Chronodromotropic Coordination in Cats

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The coordinated nervous influences on HR and atrioventricular conduction velocity (chronodromotropic coordination) were examined in wakeful cats. The wave structure and reflex reactions of *RR* and atrioventricular (AV) intervals to stress noise stimulation were studied under normal conditions and during the action of blockers of peripheral receptors in ANS. Variations of both intervals had similar wave structure (power spectrum) and similar reactions to noise stimulus. Atropine pronouncedly decreased all components of the spectra in the high, low, and very low frequency ranges. It eliminated the reactions of both intervals to noise stimulation. In *RR* intervals, the high-frequency spectrum component decreased more strongly than the low-frequency ones. By contrast, in AV intervals atropine most greatly decreased the very-low-spectrum component, while the high frequency was decreased less of all. Propranolol produced no effect on the response to noise. It did not decrease components of the wave structure in both intervals, except for the very-low-frequency peak of AV interval. The nervous chronotropic and dromotropic influences were largely coordinated, although they were not obligatorily parallel.

Key Words: *chronotropic influences; dromotropic influences; spectrum analysis*

Ample data are accumulated on the spectrum analysis and mechanisms of heart rate variation (respiratory and low-frequency waves). In dogs, regular oscillations of the atrioventricular (AV) interval were described together with waves corresponding to the respiratory rate and slow oscillations of blood pressure [11]. However, the spectrum analysis of these oscillations was not carried out. The wave structure of AV interval oscillations were examined only in few papers [6-8,10]. The nature of these oscillations was not studied in details, and the corresponding data on animals are absent. However, the wave structure of AV interval oscillations and its relevance to *RR* interval oscillations can be an important characteristic of the state of AV node, the dromotropic nervous influences, and chromodromotropic coordination reflecting fine mechanisms of nervous control of the heart.

Our aim was to describe the wave structure of AV interval oscillations in cats, to reveal its relationships to heart rate variations, and to study the role of adrenergic and cholinergic influences in the development of various elements of this oscillation pattern.

MATERIALS AND METHODS

The experiments (n=59) were carried out on mature male and female cats (n=17). The cats were places in a screened chamber, where they can freely change the posture. Two rubber strips were placed on the thorax. Each strip had two steel electrodes, which made the electrical contacts with the skin. ECG was recorded by 3 standard or 3 amplified leads. The first derivative of ECG lead with most pronounced peaks was also recorded. The signals were fed to an ECG-module of a P4Ch-02 Polygraph, 12-bit

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8-channel ADC, and PC. In all channels, the sampling time was 1 kHz. The length of a single record was 2 min. AV interval was measured as the distance between the reference points in *P* wave and *QRS*-complex. In each experiment, these points were chosen individually depending on peculiarities of the leads. For *P* wave, the reference points could correspond to its onset, maximum, end, or the maximum (minimum) of the first derivative. For *QRS*-complex, the reference points corresponded to *Q* or *R* waves, or to maximum (minimum) of the first derivative. Preliminary experiments revealed a strong correlation between the values of AV interval calculated with various reference points, so the spectrum of its oscillations did not depend on the choice of these points.

In some experiments, a short-term stress noise (a violent knock at the metal sheet) was applied, which provoked a pronounced vociferation and motor reaction. Atropine sulfate (0.5 and 1.0 mg/kg subcutaneously) and β-adrenoblocker propranolol (0.5 mg/kg intramuscularly) was used to block the parasympathetic and sympathetic influences, respectively.

Initial ECG was recorded every 10 min over 1 h; in some experiments, this period was 4 h (for evaluation of adaptation to the experimental conditions). After stabilization of the heart rate, the drug was injected at rest, thereafter ECG was recorded every 10 min over 1 h. Only one drug was injected in each experiment. The stimulating noise was presented immediately before and 20-50 min after injection of the test drug. In all animals, the intervals between the experiments were no less than 3 days needed to eliminate the drugs completely [4,5].

The data were analyzed statistically using Statistica software. Significance of differences was assessed by Student's *t* test and Pearson correlation coefficient. The spectrum analysis was performed using fast Fourier transform and 5-point Hemming window with preliminary subtraction of the mean level and elimination of the trend. The power spectrum was analyzed in the high-frequency (HF), low-frequency (LF), and the very-low-frequency (VLF) bands. According to *QRS*-amplitude analysis [3], the HF band (0.22-1.20 Hz) corresponded to the respiratory rhythm. It coincided with the pneumograms recorded in some experiments. The frequencies of LF and VLF bands were 0.04-0.22 and <0.04 Hz, respectively [9]. The spectrum power density was calculated in each band. In addition, the relative power of HF, LF, and VLF bands was calculated as percent of the total power of oscillations.

RESULTS

There was a strong correlation between *RR* and AV intervals (r=0.61). These values changed in a synchronous manner. This was true for regular wave-like oscillations and for spontaneous variations of *RR* and AV intervals, which accompanied vociferation, swallowing, and motor reactions (Figs. 1, *a*; 2, *a*). The cross-correlation function between *RR* and AV intervals showed that they oscillated strictly in the same phase (Figs. 1, *d*; 2, *d*). This suggests that variations of AV intervals have a neurogenic nature and are not determined by myogenic chromodromotropic dependence underlying the inverse proportionality of AV interval to the period of the heart beats (if the latter was true, both intervals would oscillate in antiphase). In all cases (n=16), the noise stimulation provoked a step-wise drop of both intervals followed by their slow restoration (Fig. 3, *a*, *b*).

The examined pharmacological preparations produced similar changes in the wave structure of *RR* and AV intervals (Table 1). Atropine markedly decreased all wave components of *RR* interval: HF, LF, and VLF decreased to 6.4, 9.6, and 21.2%, respectively (Fig. 1). The wave components of AV interval also decreased. The greater decrease was documented for VLF band (to 38.2%) while the smallest decrease was observed for HF band (to 49.8%). LF peak decreased to 46.6%. The less pronounced effect of atropine on rapid oscillations of AV interval (HF_{AV}) in comparison with those of *RR* interval (HF_{RR}) can be explained by the fact that the value of HF_{AV} is affected by the casual deviations of the reference point in *P* wave (inadvertent error in the recording of surface ECG), which does not depend on the action of pharmacological agents

TABLE 1. Effect of Atropine and Propranolol on Wave Structure of *RR* and AV intervals

Drug	VLF		LF		HF	
	RR	AV interval	*RR*	AV interval	*RR*	AV interval
Atropine	21.2±13.9	38.2±16.1	9.6±5.6	46.6±11.7	6.4±8.4	49.8±27.6
Propranolol	106.2±28.0	88.9±18.2	100.2±21.3	97.3±25.1	117.4±37.6	108.3±32.3

Note. The values are given in percentage of the baseline values (M±m).

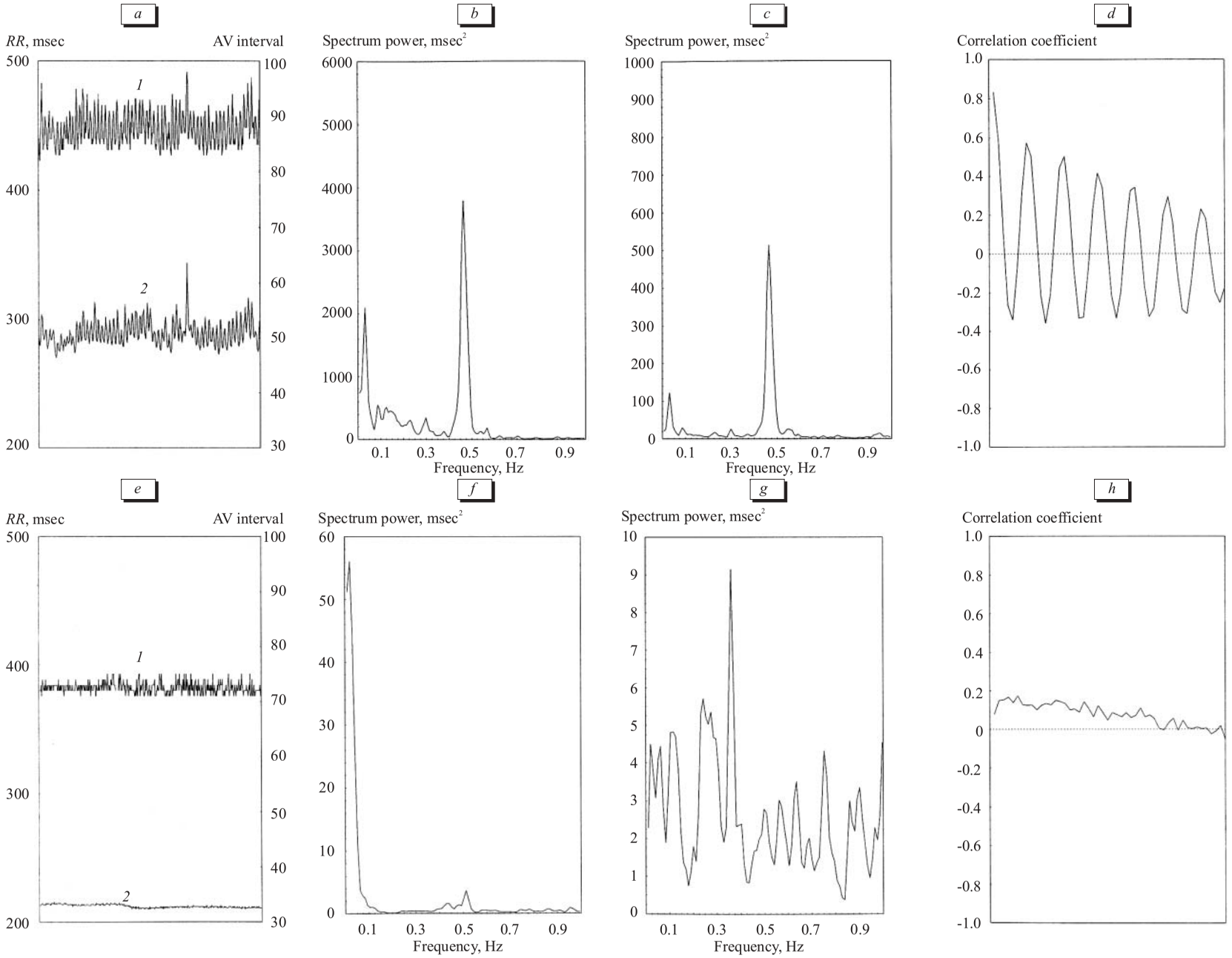

Fig. 1. Effect of atropine on oscillations of AV interval (*1*) and *RR* interval (*2*). *a-d*) before atropine; *e-h*) during the action of atropine. *a*, *e* — cardiointervalograms; *b*, *f* — power spectrum of *RR* interval; *c*, *g* — power spectrum of AV interval; *d*, *h* — cross-correlation functions. Ordinates in *f*) and *g*) are zoomed 100-fold compared to *b*) and *c*).

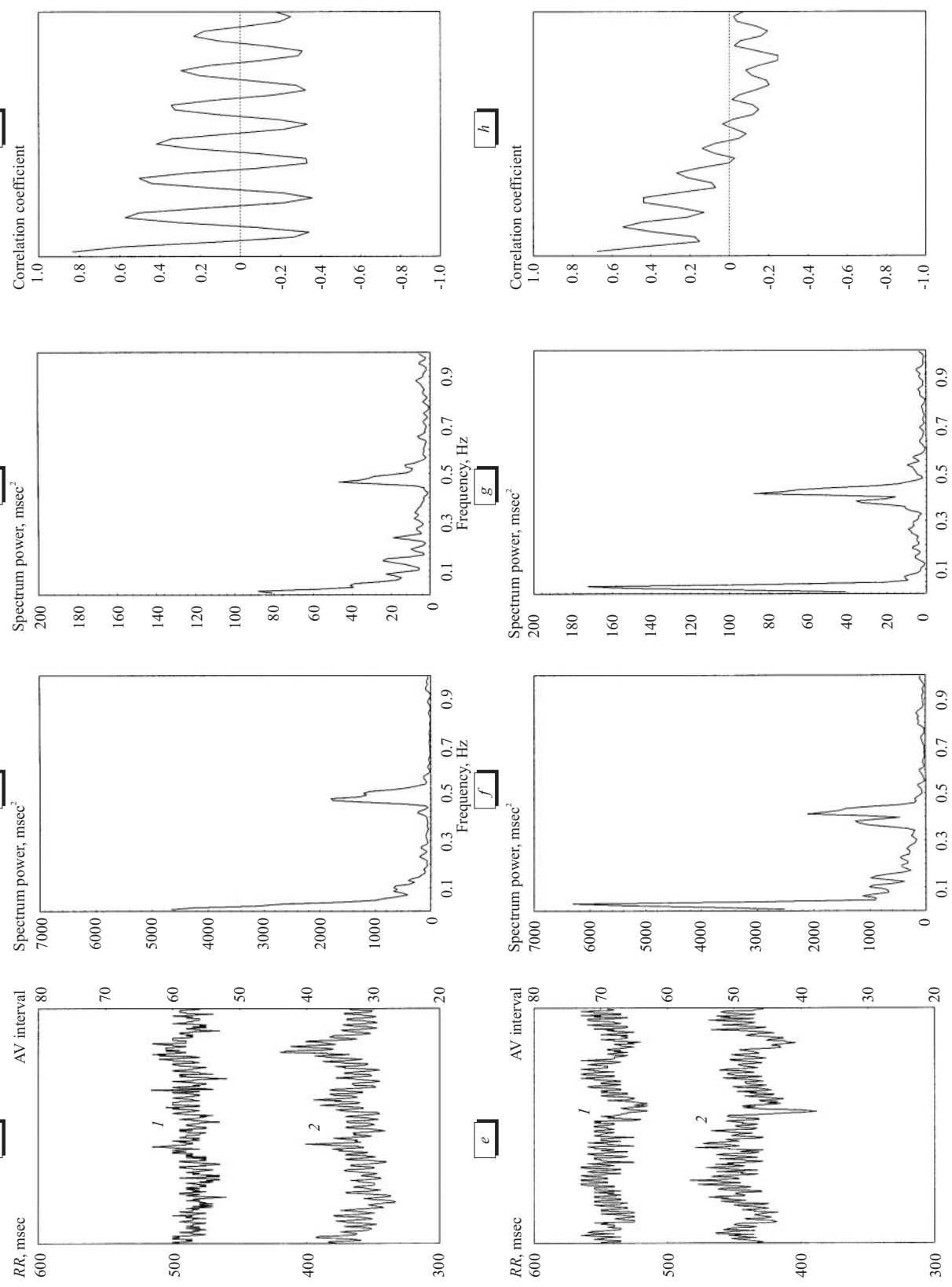

Fig. 2. Effect of propranolol on oscillations of AV interval (*1*) and *RR* interval (*2*). *a-d*) before propranolol; *e-h*) during the action of propranolol. *a*, *e* — cardiac intervalograms; *b*, *f* — power spectrum of *RR* interval; *c*, *g* — power spectrum of AV interval; *d*, *h* — cross-correlation functions.

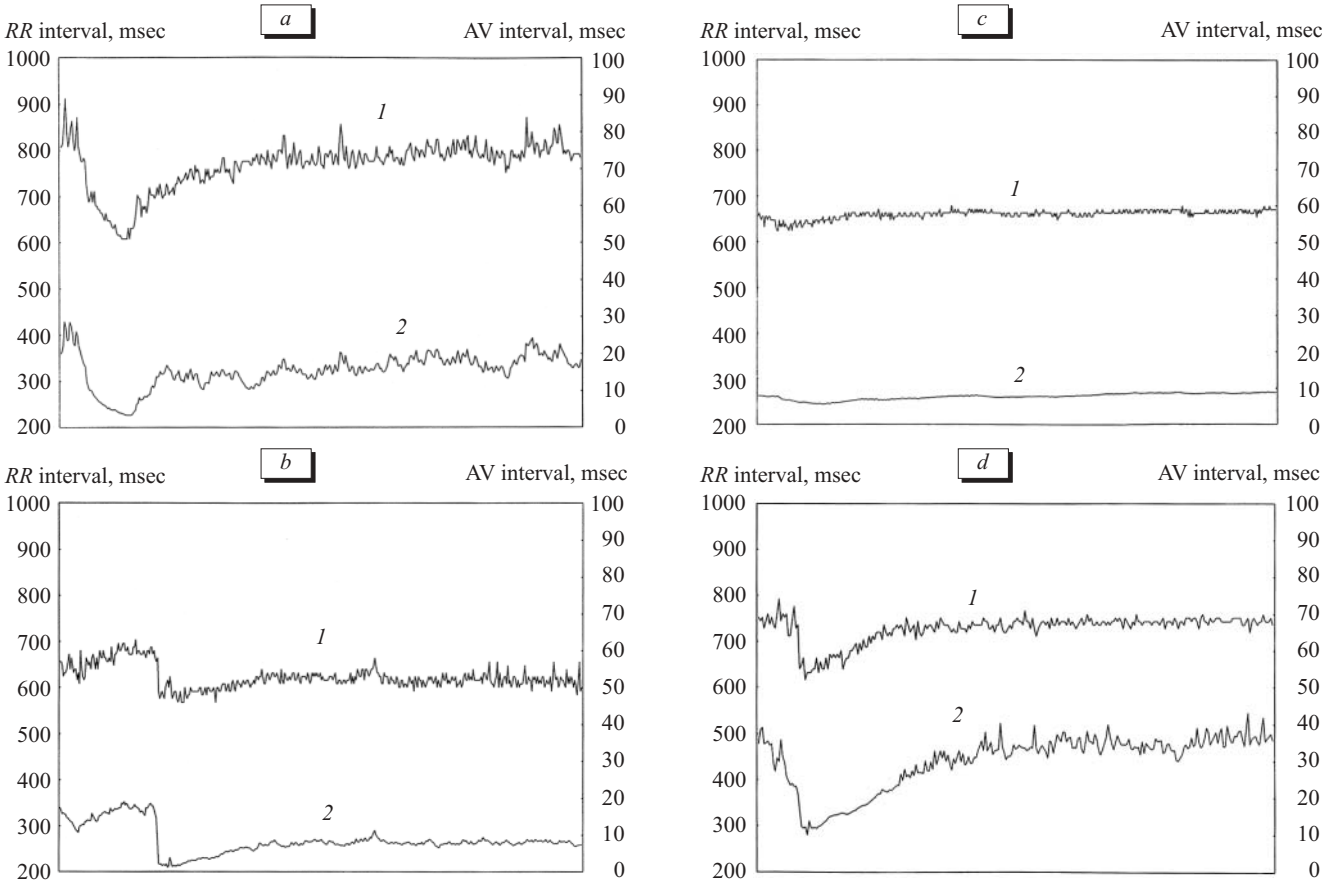

Fig. 3. Effect of atropine and propranolol on the response to noise stimulation. Cardiac intervalograms before (*a*, *b*) and after injection of atropine and propranolol (*c*, *d*), respectively. *1*) AV interval, *2*) *RR* interval.

(Fig. 1, *a*, *e*). However, this factor does not explain the less pronounced effect of atropine on VLF_{AV} and possibly LF_{AV}. It can be hypothesized that the cholinergic influences play minor role in these oscillations compared to their role in genesis of similar oscillations of *RR* interval, although other reasons cannot be excluded (for example, smaller sensitivity of AV node to atropine). Propranolol did not decrease the spectrum peaks of *RR* interval (Fig. 2). By contrast, it significantly increased HF_{RR} (to 117.4%). In addition, it slightly increased HF_{AV} (to 108.3%) and produced a moderate, but significant decrease of VLF_{AV} to 88.9%.

The basic difference in the action of atropine and propranolol on *RR* and AV-spectra focused on the VLF peak: atropine exerted weaker effect on VLF_{AV} than on VLF_{RR}, while the opposite was true for propranolol. This findings can indicate the involvement of the sympathetic nervous system into generation of very-low-frequency oscillations of AV interval, although other factors should also be considered. Specifically, propranolol can exert a central effect [2] or a tranquilizing action due to suppression of autonomic components of emotional stress [5] and the reflex effect on the heart in response to decreased blood pressure [5]. In all cases, the responses of *RR* and AV intervals to noise stimulation were suppressed by atropine and not by propranolol (Fig. 3).

Thus, in most cases the *RR* and AV intervals varied synchronously. It was true for the regular wave-like oscillation and for the responses to acoustic noise. The role of adrenergic and cholinergic influences in the control of *RR* and AV intervals was also similar in many respects, which follows from similar effects of atropine and propranolol on their spectral parameters and their response to acoustic stimulation. However, this synchronism was not absolute as indicated by the differences in the responses of VLF_{AV} and VLF_{RR} to the pharmacological agents. The later observation is corroborated by the data on non-parallel and even opposite changes of *RR* and AV interval to various reflexogenic stimuli [1]. Therefore, it can be concluded that regulation of the sinus node and AV node is mediated via the independent but correlated mechanisms of nervous chromodromotropic coordination.

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