3]. This test was carried out by means of dispersion functions, which are characteristics of correlation between processes in the case of nonlinear functions [6]. The value of correlation ( $R$ ) and dispersion ( $\eta$ ) functions coincide only in the case of a stochastic process of linear structures [4]. The value of  $\eta$  was calculated by the equations:

$$\eta_{xy}(\tau) = \sqrt{\frac{\theta_{xy}(\tau)}{D(y)}}, \quad (1)$$

$$\eta_{yx}(\tau) = \sqrt{\frac{\theta_{yx}(\tau)}{D(x)}}, \quad (2)$$

where  $\eta(\tau)$  is the dispersion function,  $\eta(0)$  and  $\eta(+1)$  are the values of the dispersion functions during shifts 0 and 1 to the right, respectively;  $\tau$  is the shift;  $\theta(\tau) = D M(x/y_1)$  is the dispersion of arbitrary mathematical expectations;  $D(x)$ ,  $D(y)$  represent dispersion of random functions of  $x$  and  $y$ .

The nonlinearity  $n(\tau)$  and the relative nonlinearity  $y(\tau)$  were determined by equations:

$$n(\tau) = \sqrt{\eta^2(\tau) - R^2(\tau)}, \quad (3)$$

$$y(\tau) = \frac{\eta^2(\tau) - R^2(\tau)}{\eta^2(\tau)}, \quad (4)$$

where  $R(\tau)$  is the correlation function;  $R(0)$ ,  $R(+1)$ , and  $R(+2)$  are the coefficients of correlation at shifts 0, 1, and 2 to the right, respectively.

## EXPERIMENTAL RESULTS AND DISCUSSION

Coefficients of cross-correlation functions "interspike interval-tension in wall" in the right and left atria at various mean values of interspike intervals are shown in Table 1. It will be clear that coefficients of correlation at shift 0 in the left atrium are practically independent of the mean duration of the interspike intervals. Coefficients of correlation likewise were not found to apply to the coefficient of rhythm variation. In both the right and the left atria coefficients of correlation practically coincided with the corresponding values of the coefficients of the dispersion functions, and low values of  $n(\tau)$  and  $y(\tau)$  are evidence that the system can be classed as a good approximation to the class of linear dynamic systems. Whereas the coefficient of correlation at zero shift  $R(0)$  makes a contribution to rhythmic ionotropic correlation, and the degree of filling of the chambers of the heart, the coefficient  $R(+1)$  is a product of rhythmic ionotropic relations only. Its negative values mean that high amplitude of the subsequent contraction corresponds to a shorter value of the interspike interval. It may be emphasized that, although "tension-interspike interval" correlation function in the atria and ventricles at frequencies of stimulation of not more than  $3.0 \text{ sec}^{-1}$  are similar in shape, other conditions being the same,  $R(0)$  and  $R(+1)$  are significantly greater in absolute magnitude than in the ventricles (Fig. 1). This probably indicates that the atria possess stronger rhythmic-ionotropic relations than the ventricles.

Investigations of correlation between isometric contractions of the atria and ventricles showed such correlation to be close;  $\bar{R}(0) = 0.92 \pm 0.03$ . Good correlation also was found between tension in the wall of the atria and the intraventricular pressure of the corresponding half of the heart (Fig. 2). Characteristically correlation  $\bar{R}(0)$  between atrium and ventricle was higher for the right heart than for the left. The "atrial tension-interventricular pressure" correlation function for the right heart differed only a little from the dispersion function:  $R(0) = 0.713 \pm 0.09$ ,  $\eta(0) = 0.745 \pm 0.07$ ;  $\bar{R}(+1) = |0.288 \pm 0.3|$ ,  $\eta(+1) = 0.322 \pm 0.05$  for a mean frequency of  $3.0 \text{ sec}^{-1}$  and  $\bar{R}(0) = 0.874 \pm 0.02$ ,  $\eta(0) = 0.878 \pm 0.04$ ;  $\bar{R}(+1) = |0.30 \pm 0.03|$ ,  $\eta(+1) = 0.36 \pm 0.07$  for a mean

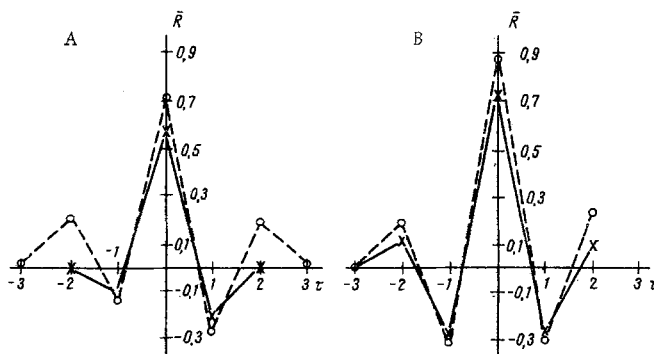


Fig. 2. Correlation functions of tension in atrial wall versus intraventricular pressure. A) Left heart, B) right. Mean values of coefficient of correlation ( $\bar{R}$ ) plotted along ordinate, Nos. of shift ( $\tau$ ) along abscissa. Crosses mark mean interspike interval of 340 msec; circles mean interspike interval of 270 msec.

frequency of  $4.0 \text{ sec}^{-1}$ . A closely similar picture was observed in the left heart, although the nonlinearity of correlation in this case was rather higher ( $y=0.16$ ) than in the right heart ( $y=0.09-0.11$ ).

It can be concluded from the results given above that close correlation between contractility of the atria (as reflected in tension) and the hemodynamic activity of the ventricles (according to the maximal value of pressure developed) over a wide range of variations of interspike intervals is the basis for construction of the control loop for the artificial heart on the basis of information on atrial contraction.

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#### CHANGES IN AMPHETAMINE STEREOTYPY IN CATS AFTER ELECTRICAL STIMULATION OF THE CAUDATE NUCLEUS

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Two types of behavioral changes arise in cats after repetitive low-frequency stimulation of the head of the caudate nucleus in cats. Behavioral inhibition is more frequently triggered from the dorsomedial zone of the head, whereas activation phenomena precede depression during stimulation of the ventrolateral zone. The assortment and pattern of stereotyped movements following injection of the minimal effective dose of amphetamine vary in different ways against the background of these changes. After stimulation of the dorsomedial zones of the nucleus stereotypy is first disorganized and then weakened, whereas caudate activation is associated with strengthening of stereotypy.

**KEY WORDS:** amphetamine stereotypy; caudate nucleus; late behavioral changes

An important place in the organization of amphetamine stereotypy of behavior, used as an experimental model in psychopathology, is ascribed to functional insufficiency of the caudate nucleus [1]. One of the neurophysiological facts confirming the validity of this opinion is the sudden abolition of stereotyped movements on electrical stimulation of that structure [4]. However, it is claimed that the stable behavioral changes which persist for a long time after the end of stimulation are much closer to the indices of natural brain function than the phasic responses arising actually during stimulation [6].

It was therefore decided to study the effect of delayed caudate phenomena on the manifestation of stereotypy.

#### EXPERIMENTAL METHOD

Ten cats of both sexes, weighing 2.2-3.4 kg, took part in 74 experiments. In the preliminary stage under pentobarbital anesthesia bipolar stimulating electrodes were inserted into different parts of the caudate nucleus and adjacent brain structures. In two animals steel needles also were inserted into various parts of the cortex

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