Effect of Pentobarbital on Spectral Characteristics and Phase Ratios of Wave Oscillations of Cardiac Contraction Period and Time of Atrioventricular Conduction in Cats

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Effects of pentobarbital on spectral characteristics and phase ratios of wave oscillations of the cardiac contraction period (*RR* interval) and time of atrioventricular conduction (AV interval) were studied in experiments of cats. Pentobarbital moderately reduced the mean values of both intervals and significantly reduced their standard deviations and spectral powers in all frequency bands (high-frequency, low-frequency, and very low-frequency). Pentobarbital treatment led to deceleration of breathing, the frequency range of respiratory oscillations of *RR* and AV intervals shifted in some cases from high to low frequencies; evaluation of spectral power in the intermittent band corresponding to respiration frequency (instead of standard fixed high-frequency band) showed that pentobarbital suppressed the respiratory oscillations in these bands. Pentobarbital induced inversion of phase ratio between respiratory oscillations of *RR* and AV intervals: oscillations of both intervals before pentobarbital coincided by phase, while after pentobarbital injection they were in antiphase. The mechanisms of the latter phenomenon deserve further investigation.

Key Words: *heart; barbiturates; spectral analysis; atrioventricular conduction*

Periodical oscillations of heart rhythms (respiratory and slow-wave) are well known. Similar wave oscillations of atrioventricular (AV) interval were detected [2,9,10,12], spectral analysis thereof was carried out, transmitter nature was investigated, and ratio between the wave structure of AV interval and cardiac contractions period (*RR* interval) was studied in cats [2]. Here we studied the effect of barbiturate narcosis, one of the most prevalent methods of anesthesia in physiological experiments, on the wave structure of AV interval and its ratio with the *RR* interval wave structure.

MATERIALS AND METHODS

A total of 57 experiments were carried out on 15 adult cats of both sexes. In order to record the initial (without narcosis) ECG, the animals were put into screened box not limiting its movements. Two elastic strips were put onto the chest, each of these strips with two steel electrodes touching the animal skin. ECG was recorded using 3 standard or 3 amplified leads from the limb and the first derivative from the ECG lead with the most pronounced waves. Signals entered the ECG block of a P4Ch-02 poly-

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graph, then were transmitted to an amplifier of a 12-order 8-channel ACP, and then to PC. The frequency of all channels interrogation was 1 kHz, duration of one recording 2 min. The records were made at 10-min intervals over 1-2 h after the animal was placed into the box. During this period the animal was get calm and heart rhythm was stabilized. The time between the reference points of *P* wave and *QRS* complex was the indicator of AV interval. These points were selected individually in each experiment depending on the leads (for *P* wave this point could correspond to its beginning, peak, end, maximum or minimum of the first derivative; for *QRS* complex to *Q* or *R* wave peaks, maximum or minimum of the first derivative). According to preliminary data, AV intervals calculated using different reference points were in strong correlation, and the pattern of AV interval wave oscillations did not depend on the type of selected reference point.

After initial ECG recording the animals received barbiturate narcosis: pentobarbital (Nembutal) 60 mg/kg intraperitoneally. Narcotized animal was put in a supine position on the operation table; ECG recording was continued for 1 h, at 10-min intervals between records. Electrograms of the atria and ventricles (EGA and EGV, respectively) were recorded in 13 experiments. For these experiments intravenous catheters were inserted, through which maintening doses of pentobarbital (20 mg/kg/min) were infused, then the second intravenous catheter was inserted through which infusion of colloid saline (5 tablets of standard Ringer-Lock solution, 250 ml rheopolygluquin, and 1000 U heparin/500 ml distilled water) was started. A catheter was inserted into the brachial artery and arterial pressure was recorded using an Elema-Shonander pickup. An intubation tube was then inserted through an incision in the trachea and forced ventilation of the lungs was started; median thoracotomy was carried out, the pericardium was dissected, and two tantalum hook electrodes were placed onto the atria and ventricles for EGA and EGV recording. Drip infusion of colloid saline was carried out at a rate needed for maintaining diastolic arterial pressure at a level of at least 50 mm Hg. EGA, EGV, and arterial pressure were computer-recorded through ACP.

The results were statistically processed using Statistica software. The significance of differences was evaluated using Student's test; correlation function was plotted using Pierson's coefficient. Spectral analysis was carried out using fast Fourier transform with preliminary deduction of the mean, elimination of the trend, and using Hamming window (5 points wide). The entire spectrum of frequencies was divided into high-frequency, low-frequency, and very-low-frequency bands (0.22-1.20, 0.04-0.22, and <0.04 Hz, respectively [2]). Absolute density of spectral power was calculated for each band, denoted, in accordance with universal abbreviations, as HF for high frequency band, LF for low frequency band, and VLF for very low frequency band.

RESULTS

Pentobarbital led to changes in *RR* and AV intervals (Figs. 1, 2). The means of both intervals decreased (*RR* interval by 11.7%, AV interval by 17.6%). Standard deviations of both intervals decreased significantly (*RR* interval by 92.8%, AV interval by 58.0%) and their oscillations in all three frequency bands (VLF, LF, HF) decreased (*RR* interval by 91.0, 95.1, and 92.3%; AV interval by 78.5, 54.0, and 38.2%, respectively). Inversion of phase ratio between respiratory oscillations of *RR* and AV intervals took place: before pentobarbital injection they (98%) took place strictly in the same phase (or phase shift was one point), while after pentobarbital injection they (76%) were in antiphase (Fig. 1).

Deceleration of respiration characteristic of barbiturate effect [5] could lead to a shift of respiratory oscillations from HF to LF, and in this case standard spectral analysis with fixed bands could fail to reflect the true effect of pentobarbital on these oscillations. We therefore additionally calculated spectral powers of respiratory oscillations not for fixed HF, standard for the cat (0.22-1.2 Hz), but in an alternating band, corresponding to respiration rate during each ECG recording. To this end, a preliminary spectral analysis of *QRS* amplitudogram was carried out [3], frequency band of respiratory movements was determined, and spectral powers of *RR* and AV intervals were then calculated for this band (its range was established at 0.4 Hz in all cases). Pentobarbital reduced the respiration rate significantly: the lower and upper levels of this part before its injection were 0.36±0.12 and 0.57±0.15 Hz, respectively (*i.e.*, 22 and 34 min^{-1}), while after injection they were 0.21±0.10 and 0.35±0.10 Hz (13 and 21 min^{-1}). Estimation of *RR* and AV interval spectral powers in the respiratory band showed that pentobarbital suppressed respiratory oscillations of both intervals (by 95.2 and 49.0%, respectively).

Artifacts could emerge during surface ECG recording because of inaccurate recognition of *P* wave reference point or positional changes of *P* wave during respiratory excursions of the chest.

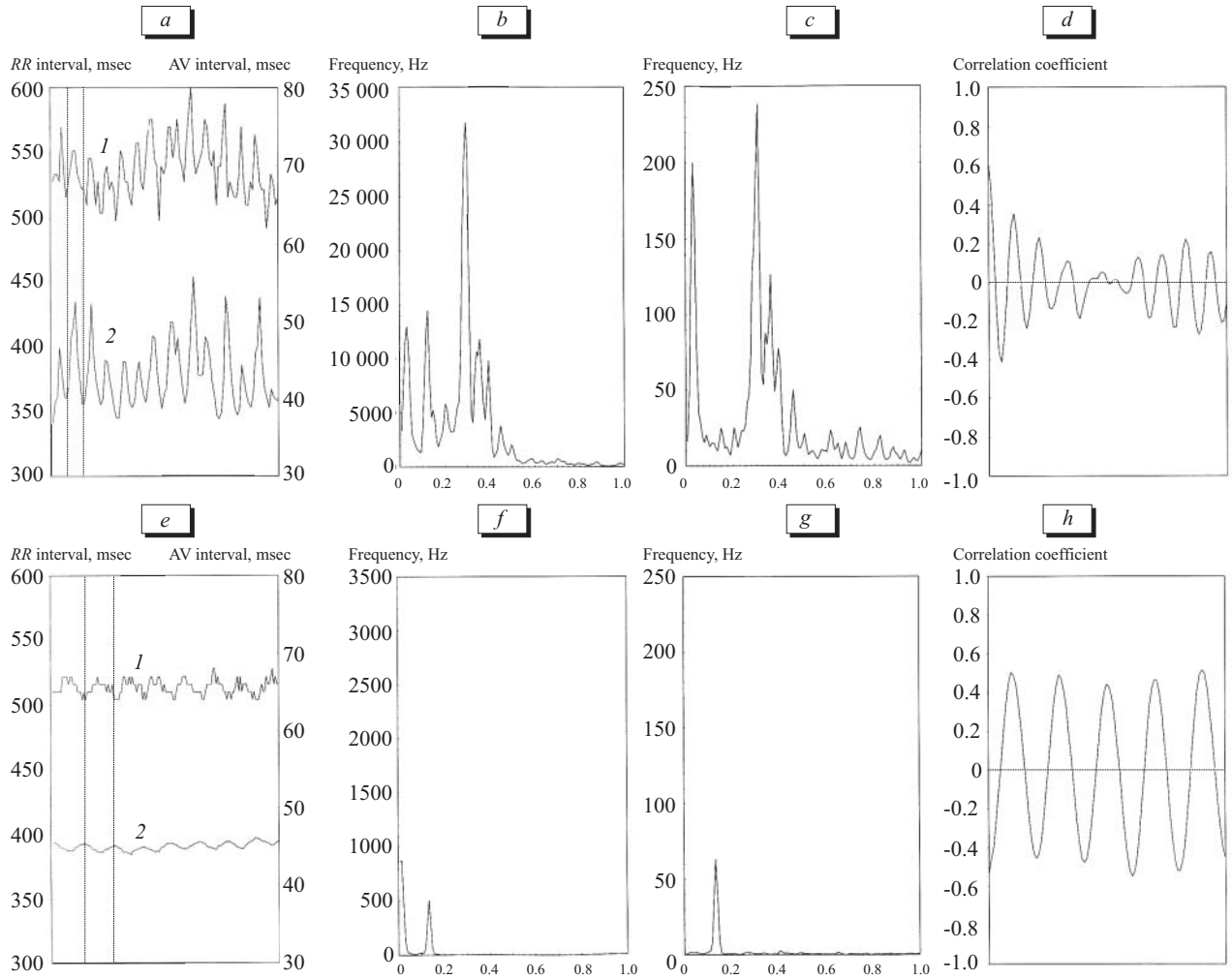

Fig. 1. Pentobarbital effects on wave oscillations of *RR* and AV intervals. *a-d*) before pentobarbital injection; *e-h*) under the effect of pentobarbital. *a*, *e*: cardiointervalograms: *1*) AV interval; *2*) *RR* interval. Vertical interrupted lines: borderlines of one respiratory wave. *b*, *f*: spectrograms of *RR* interval (ordinate: spectral power density square radical, msec). *c*, *g*: spectrograms of AV interval (ordinate: spectral power density square radical, msec). *d*, *h*: cross correlation functions.

Errors in measurements of AV interval could emerge in both cases. However, registration of EGA and EGV (no artifacts possible under these conditions) provided data similar to those obtained in recording of surface ECG. Oscillations of *RR* and AV intervals also reduced in all three frequency bands (VLF, LF, and HF: by 92.8, 94.1, and 95.2% for *RR* and by 80.0, 51.4, and 42.5%, respectively, for AV interval). Respiratory oscillations of *RR* and AV intervals were in antiphase (in 100% cases) similarly as during registration of surface ECG after pentobarbital injection.

Hence, pentobarbital caused a moderate increase in heart rate and a sharp decrease in the range of *RR* interval in all frequency bands (a known effect attributed to the vagolytic effect of barbiturates). We found that pentobarbital had a similar effect on AV interval, causing its shortening and decrease in the ranges of all frequency bands. This, together with other data [1,2], indicates a close relationship between chronotropic and dromotropic nervous effects (chronodromotropic coordination). However, it does not mean that AV delay always changes strictly parallel to the period of cardiac contractions. It was previously shown that the same reflexogenic exposure can cause opposite reactions of *RR* and AV intervals [1] and that blockers of the autonomic nervous system peripheral receptors have different effects on the spectral characteristics of *RR* and AV intervals [2]. One more manifestation of the intricate chronodromotropic coordination is presumably the inversion of phase ratio of respiratory oscillations of *RR* and AV intervals detected in this study. Its mechanisms deserve further investigation. Presumably, pentobarbital completely blocks the nervous effects on AV node, and chronodromotropic coordination is replaced by myogenic chronodromotropic relationship, when AV

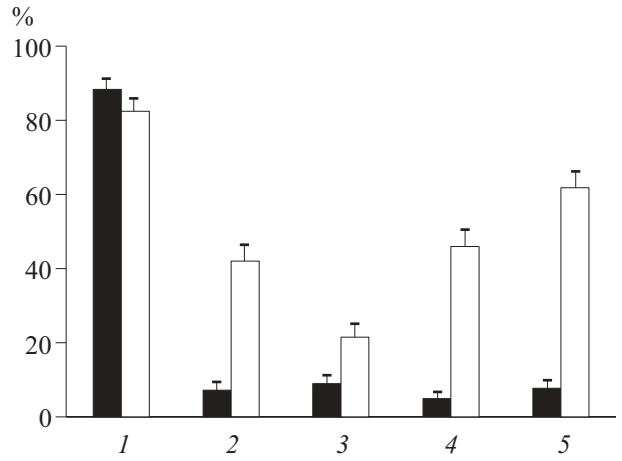

Fig. 2. Changes in the means, standard deviations, and spectral powers of *RR* and AV intervals under the effect of pentobarbital. Initial values of the parameters are taken for 100%. Dark bars: *RR* interval values (% of initial level) under the effect of pentobarbital; light bars: AV interval values (% of initial level) under the effect of pentobarbital. *1*) means of *RR* and AV interval; *2*) their standard deviations; *3*) very low frequency band; *4*) low frequency band; *5*) high frequency band.

delay changes in inverse proportion to cardiac contraction period. However, we think this explanation hardly probable. Dromotropic reflexes retained under conditions of pentobarbital narcosis indicate retained nervous regulation of AV conduction [1]. In this study we observed respiratory oscillations of AV interval in the absence of *RR* interval respiratory oscillations in many experiments, which cannot be explained by chronodromotropic relationship. Presumably, pentobarbital modifies the coordination of activities of the chronotropic and dromotropic neurons of the brain stem cardiovascular center: according to some data, these neurons are one of the targets of barbiturate effects [8]. It is also possible that inversion of phase ratio of *RR* and AV interval respiratory oscillations emerge not as a result of specific effect of pentobarbital on barbiturate receptors [5], but as a result of other mechanisms characteristic of all general anesthesias. The data on phase inversion of respiratory arrhythmia (oscillations of *RR* interval) under conditions of other than barbiturate narcosis indirectly prove it: urethane narcosis in rats [4] and isoflurane narcosis in humans [11]. The interest to spectral analysis of cardiac rhythm in general anesthesia [6,7] and high reproducibility of the effect of inversion of the phase ratio of *RR* and AV interval respiratory oscillations render theoretical and practical significance to this effect.

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