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Noninvasive Determination of Baroreflex Sensitivity in Man by Means of Spectral Analysis

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Summary

The spectral analysis technique was applied for noninvasive assessment of heart-rate baroreflex sensitivity (BRS). The coherence between fluctuation of blood pressure and heart rate at 0.1 Hz and at respiratory frequency is high. This fact enables the assessment of BRS by means of calculating the modulus (or gain) of the transfer function between variations in blood pressure and heart rate. The noninvasive continuous blood pressure registration according to Peňáz was used. During voluntarily controlled breathing intervals, the amplitude of 0.1 Hz and respiratory peaks in the spectra of heart rate and blood pressure changed markedly. Nevertheless, the average sensitivity of the baroreflex (modulus) changed insignificantly. This result indicated that the stability of BRS can be advantageous for the use of BRS in clinical practice. The difference between the modulus at 0.1 Hz and at the breathing rate indicates that baroreflex is only one of the factors causing respiratory arrhythmia. We also compared the determination of BRS by spectral analysis with the following alternative method: both lower extremities were occluded for 5 minutes. The release of pressure in the occluding cuffs decreased blood pressure which was followed by a baroreceptor-mediated increase of heart rate. Both methods correlated, but more detailed analysis revealed the role of the low pressure receptors in BRS determined by spectral analysis.

Key words
Blood pressure – Heart rate – Respiration – Rhythms – Haemodynamics physiology

Introduction

Spectral analysis was introduced into cardiovascular research in the sixties (Peňáz *et al.* 1968a). At present, attempts are being made to introduce spectral analysis into clinical practice. For example, they brought positive results in the prediction of sudden cardiac death (Myers *et al.* 1986). It was also shown that the risk of sudden cardiac death negatively correlates with the sensitivity of the baroreflex (Schwartz and Ferrari 1987). It would be useful to improve the possibility of testing baroreflex sensitivity using noninvasive methods, especially spectral analysis of the variability in the heart rate and blood pressure. Our experience with the complexity (Peňáz *et al.* 1978, Fišer *et al.* 1978) and with the interindividual variability of fluctuations in circulation and respiration (Honzíková *et al.* 1990) led us to study the physiological influence of respiration and of stimulation of the low-pressure receptors on BRS studied by means of spectral analysis.

Usually, spectral peaks are divided into frequency ranges which are given by a different origin of corresponding fluctuations of circulatory parameters: 0.03-0.06 Hz (2-3.5 cpm) – low frequency range, 0.07-0.12 Hz (4-7.5 cpm) – 10-s rhythm and 0.13-0.50 Hz (8-30 cpm) – respiratory waves. Previously, the role of respiration in the origin of fluctuation in circulation was limited to this last range. But we found (Honzíková *et al.* 1980) a new, previously undescribed relationship between the frequency and depth of respiration on the one hand, and the low-frequency circulatory waves on the other (frequency range 0.03-0.06 Hz, i.e. 2-3.5 cpm). It was thus demonstrated that the relationship between respiration and

the regulation of circulation is more important than originally supposed. Additional evidence supported our idea. We found that the changes in circulatory rhythms during mental load (Honzíková *et al.* 1988) or during isometric exercise (Honzíková *et al.* 1987) correlate with the variations in respiration better than with any tested load. It therefore seemed useful to know whether BRS also depends on the frequency of breathing and if it correlates with the amplitude of the 0.1 Hz peak.

BRS in man has been assessed for many years by two methods: the first method is neck suction (Eckberg *et al.* 1975, 1980) and the second is the administration of a vasoconstrictory substance, e.g. phenylephrin (Smyth *et al.* 1969, Brooks *et al.* 1978). Both these methods measure only one part of the baroreflex – the change in the cardiac interval after arterial baroreceptor stimulation. This change is measured quantitatively in milliseconds of interval prolongation per millimeter of mercury in the pressure rise.

New noninvasive methods of the determination of BRS are based on Peňáz's noninvasive blood-pressure measurement. Earlier, a method based on the Valsalva maneuvre was suggested. BRS is calculated from the period after the end of the Valsalva maneuvre. Mulder (1988) applied the spectral analysis technique to the noninvasive assessment of BRS. The modulus (or gain) of the transfer function between variations in blood pressure and heart rate was calculated in the range of the 10-s rhythm. The modulus expresses the ratio between changes in RR intervals and changes in systolic pressure (ms/mmHg) in a specified frequency band. Therefore, the modulus function in the frequency domain is comparable to the regression coefficient in the time domain. The modulus can be calculated only in the range where the coherence is high. The values of BRS assessed with the phenylephrin method and by means of spectral analysis correlate highly.

In this study we introduced a new method of assessment of BRS. Using inflatable cuffs on both lower extremities, we called forth changes in blood pressure which mediated stimulation of baroreceptors. At the same time, we demonstrated the stimulations of low-pressure receptors to changes in the heart interval. This mechanism can contribute to the respiratory sinus arrhythmia by changes in diastolic filling of the heart during breathing movements.

Methods

This study consists of two sets of experiments.

The first study followed the relationship between BRS and changes in the circulatory rhythms due to changes in respiratory frequency.

By means of the modulus, we assessed the baroreflex sensitivity in 8 healthy adult subjects at various breathing frequencies. The blood pressure (by means of the Peňáz volume-clamp method) and cardiac intervals were recorded in a sitting position during spontaneous quiet breathing and also during voluntarily-controlled breathing intervals. Duration of breathing intervals in experimental sessions was: 3, 4, 5, 6, 8, 10 and 17 s. The sequence of experimental periods was randomly chosen for each subject. The tidal volume was not controlled – the subjects breathed according to their need.

Our original approach for the determination of BRS which was used in the second part of the study is explained in Fig. 1. The blood pressure and heart rate were recorded in 5 subjects in the supine position. Two inflatable cuffs were placed on both thighs. The cuff pressure was increased abruptly to 24 kPa (180 mmHg) for 5 min. This occlusion elicited the vasodilatation of vessels in the legs. Following the abrupt change of pressure in the occluding cuffs from 24 to 8 kPa (180 to 60 mmHg) for 1 min caused a decrease of blood pressure followed by an increase of heart rate. During this experimental period the venous return from the legs and stimulation of low pressure receptors was blocked. After 1 min the cuff pressure was decreased to 0 kPa (mmHg) and the venous return increased. This was followed by an increase of arterial blood pressure due to increased cardiac output.

The baroreflex sensitivity was determined by three methods: 1. Modulus during the 50-second period which started 10 s after the decrease of cuff pressure from 24 to 8 kPa (180 to 60 mmHg). 2. The ratio between the average cardiac interval of 5 beats before the decrease of blood pressure ($CI_{-1}...CI_{-5}$) minus the shortest interval during the following 5 s after this decrease (CI_S) and the average systolic pressure of 5 beats before the

blood-pressure decrease ($SP_{-1}...SP_{-5}$) minus the lowest systolic pressure during following 5 s (SP_L).

$$BRS = \frac{\frac{CI_{-1}+CI_{-2}+...+CI_{-5}}{5} - CI_S}{\frac{SP_{-1}+SP_{-2}+...+SP_{-5}}{5} - SP_L}$$

3. The ratio between the difference of the longest and the shortest cardiac interval and the difference of the highest and the lowest systolic pressure during the 10-s period of increased venous return.

Results

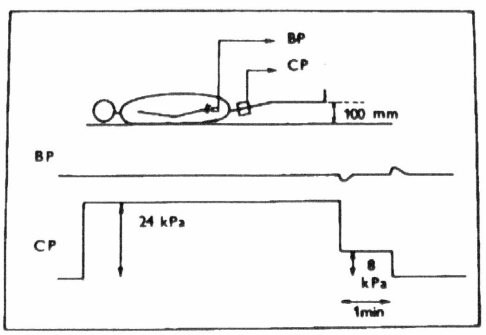

Fig. 1
Scheme of the time course of changes in finger blood pressure (BP) and in the cuff pressure (CP) during an experiment.

Fig. 2 summarizes the influence of the respiratory frequency on spectral peaks and BRS in all subjects. It shows the average values and standard deviations of power in the heart-rate spectrum and of the modulus at both frequencies (respiratory and 0.1 Hz) in each experimental period. We observed various amplitudes of 0.1 Hz peak in the spectra of cardiac intervals at various breathing rates and despite this, the modulus remained relatively constant in each subject. Also, despite the diminution of the sinus-arrhythmia amplitude with an increase of the breathing rate, the modulus at the respiratory frequency was practically independent of the breathing rate. A small decrease of the modulus at a breathing rate of 15 and 20 cpm (0.25 and 0.33 Hz) was insignificant. The ratio between maximum and minimum power at 0.1 Hz peak in the spectrum of cardiac intervals at various breathing rates ranged in some subjects between 2.31 and 57.24. Alternatively, the ratio between maximum and minimum values of the modulus at 0.1 Hz ranged from 1.16 to 3.15. This contradicts the hypothesis that the frequency and amplitude of heart-rate oscillations depend on the relative gains of the elements that modulate cardiac vagal, cardiac sympathetic, and peripheral sympathetic efferent activity (Saul 1990).

The phenomenon of resonance at the breathing frequency near the 10-s rhythm, described earlier (Peňáz 1957, Golenhofen and Hildebrandt 1962), manifests itself in a great increase in amplitude of the 10-s rhythm. It was present in half of the subjects. On the other hand, the modulus was not influenced by the resonance. This could be due to a primary increase in blood pressure oscillations and unchanged sensitivity of baroreflex control of the heart-rate frequency.

It is still an open question whether the modulus at respiratory frequency corresponds to the modulus at 0.1 Hz. The correlation between these two modulus values is positive, but insignificant ($R=0.58$). A significant difference between the average value of the modulus at 0.1 Hz and at the breathing rate, calculated for each subject for the entire experimental periods, was found in 5 subjects (in 3, $P<0.05$; in 2, $P<0.01$; t-test). It must be noted that in 4 subjects, the modulus at 0.1 Hz was higher than at the respiratory frequency and in 4 subjects an opposite relationship was observed. These facts indicate that the baroreflex is only one of the factors causing respiratory arrhythmia at rest and that additional factors also play a role.

Fig. 3 illustrates the changes of blood pressure in the set of experiments in which occluding cuffs on the lower extremities were applied. The decrease of cuff pressure from 24 to 8 kPa (180 to 60 mmHg) was followed by a decrease of blood pressure. Sometimes the decrease of blood pressure was abrupt during one interval (upper recording), mostly during 3 to 4 beats (middle recording). The changes of blood pressure after the decrease of cuff pressure from 8 to 0 kPa (60 to 0 mmHg) were uniform (lower recording).

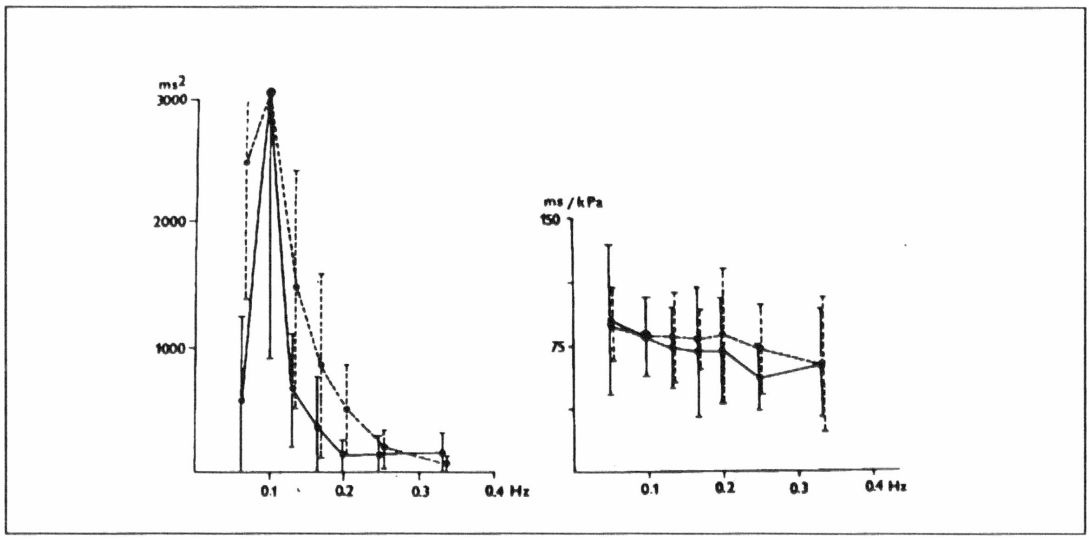

Fig. 2

Power of the peak in spectra (left) and modulus of cardiac intervals and systolic blood pressure (right) at 0.1 Hz (dots) and at respiratory frequency (circles) at various respiratory rates (abscissa). Mean values and standard deviations of 8 subjects.

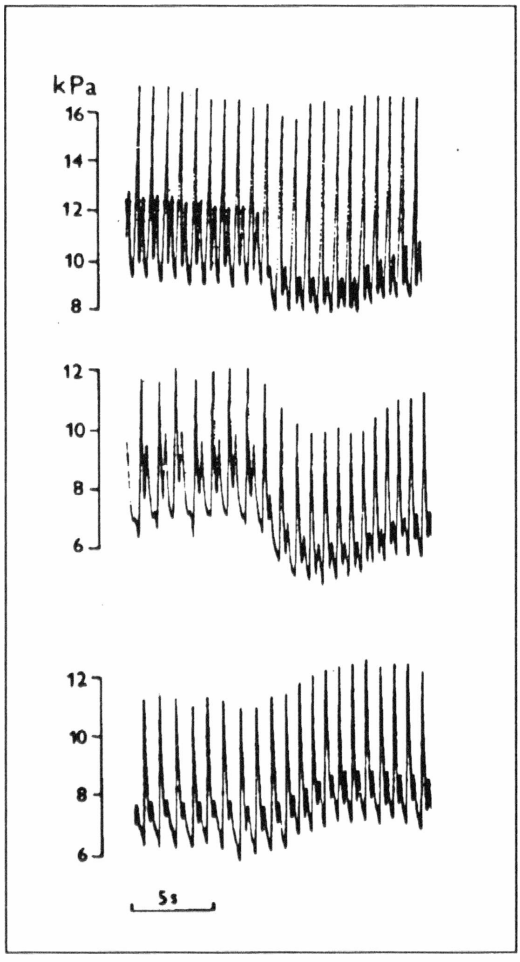

Fig. 3

Examples of records of finger blood pressure during an abrupt pressure decrease in occluding cuffs from 180 to 60 mmHg(A, B) and from 60 to 0 mmHg (C).

The average change of blood pressure and cardiac intervals in all subjects (S.D. are indicated) after the decrease of cuff pressure from 24 to 8 kPa (180 to 60 mmHg) is shown in Fig 4 (left). Cardiac intervals decreased after a latency of 1 s and a 5-second plateau is seen on the cardiac interval response curve (preceding intervals with 0.5-second linear interpolation were used for calculation).

The average change of blood pressure and cardiac intervals in all subjects (S.D. are indicated) after the decrease of cuff pressure from 8 to 0 kPa (60 to 0 mmHg) is shown in Fig. 4 (right). It is important to notice a decrease of the cardiac interval which starts before a change of blood pressure. The response of heart rate on the increase of venous return mediated by the low-pressure receptors is a plausible explanation. It is evident that the decrease of heart intervals is superposed on this reaction. The differences in individual experiments were more pronounced than on the average curve.

Summary of the results can be seen in Fig. 5. The average values and ranges of BRS were similar in all methods (calculation of the

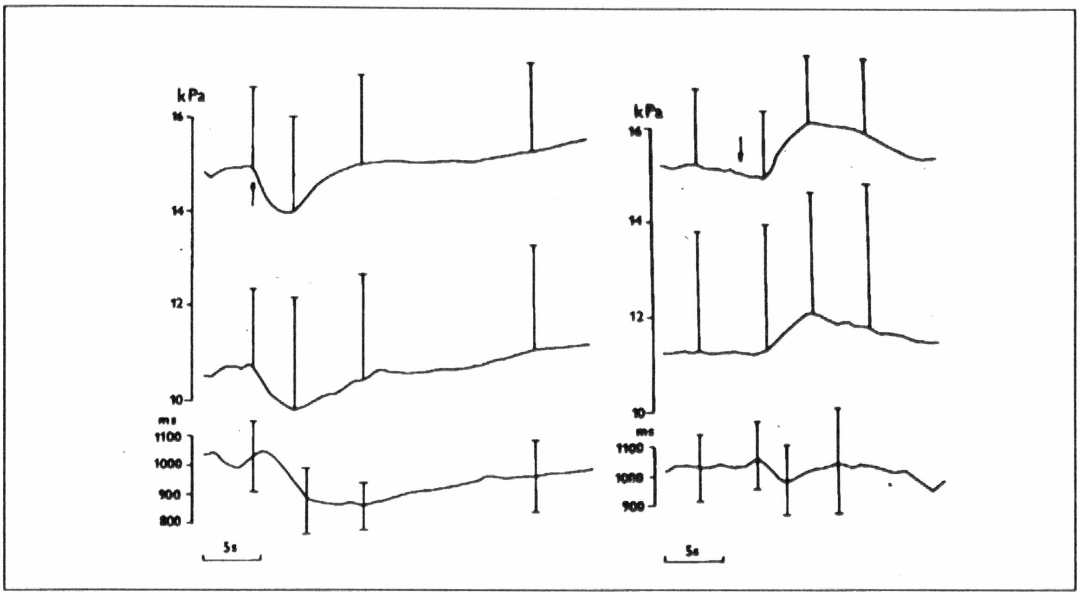

Fig. 4

Systolic pressure (top), diastolic pressure (middle) and cardiac intervals (bottom) in 5 subjects (S.D. are indicated). Decrease of cuff pressure is indicated by arrow (left - from 180 to 60 mmHg, right - from 60 to 0).

	MEAN	RANGE	MEAN	RANGE	CORRELATION		
	ms / kPa		ms / mmHg		BRS BP ↑	BRS MOD	CI
BRS BP ↓	160.4	45.0 304.7	21.39	6.00 40.62	0.4438	0.8165	0.6916
BRS BP ↑	146.0	46.9 252.7	19.47	6.25 33.69		0.7156	-0.0511
BRS MOD	166.7	60.4 284.0	22.23	8.05 37.86			0.4258
	ms						
CI	981	842 1109					

Fig. 5

Mean values, ranges and correlation of BRS (baroreflex sensitivity) calculated 1. during the blood pressure (BP) decrease, 2. during the blood pressure increase, 3. by means of modulus (MOD). CI - cardiac intervals.

change of cardiac interval per kPa or per millimeter of mercury of the blood pressure change during the blood-pressure decrease or increase and calculation of the modulus). Our preferred method based on the decrease of blood pressure correlates with the modulus

but not with the method based on the increase of blood pressure. On the other hand, the correlation between the modulus and BRS, calculated from the increase of blood pressure, was also high. This result suggests that the low pressure receptors can influence the modulus.

The total correlation coefficient between the modulus and BRS determined by means of both methods, was very high (R = 0.897). This was a value similar to the correlation coefficient between the modulus and BRS, determined by phenylephrin obtained in the study of Mulder. It is also probable that the phenylephrin method includes the stimulation of low-pressure receptors. This is a disadvantage in comparison to our noninvasive method with the occlusion of the lower extremities.

Discussion

Several different theories explain the role of the baroreflex in low-frequency blood pressure waves. The most popular theory was introduced by Sayers (1973): the spontaneous feedback rhythm is centered at the frequency of 0.1 Hz due to time constants and delays in feedback circuits. This theory, which is also documented by a recent overview (Saul 1990), is accepted by most authors. The changes in amplitude of the 10-s rhythm, accompanying changes in the respiratory rate, are undoubtedly associated with resonance, synchronization (Peňáz 1957) or with "entrainment" (Hyndman 1974). The resonance phenomenon at frequencies of 0.03-0.09 Hz was also described in blood flow in the mesenteric artery which reflects the resistance of this vascular area (Peňáz *et al.* 1968b).

According to our findings, the most plausible theory was suggested by Wesseling *et al.* (1983), which is based on two facts. The smooth muscle of blood vessels is not able to follow rapid changes of vasomotor nerve activity. The oscillations of peripheral resistance at frequencies higher than 0.066 Hz are therefore attenuated (Peňáz 1970). The low-frequency oscillations of peripheral resistance in some regions are compensated by changes in other regions by means of the baroreflex. Thus slow and fast oscillations are eliminated and the 0.1 Hz peak remains. In this sense, the origin of this peak is in the baroreflex but the 0.1 Hz peak itself is not caused by a lag in the feedback mechanism. This is important because, according to this theory, the magnitude of this peak does not depend on the sensitivity of the baroreflex. On the other hand, the oscillation of blood pressure elicits changes of cardiac intervals and the modulus between systolic pressure and cardiac intervals at 0.1 Hz corresponds to the baroreflex sensitivity expressed in ms/kPa (ms/mmHg). Baroreflex sensitivity at various respiratory rates remains constant.

An additional practical conclusion resulted from this analysis: in studies in which sympathovagal activity is determined from the amplitude of the 10-s and respiratory spectral peak, the respiratory frequency should be taken into account. It was proved in this study that the amplitude of the 10-s rhythm is dependent on respiratory frequency not only at a respiratory frequency of 6 cpm, where the respiratory and the 10-s rhythms merge into one peak. It is also dependent on respiration at a breathing frequency lower than 0.2 Hz (12 cpm).

In medical practice, many unsolved problems exist, for example – the risk of sudden cardiac death. It was shown that its occurrence negatively correlates with the sensitivity of the baroreflex. We wanted to provide new information about BRS in the physiology of man, which is possible to obtain noninvasively. Our method of assessing BRS during the blood pressure decrease has the advantage that the low-pressure receptors are not stimulated. This cannot be excluded when using phenylephrin. The modulus correlates similarly with other methods. This means that it also does not include the pure response of heart rate to the stimulation of high-pressure receptors. These results may be useful for clinical practice.

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References

BROOKS D., FOX P., LOPEZ R., SLEIGHT P.: The effect of mental arithmetic on blood pressure variability and baroreflex sensitivity in man. *J. Physiol. Lond.* **280:** 75P – 76P, 1978.

ECKBERG D.L., CAVANAUGH M.S., MARK A.L., ABBOUD F.M.: A simplified neck suction device for activation of carotid baroreceptors. *J. Lab. Clin. Med.* **85:** 167 – 173, 1975.

ECKBERG D.L., KIFLE Y.T., ROBERTS V.L.: Phase relationship between normal human respiration and baroreflex responsiveness. *J. Physiol. Lond.* **304:** 489 – 502, 1980.

FIŠER B., HONZÍKOVÁ N., PEŇÁZ J.: Power spectra of spontaneous variations of indirectly recorded blood pressure, heart rate and acral blood flow. *Automedica* **2:** 143 – 147, 1978.

HONZÍKOVÁ N., FIŠER B., PEŇÁZ J.: Relationship between power spectra of respiration and of some circulatory parameters in man. In: *Proc. of the Internat. Union of Physiol. Science.* XXVIII. Internat. Congress, Budapest, 1980, p. 477.

HONZÍKOVÁ N., PEŇÁZ J., FIŠER B.: Interpretation of differences in power spectra of blood pressure, heart rate and respiration in man. In: *Chronobiology and Chronomedicine.* G. HILDEBRANDT, R. MOOG, F. RASCHKE (eds), Peter Lang, Frnkfurt/Bern/New York/Paris, 1987, pp. 172 – 176.

HONZÍKOVÁ N., PEŇÁZ J., FIŠER B.: Power spectra of blood pressure and heart rate fluctuations during mental load. *J. Interdiscipl. Cycle Res.* **19:** 75 – 79, 1988.

HONZÍKOVÁ N., PEŇÁZ J., FIŠER B.: Individual features of circulatory power spectra in man. *Eur. J. Appl. Physiol.* **59:** 430 – 434, 1990.

HYNDMAN B.W.: The role of rhythms in homeostasis. Kybernetik 15: 227 – 236, 1974.

MULDER L.J.M.: Assessment of cardiovascular reactivity by means of spectral analysis. Proefschrift, University Groningen 1988.

MYERS G.A., MARTIN G.J., MAGID N.M., BARNETT P.S., SCHAAD J.W., WEISS J.S., LESCH M., SINGER D.H.: Power spectral analysis of heart rate variability in sudden cardiac death: Comparison to other methods. *IEEE Trans. Biomed. Eng.* **33:** 1149 – 1156, 1986.

PEŇÁZ J.: Oscillations de la fréquence cardiaque et du tonus vaso-moteur au cours de respiration ralenti et accélérée. *J. Physiol. Paris* **49:** 346 – 349, 1957.

PEŇÁZ J.: Czechoslovak patent No. 133205, 1969.

PEŇÁZ J.: The blood pressure control system: A critical and methodological introduction. In: *Psychosomatics in Essential Hypertension.* M. KOSTER, H. MUSAPH, P. VISSER (eds), Karger, Basel-München-New York, 1970, pp. 125 – 150.

PEŇÁZ J., ROUKENS J., VD WAAL H.J.: Spectral analysis of some spontaneous rhythms in the circulation. In: *Biokybernetik I.* Karl-Marx-Univ., Leipzig, 1968a, pp. 233 – 236.

PEŇÁZ J., BURIÁNEK P., SEMRÁD B.: Dynamic aspects of vasomotor and autoregulatory control of blood flow. In: *Circulation in Skeletal Muscle.* O. HUDLICKA (ed), Pergamon Press, Oxford, 1968b, pp. 255 – 276.

PEŇÁZ J., HONZÍKOVÁ N., FIŠER B.: Spectral analysis of spontaneous variability of some circulatory parameters in man. *Physiol. Bohemoslov.* **27:** 349 – 357, 1978.

SAUL J.P.: Beat-to-beat variations of heart rate reflect modulation of cardiac autonomic outflow. *NIPS* **5:** 32 – 37, 1990.

SAYERS B.McA.: Analysis of heart rate variability. *Ergonomics* **16:** 17 – 32, 1973.

SCHWARTZ P.J., DE FERRARI G.M.: The influence of the autonomic nervous system on sudden cardiac death. *Cardiology* **74:** 297 – 309, 1987.

SMYTH H.S., SLEIGHT P., PICKERING G.W.: Reflex regulation of arterial pressure during sleep in man: a quantitative method of assessing baroreflex sensitivity. *Circ. Res.* **24:** 109 – 121, 1969.

WESSELING K.H., SETTELS J.J., WALSTRA VAN ESCH H.J., DONDERS J.J.H.: Baromodulation as the cause of short term blood pressure variability? In: *Proc. of the Internat. Conf. on Applications of Physics to Medicine and Biology.* G. ALBERI, Z. BAJZER , P. BAXA (eds), World Scientific Publishing, Singapore, 1983, pp. 247 – 276.

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