Effects of +Gz acceleration on indices of heart rate variability

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ABSTRACT

The effect of +Gz acceleration on autonomic control of heart was assessed using time and frequency domain analysis of Heart Rate Variability (HRV) in an experiment involving centrifugation of 17 healthy male subjects at +3Gz. The procedure resulted in a significant decrease in all the time domain indices of HRV (namely, variance, SDNN, pNN50 and RMSSD) suggesting a reduction in parasympathetic influences. Amongst the frequency domain indices of HRV, total spectral (0.04-0.40 Hz) and HF (0.15-0.40 Hz) power exhibited a significant reduction during centrifugation. LF (0.04-0.15 Hz) showed a significant increase. However, the latter was appreciable only when it was normalized to total power. LF/HF ratio increased significantly during centrifuge run. Both time and frequency domain indices reverted back to 'resting-sitting' values almost immediately (within the first minute) after the run. There was a significant increase in heart rate during centrifuge run. During recovery, heart rate attained a value which was significantly lower than that observed in resting-sitting. This 'overshoot' could be reasonably attributed to psychological excitation of subjects before exposure to centrifuge run. Additionally, a leftward shift of the 'peak power frequency' (the frequency around which maximum power was concentrated) in the LF band was seen during centrifuge run signifying a change in the responsiveness of the sympathetic effector organs.

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Head-ward acceleration (+Gz) in military aviation environment imposes a physiological (and also psychological) stress, like none other. +Gz acceleration causes immediate major changes in the distribution of pressure in the arterial and venous systems. These early disturbances evoke reflex compensatory changes which tend to reduce the magnitude of the initial effects [1].

The modulation of the response of the circulatory system to headward acceleration alters the dynamic balance between the sympathetic and parasympathetic control mechanisms. Simultaneous assessment of sympathetic and

vagal nerve activities on cardiovascular regulation during exposure to +Gz is possible by parameters derived from analysis of Heart Rate Variability (HRV). Analysis of beat-to-beat variability of heart rate has been stated to represent one of the promising quantitative markers of autonomic activity [2].

The present study addresses specifically to the behaviour of the two branches of Autonomic

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Nervous System (ANS) during human centrifugation with an aim to study the autonomic control of heart rate using both time and frequency domain analysis of HRV during +Gz acceleration. It was also intended to find out if HRV indices could be useful in providing information additional to what was generally available through the examination of heart rate alone.

Material and Methods

A total of 17 subjects with mean age 29 ± 4 years (range 23-34 years) participated in this study. They were all males, with a mean height of 170 ± 4 cm (range 164-178 cm) and weight 68 ± 6 kg (range 57-79 kg). The subjects were ascertained to be healthy after a thorough clinical examination and resting ECG. They were subjected to +3Gz acceleration in a human centrifuge at the Department of Acceleration Physiology at Institute of Aerospace Medicine (IAM), Indian Air Force after approval of the Ethical Committee at the Institute. An informed consent was obtained.

The subjects were instructed to abstain from smoking and caffeine for 2 hr and alcohol for 36 hr prior to the experiment, have adequate rest, get at least 8 hours of uninterrupted sleep on the night prior to the experiment, have a normal breakfast on the morning of the experiment and to void urine prior to the centrifuge run. All runs were conducted between 1030 to 1300 h.

After comfortable strapping and rest for 5 min in the gondola, ECG was recorded using disposable Ag/AgCl electrodes in standard lead II configuration. Respiratory rate and blood pressure were also measured. These recordings served as 'Resting-Sitting' values. The subjects were then exposed to +3Gz acceleration. They remained at +3Gz for a total duration of 1 minute (time of onset and offset excluded). The onset

rate was 1 G/sec. The rate of offset was 1G/sec until 2G, 0.5G/sec until 0.5G and 0.1G/sec until halt. A continuous recording of ECG signal was done from the start of the run until 1 min during recovery. From this recording, suitable sections of 50 sec each were taken out leaving behind the time of onset, initial 10 sec at peak G and offset. These two recordings were designated as 'Run' and 'Recovery 0 min'. This was followed by two more 50 sec recordings at 5th and 10th min ('Recovery 5 min' and 'Recovery 10 min' respectively).

The subjects were monitored on close circuit TV screen for respiratory rate and any possible discomfort or motion sickness during the runs. The subjects were instructed to be as still and relaxed as possible while the ECG recording was done in order to obtain a noise free recording and was not given any task to perform while in gondola. It was ensured that the temperature of the gondola was comfortable by keeping the gondola door open before and after the run.

ECG data in standard lead II configuration was acquired using portable ECG acquisition equipment (Niviqure Meditech Systems, Bangalore, India). This system is a multi-channel digital data acquisition system. It consists of a module with capabilities for real time capture and display of two channels of data. The system comprises of a package that processes acquired data from a custom-built, portable, biomedical electronic digital acquisition system (battery operated) which can be kept in the subject's pocket. It is capable of storing digital data sampled between frequencies varying from 100 to 1024Hz. ECG signals are stored in the memory in form of time blocks of 2 sec each. The signals are then downloaded to the computer for 'off-line' analysis.

ECG sampling rate was 1024 Hz using a microprocessor chip with 12 bit resolution, suitably filtered, amplified, digitized and stored on a computer. After examination of ECG waveform for any artifacts or ectopics, a manual computation of successive RR intervals was resorted to. This series of RR intervals was subjected to both time domain and frequency domain analyses.

From the original R-R interval sequence, the mean R-R interval (RR), standard deviation (SD), root mean squared difference of successive intervals (RMSSD), the number of successive R-R intervals that differed by more than 50 ms (NN50) and their proportion to total number of beats analysed (pNN50), were calculated manually.

Sequence of R-R intervals was converted into an evenly spaced time series by spline interpolation at 250 ms (4 Hz). Power spectral estimates were computed using both parametric as well as non-parametric methods. In the parametric method, spectral analysis was done by maximum entropy method (MEM), which is known to provide a much greater spectral resolution and is specially suited for the spectral analysis of relatively short data records. Autoregressive coefficients were computed using forward-backward approach. Model order was estimated by minimizing Akaike information criterion [3]. Mean model order was 21 ± 13 . Spectral estimation was done with 'PMEM' command using Matlab® version 5.1.0.421. Frequency resolution was 0.02Hz. Nonparametric estimation involved averaged periodogram method of Welch. In this method, entire data length is divided into overlapping sections, each section is detrended and Fast Fourier transformed and periodogram values are averaged. In the present study, a data length of

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50 seconds was analyzed wherein it was divided into overlapping sections of 175 data points each (43.7 sec) with an overlap at 97 percent. A Hanning window was used. Frequency resolution was 0.023 Hz.

Spectral estimates of RR intervals were calculated in both the methods by integrating the power as total power from 0.04 to 0.40 Hz, LF power from 0.04 to 0.15 Hz, HF Power from 0.15 to 0.40 Hz. Additionally, the frequencies, at which the peaking of power in LF band of the spectra occurred, were also noted. These were designated as 'Peak Power Frequency' and 'Peak LF Power'. Power contained in VLF band was not calculated because of its dubious physiologic significance [2].

The data was analyzed using Wilcoxon matched pairs test. This statistic was chosen because of significant departures of most of the data from normality as ascertained through Shapiro-Wilk's 'W' test. Significance was accepted at p<0.05. All values are presented as mean±SD.

Results

Values of RR intervals (and heart rate), respiratory frequency and results for time domain analyses are presented in Table 1. The results of frequency domain analyses using Welch's averaged periodogram method and Maximum Entropy Method are given in Tables 2 and 3, respectively. Power spectra averaged across all the subjects are given in Fig 1. The changes in power around the centrifuge frequency and peak power frequency (with the corresponding value of power) in LF are shown in Table 4.Values of RR intervals and respiratory frequency are repeated in each table so that changes in HRV indices can be appreciated in the light of changes in these variables.

	Resting- Sitting	During Run	Recovery		
			0 min	5 min	10 min
RR Intervals (ms)	750±134*	545±103	706±142*#	788±111*#	791±108*#
Heart Rate (bpm)	83±16*	114±25	84±22*#	76±11*#	75±10*#
Total Variance (ms ²)	4716±3888*	1860±1305	6508±5877*	2872±2424 [#]	3342±2393
SDNN (ms)	63±25*	40±16	74±34*	49±22	53±23
NN50	11±8*	2±3	11±10*	10±8*	10±8*
pNN50	18±14*	2±3.5	19±19*	17±14*	17±14*
RMSSD (ms)	55±29*	21±9	49±27*#	44±23*#	46±22*#

Table 1: RR interval and time domain HRV indicesResting-Sitting, during centrifuge run and recovery (n=17)

Table 2: RR intervals and frequency domain HRV indices (Welch's Method)Resting-Sitting, during centrifuge run and recovery (n=17)

	Resting- Sitting	During Run		Recovery	
			0 min	5 min	10 min
RR Intervals (ms)	750±134*	545±103	706±142*#	788±111*#	791±108*#
Respiratory Frequency	15±1.3*	17±1.2	16±1.7*	16±1.3*	16±0.95*
(per minute)					
Total power	5556±5504*	1637±1728	3914±4180*#	2825±2066*#	4442±4324*
(0.04-0.50 Hz) (ms ²)					
LF Power	2992±3323*	1073.5±1069	1330±1226#	1356±993 [#]	2373±2139*
(0.04-0.15 Hz) (ms ²)					
HF Power	2564±2391*	563.5±802	2583±3658*	1469±1198*#	2069±3380*
(0.15-0.50 Hz) (ms ²)					
LF Power Normalized	52±15*	65±18	42±24*	49±13*	57.5±19
HF Power Normalized	48±15*	35±18	58±24*	51±13*	42.5±19
LF/HF	1.37±1*	3.33±3.9	1.59±2.6*	1.09±0.5*	1.86±1.4

* Significantly different from corresponding values during run

Significantly different from resting-sitting values

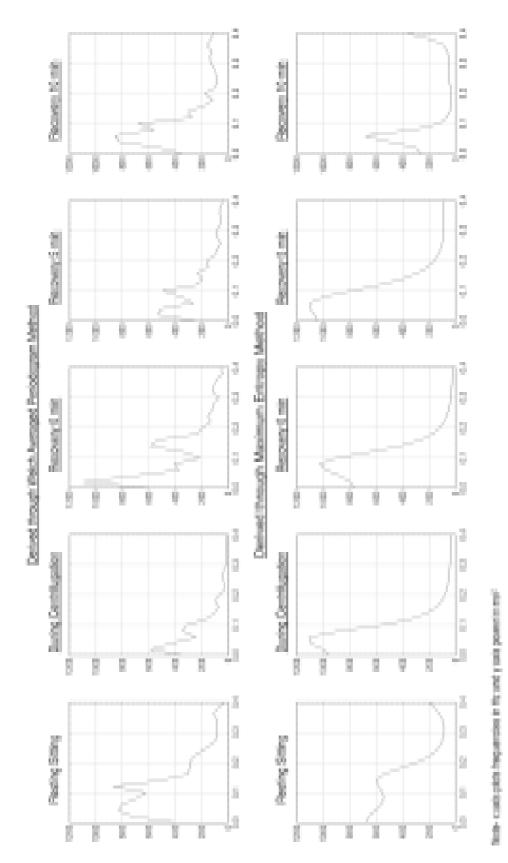


Fig 1 : HRV Power Spectra averaged across subjects

+Gz and HRV:Pipraiya, Tripathi & Dogra

	Resting & Sitting	During Run		Recovery	
			0 min	5 min	10 min
RR Intervals (ms)	750±134*	545±103	706±142* [#]	788±111* [#]	791±108*#
Respiration Frequency	15.7±1.3*	17.6±1.2	16.4±1.7*	16.3±1.3*	16.1±0.95*
(Per minute)					
Total power	5932±5729*	1726±1666	5525±4306*	3898±3630*	4516±3777*
(0.04-0.50 Hz) (ms ²)					
LF Power	3261±3423*	1159±1043	2652±1721*	2142±1949*	2744±2943*
(0.04-0.15 Hz) (ms ²)					
HF Power	2672±2671*	566±766	2873±3354*	1755±1755*#	1771±1601*
(0.15-0.50 Hz) (ms ²)					
LF Normalized	57±14*	68±14	56±19	52±11*	55±17*
HF Normalized	43±14*	32±14	44±19	48±11*	45±17*
LF/HF	1.54±0.8*	2.76±1.7	1.85 ± 1.9	1.22±0.6*	1.66±1.3* [#]
Peak Frequency	$0.088 \pm 0.04*$	0.051 ± 0.02	0.071 ± 0.03	$0.088 \pm 0.04*$	$0.079 \pm 0.03*$
in LF Band (Hz)					
Peak Power	1145±1534*	479±378	1307±1283*	646±553	`927±1078
in LF Band (ms ²)					

Table 3: RR intervals and frequency domain indices of HRV (Maximum Entropy Method)Resting-Sitting, during centrifuge run and recovery (n=17)

Table 4: Respiratory frequency, power around centrifuge frequency and peak powerfrequency in LF band: Resting-Sitting, during centrifuge run and recovery (n=17)

	Resting- During Sitting Run		Recovery			
Respiratory Frequency (per minute)	15±1.3*	17±1.2	0 min 16±1.7*	5 min 16±1.3*	10 min 16±0.95*	
Power around Centrifuge frequency (ms ²)	440±450	69±101	426±520*	325±321*	688±1565*	
Power around Centrifuge (Normalized)	9±7	8±9	13±9	11±7	12±11	
Peak Frequency in LF Band (Hz)	0.088±0.04*	0.051±0.02	0.071 ± 0.03	0.088±0.04*	0.079±0.03*	
Peak Power in LF Band (ms ²)	1145±1534*	479±378	1307±1283*	646±553	927±1078	

*Significantly different from corresponding values during run # Significantly different from resting-sitting values Results of the present study indicate that mean RR interval decreased from its resting sitting value of 750 ± 134 ms to 545 ± 103 ms at +3Gz. This translates in terms of an increase in heart rate by 32 ± 14 bpm from its resting value of 83 ± 16 bpm to 114 ± 25 bpm during centrifuge run. All these changes are significant and comparable to those reported in the literature for this level of acceleration [4,5]. This decrease in RR interval is reported to be due to sympathetic stimulation in response to hypergravity (the acceleration) as a stressor and is mediated by a baroreceptor compensatory reflex to a reduced arterial blood pressure at the site of carotid sinus and decrease in cardiac output [5].

After the centrifuge run, RR interval increased and attained a value which was significantly higher than in resting-sitting. In other words, heart rate during recovery attained a value which was significantly lower than resting-sitting value. This 'overshoot' effect was observable in the 0 min of recovery and persisted till 10th min (of recovery). It is in consonance with what is reported by others as well [6]. Apparently, there can be two explanations for this 'overshoot': first, an increase of RR interval (decrease in heart rate) due to a shift of sympathovagal interaction in favour of parasympathetics and second, settlement of pre-exposure psychologic excitement of subjects. This might have resulted into higher than 'baseline' values during resting-sitting. However, recovery pattern of HRV parameters did not follow similar pattern. All HRV indices settled down in the '0' min of recovery and there was no 'overshoot' (vide infra). This lends support to the latter hypothesis.

All the time domain measures of HRV (e.g.,

SDNN, Variance, pNN50 and RMSSD) exhibited a significant change during centrifuge run compared to resting values. All these variables estimate predominantly high frequency variation in heart rate [2]. Following the centrifuge run, all these time domain parameters of HRV reverted back to resting values in '0' min of recovery. No other information was evident from these time domain indices of HRV.

Total power exhibited changes similar to variance. This was expected because variance is the time domain counterpart of total spectral power. However, it is to be appreciated that the values of variance (Table 1) and total spectral power (Tables 2 and 3) observed in the present study are not identical because of transformations of RR interval sequences (e.g., interpolation, windowing etc.).

LF power, expressed in absolute terms (ms²) showed a significant reduction during centrifuge run compared to resting-sitting. This, at first instance, seems paradoxical in view of the expected increase in the sympathetic activity. When the values were normalized relative to total spectral power, a significant increase was identified. This reiterates that, for an appropriate appreciation of various autonomic modulations, it is necessary to normalize the component power to avoid the confounding influence of change in total power [2]. HF power, on the other hand, showed a significant decrease during run compared to resting-sitting value. This was apparent when the power was expressed in absolute as well as normalized terms. Recovery of all the spectral measures followed the same temporal pattern as seen in case of time domain indices (values reverted to normal during '0' min of recovery).

Task Force of European Society of

Cardiology and North American Society of Pacing and Electrophysiology [2] recommends that for short-term physiologic studies, ECG recorded over a period of 2-5 min should be analyzed. However, the above recommendation of the task force is principally for standardization. Technical considerations do permit a meaningful spectral analysis from a signal recorded for as short a period as twice the period of the slowest frequency component of interest. In the present study, the slowest frequency component analyzed was 0.04 Hz corresponding to a period of 25 sec. Therefore, a recording period of 50 sec was considered adequate. Published reports are available in standard, peer reviewed psychophysiologic texts, using a comparable or even a smaller period of recording [7,8]. Because of this constraint, spectral estimation was made also with a nonlinear technique (viz., Maximum Entropy Method) [9].

There could be three reasons which explain the above noted changes in heart rate variability parameters:-

(a) A change in the breathing frequency from resting-sitting to centrifugation.

(b) Entrainment of power spectra with centrifuge

frequency (0.38 Hz).

(c) An increase in sympathetic and/or decrease in parasympathetic influences.

Respiration is known to be a confounding factor in the spectral analysis of HRV [10,11,12]. During centrifuge run, a significant increase (of 12.5%) in the breathing rate was observed. It increased from 16±1 breath per min during restingsitting to 18 ± 1 during centrifuge run (p<0.05). It was interpretable as a change from 0.26 Hz during resting-sitting to 0.29 Hz during centrifugation. Glaister [13] reported an increase of 18% in the breathing frequency during a +3Gz run. An increase in the respiratory frequency has been reported to reduce the total power [10,11,12]. It can be argued that this change in respiratory frequency accounts, at least partially, for a reduction in all the time and spectral domain measures (in absolute terms) of HRV.

However, a closer examination reveals that the extent of reduction in these measures observed in the present study was much more than could be explained due to an increase in respiratory frequency. It can be regressed from the data of Schipke et al. [11] and Stark et al. [12] that a change of respiratory frequency from 0.26 Hz to

Table 5:	Effect of breathing frequency on HRV spectral power and i	ts constituents
	Schinke et al. (1999) (n=15)	

0.03 Hz 0.08 Hz 0.10 Hz 0.13 Hz 0.25 Hz 0.50 Hz LF Power (ms²) 570 ± 290 609 ± 337 692 ± 354 615 ± 336 412 ± 184 399 ± 221 HF Power (ms²) 468 ± 343 436 ± 386 496 ± 364 482 ± 371 596 ± 529 437 ± 432		Sempke et al. (1999) (ll 15)					
		0.03 Hz	0.08 Hz	0.10 Hz	0.13 Hz	0.25 Hz	0.50 Hz
HF Power (ms ²) 468 ± 343 436 ± 386 496 ± 364 482 ± 371 596 ± 529 437 ± 432	LF Power (ms ²)	570±290	609±337	692±354	615±336	412±184	399±221
	HF Power (ms ²)	468±343	436±386	496±364	482±371	596±529	437±432

Stark et al. (2000) (n=40)						
0.15 Hz 0.20 Hz 0.25 Hz 0.30 Hz						
LF Power log (ms ²)	3.34	2.66	2.61	2.64		
HF Power log (ms ²)	3.03	2.84	2.59	2.42		

0.29 Hz, observed in the present study, will lead to a reduction in total power merely by 2.6-7.5% (Table 5).

Additionally, in the study by Schipke et al. [11], subjects were in supine position. Effects of breathing on spectral power are likely to be further attenuated during sitting/standing postures and centrifugation due to disappearance of vagal motoneurone responsiveness explained on account of respiratory gating [14]. Therefore, a reduction in spectral power and variance cannot be explained solely on the grounds of an increase in the breathing frequency.

Not withstanding the above, the spectral power in low frequency band is reported not to be influenced to any significant extent due to variations of breathing rate in the frequency range in which the analysis of HRV was done in the resent study. For example, Schipke et al [11] and Stark et al. [12] have reported an insignificant change in low frequency power during a shift in breathing frequency from 0.15 Hz to 0.20 Hz during metronomic breathing. Therefore, it can be reasonably construed that absolute values of low frequency power are definitely free from the confounding effect of respiration.

Entrainment of HRV power spectra of nonlinear physiologic signals with stimulus frequency is a well-recognized phenomenon [15]. Non-linear phenomena determined by complex interaction of haemodynamic, electrophysiological and humoral variables as well as by the autonomic and the central nervous system regulations, are believed to be involved in the genesis of HRV [2]. Entrainment of power spectrum was expected from centrifuge frequency (23 rpm or 0.38 Hz). This aspect was examined through a visual inspection of spectra as well as by comparing power in a frequency band from 0.35 to 0.41 Hz (around centrifuge frequency which was 0.38±0.03 Hz). The HRV spectrum derived through autoregressive (MEM) method clearly ruled out any entrainment on visual inspection. Power around centrifuge frequency, when normalized with respect to total power, was found not to be significantly different during run compared to resting- sitting or during recovery.

From the above, it appears that an increase in sympathetic and a decrease in parasympathetic influences is the only plausible explanation for the changes that are seen during centrifugation in this study. This inference is further supported from a concomitant decrease in RR (increase in the heart rate).

Additional information from LF spectral power

The present study also examined any shift in the frequency around which maximum power was concentrated in the LF band. According to the resonance theory of low-frequency RR interval rhythms, the sinoatrial node and arteriolar response to brief sympathetic stimulation develop and dissipate slowly with a total period of about 10 sec [16]. Therefore, a single sympathetic burst or a brief volley of sympathetic bursts can initiate a cycle of rising and falling arterial pressures and decreasing and increasing sympathetic nerve activities at about 0.1 Hz. It was conceived that a shift of 'peak power frequency' would indicate a change in the time constant of effector responses. Alternatively, it could also indicate a change in the pacemaker frequency [17].

The frequency around which maximum power was concentrated changed from 0.08 ± 0.04 Hz in resting-sitting to 0.051 ± 0.02 Hz during centrifugation. This represented a significant

change in the responsiveness of effectors. However, Cooke et al [17] did not observe any change in the center frequency of LF spectrum during graded head up tilt up to 80° in humans despite a significant change in power. The authors argued that the level of arterial baroreceptor input modulated intensity but not center frequency of spectrum. This is at variance with the findings of present study. It is difficult to comment on this difference based on the present experimental design. However, it could be because of a different nature of the stress (different from 80° tilt). Since a change of center frequency is also interpreted as an alteration in responsiveness of effector organs, this parameter seems to have great potential in examining baroreflex responsiveness after single/multiple +Gz exposures. Such an exploration is much desired in the field of Aerospace Medicine. In view of the above, it needs further exploration with a simultaneous monitoring of BP variability, preferably, over longer time durations.

References

1 Glaister DH, Prior ARJ. The effects of long duration acceleration. In: John Ernsting, Nicholson AN, Rainford DJ, editors. Aviation Medicine. 3rd ed. Oxford: Butterforth-Heinemann, 1999; 128-47.

2. Malik M. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, Heart Rate Variability-Standards of Measurement, Physiological Interpretation and Clinical Use-Special Report. Circulation 1996; 93:1043-65.

.3. Akaike H. Statistical predictor identification. Ann Inst Stat Math 1970; 22: 203–17.

4. Burton RR, Arthur HS. Adaptation to acceleration environment. In: Fregley MJ, Blattis C, editors. Hand

book of physiology. 1st ed New York: Oxford University Press, 1996; 943-70.

5. Burton RR, Whinnery JE. Biodynamics: Sustained Acceleration. In: DeHart RL, editor. Fundamentals of Aerospace Medicine. 2nd ed. Philadelphia: Lea and Febiger, 1996; 201-60.

6. Parkhurst MJ, Leverett SD Jr, Shubrooks SJ. Human tolerance to high sustained +Gz acceleration. Aerosp Med 1972; 43 (7):708-12.

7. Veltman JA, Gaillard AWK. Physiological indices of workload in a simulated flight task. Biol Psychol 1996; 42: 323-42.

8. Tripathi KK. Psychophysiologic evaluation of human mental workload (disseratation). Bangalore, India. National Institute of Mental Health and Neuro Sciences: 2001.

9. Haykin S. Prediction-error filtering and maximum entropy spectral estimation. In: Topics in applied physics: Non linear methods of spectral analysis. New York: Springer-Verlag, 1979; 34: 9-72.

10. Brown TE, Beightol LA, Koh J, Eckberg DL. Important influence of respiration on human RR interval power spectra is largely ignored. J Appl Physiol 1993; 75: 2310–17

11. Schipke JD, Pelzer M, Arnold G. Effect of respiration rate on short-term heart rate variability. J Clin Basic Cardiol 1999; 2: 92.

12. Stark R, Schienle A, Walter B, Vaitl D. Effects of paced respiration on heart period and heart period variability. Psychophysiol 2000; 37: 302-09.

13. Glaister DH. Ventilation and Mechanics of Breathing. In: The effects of gravity and acceleration on lung.AGARDograph No. 133. England, Technivision services, Slough. 1970; 19-36.

14. Eckberg, DL, Orshan CR. Respiratory and baroreceptor reflex interactions in man. J Clin Invest 1977; 59: 780-85.

15. Kitney RI. The use of entrainment in analysis of the human thermoregulatory system. J Physiol 1972; 229:1043-65.

16. Wallin BG, Nerhed C. Relationship between spontaneous variations of muscle sympathetic activity and succeeding changes of blood pressure in man.

Journal of the Autonomic Nervous System 1982; 6: 293-302.

17. Cooke WH, Jeffrey BH, Alexandra AC, Tom AK, Kari UOT, Eckberg DL. Human responses to upright tilt: a window on central autonomic integration. J Physiol 1999; 517: 617-28