CAN SPECTRAL COHERENCE BETWEEN BLOOD PRESSURE AND INTER-BEAT INTERVALS DISCRIMINATE THE STAGES OF HYPERTENSION

S. Danev[1], E. Datzov[1], S. Svetoslavov[3], D. Mikhov[2], P. Markova[2], R. Girchev[2],

1. National Center of Hygiene, Medical Ecology and Nutrition, Sofia, Department of Physiology, Psychology and Ergonomics
2. Medical University, Sofia, Department of Physiology
3. Technical University, Sofia, Department of High Technology Communications

Key words: heart rate variability, blood pressure, power spectrum, cross-spectrum.

Address for correspondence: Prof. S. Danev, National Center of Hygiene, Medical Ecology and Nutrition, Department of Physiology, Psychology and Ergonomics, Blvd. D. Nestorov N 15, Sofia 1431, Bulgaria,
FAX: 95-81-277.

CAN SPECTRAL COHERENCE BETWEEN BLOOD PRESSURE AND INTER-BEAT INTERVALS DISCRIMINATE THE STAGES OF HYPERTENSION

S. Danev, E. Datzov, S. Svetoslavov, D. Mikhov, P. Markova, R. Girchev

SUMMARY

Continuous registration of blood pressure (BP) was obtained in 31 normotensives and 76 hypertensives (divided into 3 stages of hypertension) by a method in which the blood pressure in a human finger is measured non-invasively in a beat-by-beat fully calibrated manner. From this signal, the power density spectra of inter-beat intervals (IBI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were derived. Total spectral power (TP) and Low/High spectral frequency ratios of all spectra were calculated. Cross-correlation analysis revealing the amplitude and the phase coherence (calculated by means of appropriate mathematical formulas) between IBI, SBP and DBP spectra shows that the level of coherence is strongly dependent of the stage of hypertension. By multiple step regression analysis was pointed out that this relationship is highly significant for both - amplitude and phase spectral coherence ($p<0.01$).

INTRODUCTION

Essential hypertension seems to depend on many factors, as family history, increased body weight, vascular hypertrophy etc. A very reliable marker of sympathetic predominance is the decreased IBI variability (IBIV) (1) and the increase of low-frequency associated spectral power (LFP), respectively the decrease of the high-frequency associated spectral power (HFP) of IBIV in hypertensive subjects as compared with normotensive subjects - Guzzetti et al.(2), Dassi et al. (3).

By spectral analysis of IBIV and blood pressure variability (BPV), Pagani et al. (4) confirmed also the existence of enhanced sympathetic tone in hypertensive subjects. Although the relationship between hypertension and the decreased IBIV, its total spectral power (TP) and the HFP is well-described, the effect of chronic vasoconstriction upon spectral coherence between cardiac and vascular functions is almost unknown.

One of the first who proposed cross-spectral analyses of IBIV and BPV spectra to be used in order to reveal the pathophysiological background of the central origin of hypertension was Levy (5). We have found, in this relation that the amplitude and the phase-based spectral coherence (SC) of IBIV and BPV spectra show tendency to be decreased in subjects with overstress (6) and as a consequence of pharmacologically induced autonomic disequilibrium towards prevailing sympathetic tone (7). A decrease of TP in both spectra, as well as an increase of LFP/HFP ratio was also found.

The aim of the study was to examine the relationship between IBIV and BPV spectra by comparing their SC in normotensive and hypertensive subjects.

MATERIAL AND METHODS

SUBJECTS. One hundred and seven subjects aged 20 to 65 years were followed up. All of them were without medication for the preceding 3 days period and were maximally equalized for smoking habits, alcohol consumption and physical activity (the subjects filled in a standardized health questionnaire for past medical history). The major part of hypertensive outdoor patients were from cardiological clinics as well as from the consulting cardiological rooms of some district's polyclinics. Some of them had received previously antihypertensive medication (beta-blockers, ACE inhibitors, calcium antagonists, and diuretics). The cardiovascular state was consulted with cardiologists. All subjects were divided into four groups according to WHO criteria for hypertension (SBP > 140 mm Hg, DBP > 90 mm Hg): - normotensive (n=31, mean age 42.6±6.2); hypertensive - I stage (n=27, mean age 40.4±3.6); II stage (n=25, mean age 52.2±7.6); III stage (n=24, mean age 48.8±3.9).

PROCEDURE. BPV and IBIV spectra were obtained after 10-min. resting period in lying position (between 9-11 a.m.) from 7 min registration period. BP was measured 3 times consecutively from the right arm and the mean value was used.

The power density spectra (PDS) as well as the ASC and PSC of the assessed signals were obtained by the following mathematical algorhythms:

Let us accept that X (n) is a real entrance signal and Y (n) is a spectral signal of X (n).

$$Y(n) = 1/2\pi \int_{-\pi}^{+\pi} x(e^{iw}) e^{iwn} dw ,$$

where $X(e^{iw})$ is a periodical function with period of 2 π.

This equation can be transformed for number “N” of entrance signals and it looks like:

$$Y(n) = \sum_{n=0}^{N-1} x(n)e^{-j2\pi k/N}$$, 0≤ k <N

If indicate $Wn = e^{-j2\pi/N} = \cos(\frac{2\pi}{N}) - j\sin(\frac{2\pi}{N})$,

then:

$$Y(n) = \sum_{n=0}^{N-1} x(n)Wn^{nk}$$, 0≤ k <N

This is the algorhythm for Direct Fourier Transform and it is used for spectral analysis of the discreet signals.

If two signals are summited to Direct Fourier Transform – they have accordingly Y (n) and U (n) imaginary spectral signals. On their basis the correlation analysis can be accomplished in accordance with the equation:

C (n) = Y(n) U*(n),

where C(n) is the correlation function.

In order to accomplish the correlation analysis is necessary the two entrance signals to have equal enter discreets and equal frequency of discreets.

From the obtained correlation function the amplitude coherence spectrum can be elected by:

$$\text{Ca(n)} = \sqrt{\text{Re}(C(n))^2 + \text{Im}(C(n))^2}$$,

and the phase coherence spectrum can be elected by:

$$\text{Cf(n)} = arctg\frac{\text{Im}(C(n))}{\text{Re}(C(n))}$$,

Examples of Power Density Spectra of IBIV, SBPV and DBPV are presented in fig.1.

Beat-to-beat systolic BP (SBP), diastolic BP (DBP) and IBI were registered by the non-invasive method (based on employment the principle of the Penaz method (8)) of vascular unloading on the fingertip. Changes in the vascular volume of the finger are detected by a photoplethysmographic device consisting of a light source and a photoelectric cell. The photoelectric equipment is incorporated into an inflatable cuff surrounding a finger. Arterial pressure signal, sampled at 200 Hz, was digitally lowpass filtered by a five point rectangular moving average filter and down-sampled to 100 Hz in order to derive the consecutive maximum and minimum values from which SBP and DBP spectra were obtained. The IBIV spectrum was derived from IBI. These three spectra were compared by cross-correlation analysis in order to assess their mutual amplitude spectral coherence (ASC) and phase spectral coherence (PSC). The ASC was measured by the value of the correlation coefficient (K). The PSC was measured in radians (rad) only for middle-frequency (MF) band, as in this area the ASC seems to be higher expressed. The total spectral power of every spectrum was divided into three frequency bands – low frequency (LF), middle frequency (MF) and high frequency (HF): LF - 0.01-0.06 Hz; MF - 0.07-0.14 Hz and HF - 0.15-0.40 Hz. The total spectral power (TP= S^{-2}/Hz), low frequency power (LFP), middle frequency power (MFP), high frequency power (HFP) and the ratio LFP/HFP were computed.

STATISTICS: Student's t-test for independent variables was used for comparing the obtained mean groups values of normotensive and hypertensive subjects. Significant differences in baseline variables between the groups were taken into account by means of covariance when comparing the measures of SBP and DBP between hypertensive and normotensive subjects. The associations between measures of SBP or DBP and the other variables were analyzed by a sample correlation procedure. The variables that had a significant univariate relation to the levels of SBP and DBP were assessed by stepwise linear multiple regression analysis.

RESULTS

All obtained mean groups values ± SEM are presented in table 1. The major part of the followed up parameters showed statistically significant difference when compare normotensive with hypertensive subjects. This is confirming the reliability of the experimental procedure.

The obtained by multiple step regression analysis coefficients of correlation are:

- SBP – $ASC_{IBIV-SBPV}$: r = -0.8776; p<0.001; SBP – $ASC_{IBIV-DBPV}$: r = -0.9106; p<0.001;
- DBP - $ASC_{IBIV-SBPV}$: r = -0.9015; p<0.001; DBP – $ASC_{IBIV-DBPV}$: r = -0.8767; p<0.001.
- SBP – $PSC_{IBIV-SBPV}$: r = -0.9000; p<0.001; SBP – $PSC_{IBIV-DBPV}$: r = -0.9198; p<0.001;
- DBP - $PSC_{IBIV-SBPV}$: r = -0.8911; p<0.001; DBP – $PSC_{IBIV-DBPV}$: r = -0.9212; p<0.001.

The model fitting results for SBP or DBP (≡ y) give the following ratios:

1. $y = 230{,}07 - 24{,}34.x_1 - 59{,}41.x_2 - 0{,}34.x_3 - 0{,}62.x_4 + 5{,}11.x_5 - 0{,}51.x_6 + 0{,}61.x_7$; where: y = SBPV; $x_1 = ASC_{IBIV-SBPV}$; $x_2 = ASC_{IBIV-DBPV}$; $x_3 = PSC_{IBIV-SBPV}$; $x_4 = PSC_{IBIV-DBPV}$; $x_5 = LFP_{IBIV}/HFP_{IBIV}$; $x_6 = TP_{SBPV}$; $x_7 = TP_{DBPV}$;
2. $y = 153{,}63 - 24{,}6.x_1 - 13{,}24.x_2 - 0{,}19.x_3 - 0{,}43.x_4 - 0{,}6.x_5$; where: y = DBPV; $x_1 = ASC_{IBIV-SBPV}$; $x_2 = ASC_{IBIV-DBPV}$; $x_3 = PSC_{IBIV-SBPV}$; $x_4 = PSC_{IBIV-DBPV}$; $x_5 = TP_{SBPV}$.

By means of ANOVA analysis (at F-Ratio = 178.175 and p<0.001 for the significance of this model) it was settled down that 92.65% of the changes in y = SBPV and 92.09% in y = DBPV are due to the changes in x.

According to t-values, the main predictors of SBP are: $ASC_{IBIV-DBPV}$, $PSC_{IBIV-DBPV}$ and $PSC_{IBIV-SBPV}$ (t-values = -4.59, -2.45 and -1.81; sig. levels = 0.00, 0.016, 0.072) whereas the main predictors of DBP are: $ASC_{IBIV-SBPV}$, $PSC_{IBIV-DBPV}$ and $TP_{IBIV-SBPV}$ (t-values = -3.57, -3.20 and -3.07; sig. levels = 0.00, 0.002, 0.003).

The amplitude and phase coherence in cross-spectrum between inter-beat intervals and systolic blood pressure in four persons (normrotensive, with I-st, II-nd and III-rd stage of hypertension) are presented in fig.2.

DISCUSSION

The obtained results suggested that a discrepancy between the activity of the both parts (the cardiac and the vascular), of the cardiovascular center is possibly to exist being the cause or the consequence of hypertension. This phenomenon is the physiological basis of Danev's model for developing of hypertension. According to this model the chronic stress provokes a long-term lasting augmentation of the overall sympathetic tone. In some persons this process can engage predominantly the vasoconstricting part of the cardiovascular regulatory centers, whereas the cardiac activity remains almost unchanged. This is why we actually do not find any relationship between the stage of hypertension and heart rate. The pathogenetical mechanism of hypertension probably includes also a decreased effectiveness of the negative feed-backs taking part in the neurovegetative vascular brain control, as an outcome of the decreased baro- and beta-receptor sensitivity. Parati et al. (9) and Pagani et al. (10) found that the arterial baroreceptor sensitivity is much lower in hypertensive than in normotensive subjects for each hour of the 24 hours lasting following up. So why the chronically increased sympathetic drive found in hypertensives is predominantly vascular than cardiac oriented, which coincides with clinical data. The reliability of this model can be confirmed if hypertension is accompanied by a more increased LFP/HFP ratio of SBPV and DBPV when compare with the same values for IBIV, because LFP spectral band is sympathetically modulated (11). Our results coroborate such a confirmation.

It was reported from Guzzetti et al. (2) that, essential hypertension is characterized by a increase low-frequency power (defined as the power around 0.1 Hz) and a decreased high-frequency power of IBIV during supine rest, what is coinciding with our data.

As can be seen from fig.2 the ASC and PSC between IBIV and BPV spectra decrease with the level of hypertension, but it is disputable if this phenomenon possess the potency to predict progressing of hypertension. There exists some lack of knowledge about the basic question: is the decrease of SC preceding or just accompanying the hypertension. This problem can be resolved by a further longitudinal following up of groups of borderline normotensive persons being at high level of risk for hypertension according to SC data. From table 1 it can be seen that such a possibility is very probable.

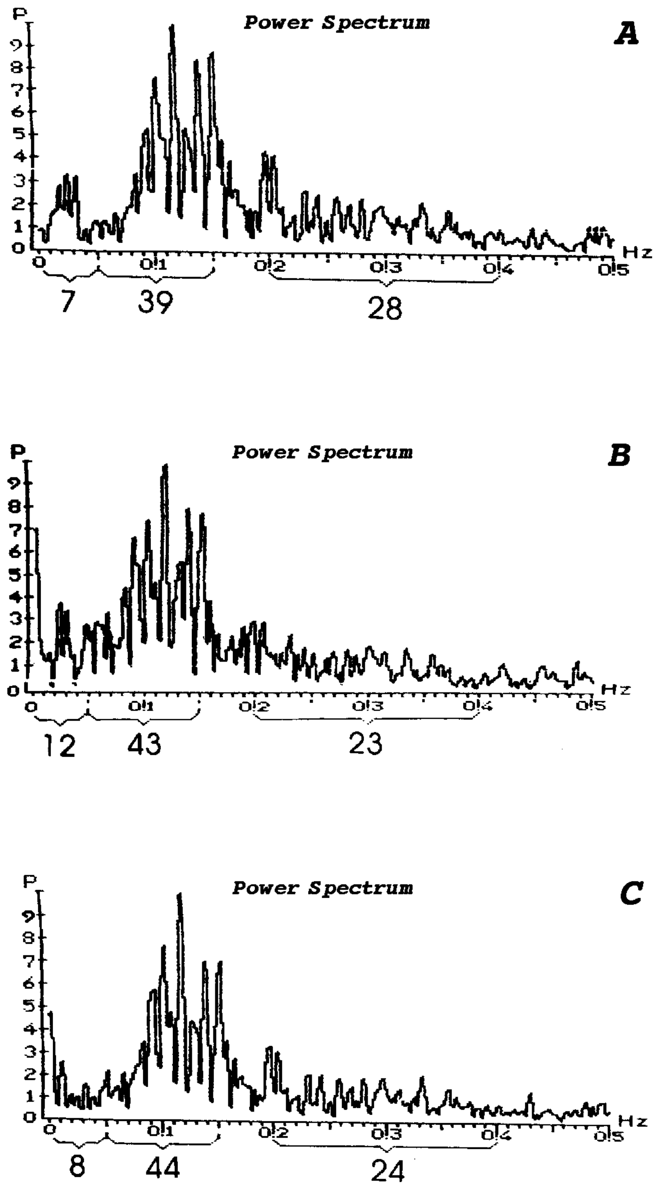
The higher level of SC found in normotensives when compare with hypertension, is confirming the proposed by us model, because the best way to assess the discrepancy between the activity of cardiac and vascular parts of the cardiovascular centers is the SC between IBIV and BPV.

REFERENCES

1. **Julius, S., Schork, M.A.:** Predictors of hypertension. Annals of the New York Academy of Science 304, 1978, 38-42.
2. **Guzzetti, S., Piccaluga, E., Casati, R., Cerutti, S., Lombardi, F., Pagani, M., Malliani, A.:** Sympathetic predominance in essential hypertension: a study employing spectral analysis of heart rate variability. J. Hypertens. 6, 1988, 711-717.
3. **Dassi, S., Balsama, M., Guzzetti, S., Ponti, G.B., Magni, L., Pagani, M., Malliani, A.:** Twenty-four hour power spectral analysis of heart rate variability and of arterial pressure values in normotensive and hypertensive subjects. J. Hypertens. 9, Suppl 6, 1991, S72-S73.
4. **Pagani, M., Lombardi, F., Guzzetti, S., Sandrone, G., Rimoldi, O., Malfatto, G., et al.:** Power spectral density of heart rate variability as an index of sympato-vagal interaction in normal and hypertensive subjects. J. Hypertens. 2, 1984, 383-385.
5. **Levy, M.N.:** Autonomic interactions in cardiac control. Ann. N.Y. Acad. Sci. 601, 1990, 209-221.
6. **Datzov, E., Danev, S., Svetoslavov, S.:** Stress evaluation: comparative assessment of the spectra of basic physiological functions. Acta Med. Bulg. 24, 1, 1997, 47-53.
7. **Danev, S., Datzov, E., Svetoslavov, S.:** Pharmacologically induced sympathetic or parasympathetic influence upon cross spectrum of basic physiological functions. Comptes Rendus de l'Akademie Bulgare des Sciences 51, 2, 1998.
8. **Penaz, J.:** Photo-electric measurement of blood pressure, volume and flow in the finger. In: Digest of the 10-th International Conference on Medical and Biological Engineering, ed. Albert, R., Vogt, W., Helbig, W., Dresden, 1973, 104-111.
9. **Parati, G., Omboni, S., Frattola, A., Di Rienzo, M., Zanchetti, A., Mancia, G.:** Dynamic evaluation of the baroreflex in ambulant subjects. In: **Di Rienzo, M., Mancia, G., Parati, G., Pedotti, A., Zanchetti, A. (Eds)** Blood pressure and heart rate variability. Amsterdam, Netherlands: IOS Press, 1992, 123-137.
10. **Pagani, M., Somers, V., Furlan, R., Dell'Orto, S., et all.:** Changes in autonomic regulation induced by physical training in mild hypertension. Hypertens. 12, 1988, 600-610.
11. **Akselrod, S., et all.:** Hemodynamic regularion: investigation by spectral analysis. Am. J. Physiol. 249,1985, 867-875.

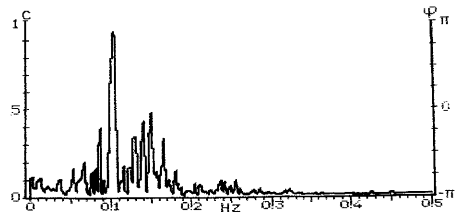
PARAMETERS	NORMOTENSIVES n=31	HYPERTENSIVES		
		I stage n=27	II stage N=25	III stage n=24
Heart Rate (b/m)	74.3 ± 1.5	76.2 ± 2.1 ns	72.8 ± 1.5 ns	71.9 ± 1.1 ns
IBIV (ms)	38.3 ± 1.4	33.9 ± 2.4 ns	29.6 ± 1.8 ns	22.3 ± 1.4 *
SBP (mm Hg)	123.3 ± 1.5	151.1 ± 1.4 **	177.2 ± 2.0 **	203.4 ± 1.9 **
DBP (mm Hg)	72.2 ± 0.7	90.3 ± 0.7 **	105.8 ± 1.4 **	117.4 ± 1.9 **
TP_{IBIV} (s^{-2}/Hz)	47.6 ± 1.3	44.8 ± 1.3 ns	44.2 ± 1.9 ns	39.6 ± 1.6 *
TP_{SBPV} (s^{-2}/Hz)	41.5 ± 0.6	37.9 ± 1.0 *	30.5 ± 0.8 **	24.8 ± 0.9 **
TP_{DBPV} (s^{-2}/Hz)	41.7 ± 0.02	35.5 ± 0.5 *	31.0 ± 0.7 *	23.3 ± 0.9 **
LFP/HFP_{IBIV} (a.u.)	0.8 ± 0.02	1.0 ± 0.02 ns	1.1 ± 0.02 ns	1.9 ± 0.08 *
LFP/HFP_{SBPV} (a.u.)	0.6 ± 0.02	1.0 ± 0.02 *	1.2 ± 0.04 **	1.8 ± 0.06**
LFP/HFP_{DBPV} (a.u.)	0.9 ± 0.02	1.1 ± 0.02 ns	1.2 ± 0.04 *	1.7 ± 0.06 **
$ASC_{IBIV-SBPV}$ (K)	0.8 ± 0.02	0.6 ± 0.02 **	0.5 ± 0.02 **	0.4 ± 0.02 **
$ASC_{IBIV-DBPV}$ (K)	0.9 ± 0.02	0.7 ± 0.02 **	0.5 ± 0.02 **	0.4 ± 0.02 **
$PSC_{IBIV-SBPV}$ (Rad)	3.9 ± 0.1	2.8 ± 0.2 ns	2.1 ± 0.3 ns	0.9 ± 0.06 *
$PSC_{IBIV-DBPV}$ (Rad)	3.4 ± 0.05	2.3 ± 0.3 ns	1.5 ± 0.1 *	0.8 ± 0.04 **

Student's "t" test for independent variables:
* $p < 0.05$ when compare with normotensive
** $p < 0.01$ when compare with normotensive

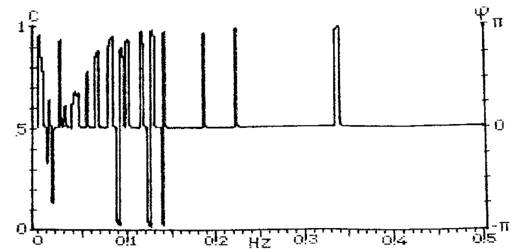

Power Spectrum
A
P
Hz
7
39
28
Power Spectrum
B
P
Hz
12
43
23
Power Spectrum
C
P
Hz
8
44
24

A **B**

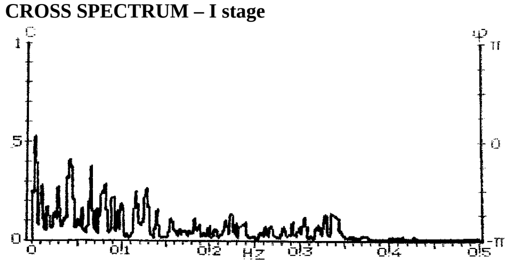
CROSS SPECTRUM – normotensive



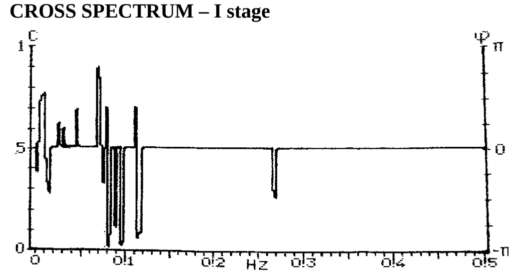
CROSS SPECTRUM - normotensive



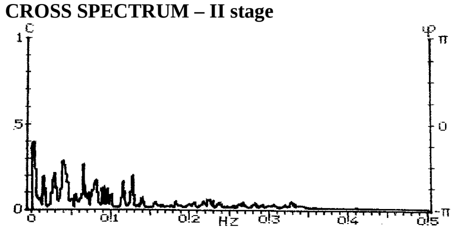
CROSS SPECTRUM – I stage



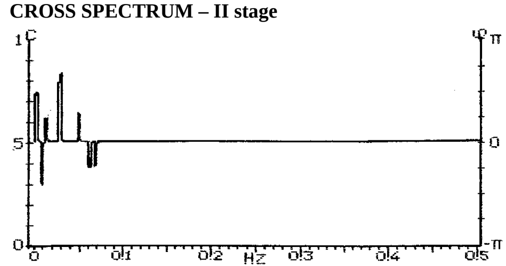
CROSS SPECTRUM – I stage



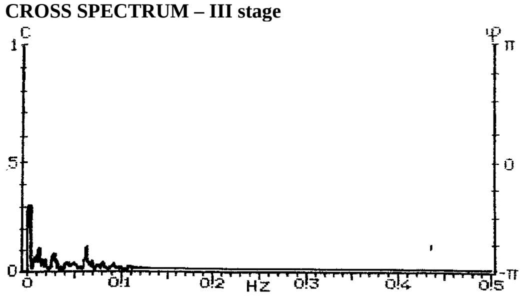
CROSS SPECTRUM – II stage



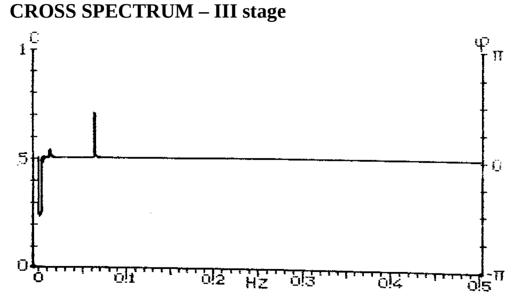
CROSS SPECTRUM – II stage



CROSS SPECTRUM – III stage



CROSS SPECTRUM – III stage



Legends for tables and figures.

Table 1. Mean groups values ± S.E.M. of the followed up parameters.

Fig.1. Power density spectra of: A. IBIV; B. SBPV; C. DBPV.

Fif.2. Amplitude (A) and phase (B) coherence in cross-spectrum between inter-beat intervals and systolic blood pressure in four persons - normotensive, with I-st, II-nd and III-rd stage of hypertension.

Table 1.

Fig. 1