HEART RATE AND BLOOD PRESSURE VARIABILITY UNDER MOON, MARS AND ZERO GRAVITY CONDITIONS DURING PARABOLIC FLIGHTS

Wouter Aerts[1], Pieter Joosen[1], Devy Widjaja[1,2], Carolina Varon[1,2], Steven Vandeput[1,2], Sabine Van Huffel[1,2], and André E. Aubert[3]

[1]*Department of Electrical Engineering - ESAT, SCD-SISTA, KU Leuven, Kasteelpark Arenberg 10, B-3001 Leuven, Belgium, Email: carolina.varon@esat.kuleuven.be*

[2] *IBBT Future Health Department, Kasteelpark Arenberg 10, B-3001 Leuven, Belgium, Email: carolina.varon@esat.kuleuven.be*

[3]*Laboratory of Experimental Cardiology, Faculty of Medicine, KU Leuven, O&N I Herestraat 49, B-3000 Leuven, Belgium, Email: andre.aubert@med.kuleuven.be*

ABSTRACT

Gravity changes during partial-G parabolic flights (0g - 0.16g - 0.38g) lead to changes in modulation of the autonomic nervous system (ANS), studied via the heart rate variability (HRV) and blood pressure variability (BPV). HRV and BPV were assessed via classical time and frequency domain measures. Mean systolic and diastolic blood pressure show both increasing trends towards higher gravity levels. The parasympathetic and sympathetic modulation show both an increasing trend with decreasing gravity, although the modulation is sympathetic predominant during reduced gravity. For the mean heart rate, a non-monotonic relation was found, which can be explained by the increased influence of stress on the heart rate. This study shows that there is a relation between changes in gravity and modulations in the ANS. With this in mind, countermeasures can be developed to reduce postflight orthostatic intolerance.

Key words: parabolic flight; heart rate; blood pressure; variability; ESA.

1. INTRODUCTION

Postflight orthostatic intolerance is a phenomenon from which many astronauts suffer on their return to a normal gravitational environment. Effective countermeasures are needed to prevent this disorder of the autonomic nervous system (ANS) and the cardiovascular system (CVS). Examples can be found in the training devices of the astronauts to prevent weakening of the muscular system and in the lower body where negative pressure trousers are used to prevent a decrease of blood volume in the legs [1]. Development of countermeasures requires the understanding of how the CVS adapts to gravity changes. Many researches are dedicated to study this response of the CVS. Some of these studies use data from experiments in outer space [5, 7, 8], however, ground-based studies simulating weightlessness, are more cost-effective. These simulation possibilities are among others head-down-bedrest, head-out-of-water immersion and parabolic flights. All of these microgravity simulations have their own differences as to real microgravity, but many of the changes in human physiology induced by simulation are similar to those in real space flight [1]. In this study, parabolic flights were used to assess the heart rate variability (HRV) and blood pressure variability (BPV) during reduced gravity conditions.

Due to gravity changes during parabolic flights, body fluid hydrostatic pressure gradients arise, leading to a blood and body fluid redistribution. Within a parabolic flight, the microgravity is preceded and followed by a hypergravity phase. During this hypergravity, blood is shifted to the lower extremities, resulting in a reduction of venous return and hence stroke volume [9]. During microgravity the opposite is true [1, 4, 12]. This hemodynamic alternation will result in a parasympathetic and sympathetic modulation, via the baroreflex and cardiopulmonary reflex, leading to hemodynamic and cardiac adaptations [17]. Parasympathetic modulation is found to have a global inhibitory effect, decreasing heart rate, arterial resistance and venous tone, while the sympathetic modulation is found to have a more excitatory effect [9]. HRV and BPV are two unique tools for obtaining insight into this modulation of the cardiovascular system. HRV, derived from electrocardiogram (ECG) recordings, and BPV, derived from finger pressure measurements, can both be measured non-invasively and continuously. The sympathovagal balance of the ANS can be estimated using classical signal analysis methods in time and frequency domain, calculated in a standardized way as described in the Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology[16].

The purpose of this study is to analyse the HRV and BPV during Moon, Mars and zero gravity conditions. The hypothesis is that there is a monotonic relationship between

the HRV and BPV, and the gravity level. In studies from the Laboratory Experimental Cardiology at KU Leuven [4, 15, 17] the HRV is examined during parabolic flights as a function of the hypergravity (1.8g), normogravity (1g) and microgravity phase (0g). Other studies [10, 12] also analyzed the BPV during these gravity levels. However with the present study it is also possible to analyse the cardiovascular behaviour at intermediate gravity conditions, those from Moon (0.16g) and Mars (0.38g).

2. METHODS

2.1. Data acquisition

During the Joint European Partial-G parabolic flight campaign, gravity conditions of Moon (0.16g - 12 parabolas), Mars (0.38g - 12 parabolas) and weightlessness (6 parabolas) were simulated. Six healthy non-smoking male volunteers between 22 and 32 years of age (mean $\pm$ SD: 28 $\pm$ 5 year; stature: 181 $\pm$ 2 cm; mass: 76 $\pm$ 7 kg; BMI: 23 $\pm$ 2), were selected for this study. They were free from any cardiovascular pathology and a special flight medico-physical examination was performed at the Medical center of the Belgian Air Force, Brussels, 2 months before the flight campaign in order to pass FAA III tests. To eliminate the effects of pharmacological agents that might alter cardiovascular ANS control, neither general medication nor medication for the control of motion sickness were taken before or during the flights. One subject suffered from severe nausea during the second parabola and received scopolamine, a medication for control of motion sickness. Therefore his data are not used in this study. Another subject suffered from nausea during two parabolas and only the data obtained during these parabolas are discarded.

In these six healthy volunteers, ECG and blood pressure signals were continuously measured in sitting position. During each flight, the biomedical data of 2 subjects were collected using 2 ccNexfin monitors (BMEYE, Amsterdam, The Netherlands). Lead II ECG was recorded with gel electrodes. Blood pressure was measured with an inflatable finger cuff in combination with an infrared plethysmograph using the volume-clamp method of Finapres technology (Finapres Medical Systems, Amsterdam, The Netherlands). Acceleration data were recorded as well. The ECG signal was measured with a sampling frequency of 1000 Hz, the blood pressure was sampled at 200 Hz. Before and after each flight, baseline measurements were collected in a protocol of 10 minutes in supine, standing and sitting position each. The experiment protocol was approved in advance by the local ethical committee, the ESA Medical Board and the French authorities. Each subject provided written informed consent before participating.

2.2. Data pre-processing

A tachogram, containing the RR-intervals as a function of time, is derived from the ECG signal. First the ECG signal is transformed with Pan-Tompkins algorithm to a signal with enhanced R-peaks. The R-peaks of the QRS complexes are detected, using an adaptive thresholding algorithm with a blanking period [14, 18]. A search back procedure is implemented, in order to correct for missing R-peaks. The time difference between two successive R-peaks determines the RR-interval, which is the reciprocal of the instantaneous heart rate.

The blood pressure is pre-processed to obtain a systogram and a diastogram, which are the systolic blood pressure (SBP) and diastolic blood pressure (DBP) values as a function of time. These blood pressure values were obtained by filtering the blood pressure signal with a high pass filter and using an adaptive thresholding algorithm to detect the SBP values. The DBP values were found as the minima of the blood pressure between two successive SBP values. The blood pressure signal contains some calibration periods, needed to estimate the unloaded diameter of the finger artery for the Finapres technology, using two constant pressure levels. Within these calibration periods the blood pressure signal is interpolated using a third order cubic spline on time instances determined via forward and backward extrapolation.

Fig. 1 shows an example of the segmentation of a Moon parabola. Different phases can be distinguished: a normogravity phase before the start (phase 1) and one after the end of the parabola (phase 5), a hypergravity phase before (phase 2) and one after (phase 4) the reduced gravity phase (phase 3). Each phase has a certain duration, of which the mean duration and the range is given in Tab. 1. To analyse the HRV and BPV as function of the gravity, a fixed window of 20 seconds is chosen. A smaller window would lead to less data for the calculation, while the length of this window is limited by the duration of the reduced gravity phase of the zero gravity parabolas, as shown in Tab. 1. Due to the small duration of phase 2 and phase 4, only phase 1, 3 and 5 are considered in the analysis. The middle part of the reduced gravity phase is chosen.

2.3. Data analysis

The influence of the gravity on HRV and BPV will be assessed by computing several indices which characterize the variability. The time domain indices are the mean, the standard deviation (std) and the root mean square of the squared differences (rmssd), calculated as described in [16]. The frequency domain indices include: the normalized high frequency (HFnu), the normalized low frequency (LFnu) component and their ratio (LF/HF). HFnu is calculated as HF/(LF+HF) and LFnu is calculated as LF/(LF+HF). These LF and HF components are calculated as the integral of the power spectral density (PSD) in specific bands, from 0.05 Hz to 0.15 Hz for LF, and

Table 1. Mean duration and range of the different phases.

	Mean (s)	range (s)
phase 2	13.6	(8.0 - 17.5)
phase 3 (Zero)	21.6	(20.5 - 22.2)
phase 3 (Moon)	24.5	(21.0 - 26.0)
phase 3 (Mars)	30.2	(26.5 - 32.5)
phase 4	11.9	(2.8 - 18.0)

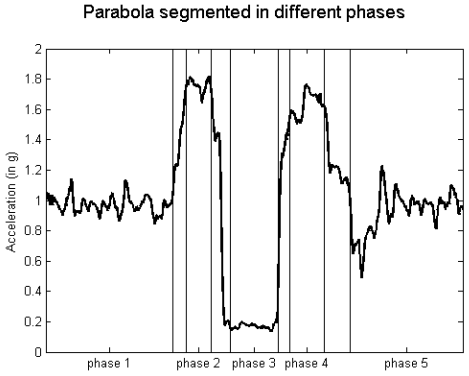

Figure 1. Example of a segmented parabola into the different phases.

from 0.15 Hz to 0.4 Hz for HF. Due to the short duration of the segments, pre-processing of the signals is needed before calculation of the PSD. These pre-processing steps are: resampling at 2 Hz, linear trend removal, tapering with a Hamming window, stationarity assessment and zero padding to 256 points to increase frequency resolution. This procedure is described in detail in [2, 17]. To reduce the effect of excitement on the cardiovascular response, only the last 6 parabolas of each gravity level were used for the statistical analysis. In previous studies, it is proven that the indices are related to the modulation of our ANS [16]. Std corresponds to the total power of the modulation, while the rmssd is related with the parasympathetic modulation. The ratio between those two indices reveals the relative importance of the parasympathetic modulation with respect to the sympathetic modulation. For the frequency domain measures, the LF component is related to the sympathetic modulation with vagal influences, while the HF component indicates the parasympathetic modulation. The ratio LF/HF reveals therefore the predominance of the sympathovagal balance. Due to spectral leakage in the frequency domain by the Hamming window, the value of the LF component could be larger than in reality. In the short duration of 20 seconds, only one or two waves at the low frequencies are measured. Therefore these components should be interpreted carefully.

2.4. Statistical analysis

A repeated measures one-way ANOVA is used to test the influence of gravity on the ANS, using the time and frequency domain indices. This statistical analysis takes into account the inter-subject variability and the repeated design of the experiments. To fulfil the normality assumption for performing an ANOVA, the data is transformed using a Box-Cox transformation. The Box-Cox transformation is a member of the family of power transform functions which create a rank-preserving transformation of the data. The normality assumption is verified by performing the Lilliefors test on the residuals and the assumption of constant variances is verified by performing the Levene's test. Unless mentioned otherwise, these assumptions are fulfilled for all results.

3. RESULTS

Fig. 2 and Fig. 3 show the statistical results for the HRV and the BPV, respectively, as function of gravity (0g - 0.18g - 0.38g - 1g). The plots show the mean $\pm$ 2std and the asterix indicates a significant ($p < 0.05$) difference with the baseline normogravity. The meanRR shows a non-monotonic relation with the gravity, in contrast with the hypothesis. A slightly lower meanRR, and thus higher heart rate, is found during Moon parabolas. However the stdRR and rmssdRR show a decreasing trend (shown in plot a. and b. of figure 4), meaning that there is a decrease of total and parasympathetic modulation for higher gravities. The relative importance of parasympathetic modulation, characterized by rmssdRR/stdRR, is significantly lower for Moon and Mars parabola compared to the other gravities. This inference can also be seen in the HFnu component, which shows a slightly lower value during Moon parabolas. The LFnu component can be deduced from the HFnu, LFnu = 1 - HFnu. However the dissimilarity between the HFnu component and rmssdRR/stdRR, can be explained due to the vagal influences in the LF component. The ratio LF/HF shows a slightly higher value during Moon parabolas, meaning that there is a higher sympathetic predominance, leading to the higher mean heart rate during the Moon parabolas.

For the BPV, meanSBP and meanDBP shows an increasing trend as a function of gravity, except for the zero gravity. Due to the short duration of the microgravity of these zero gravity parabolas (see Tab. 1), the influence of the hypergravity plays an important role, resulting in a higher meanSBP and meanDBP. This was also found in a study of Liu et al. [10], which found a transition period of about 3-5 seconds in blood pressure between hypergravity and microgravity. For both blood pressures the rmssd and std show a monotonic decreasing trend towards increasing gravity (shown in plot c. and d. of figure 4), but the ratio rmssdSBP/stdSBP and rmssdDBP/stdDBP of the reduced gravity parabolas is significantly lower compared to the normogravity, meaning that there is a higher sympathetic predominance during the parabolas.

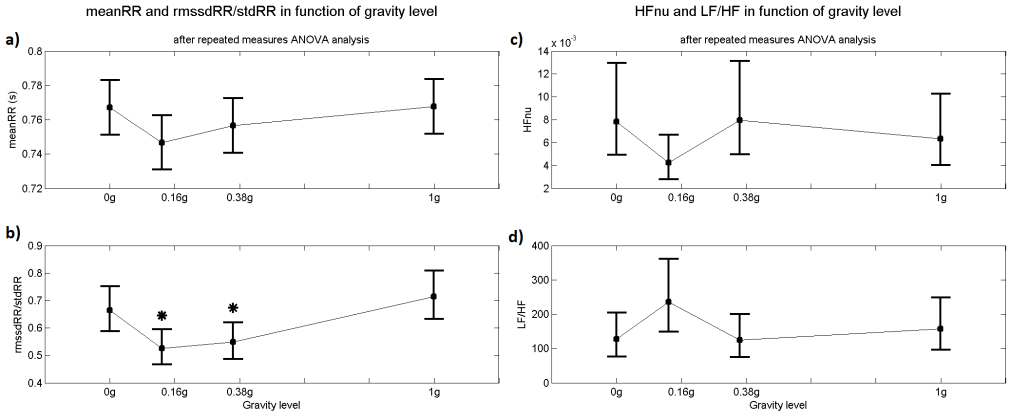

Figure 2. From a to d, statistical results for: meanRR, rmssdRR/stdRR, HFnu RR and LF/HF RR.

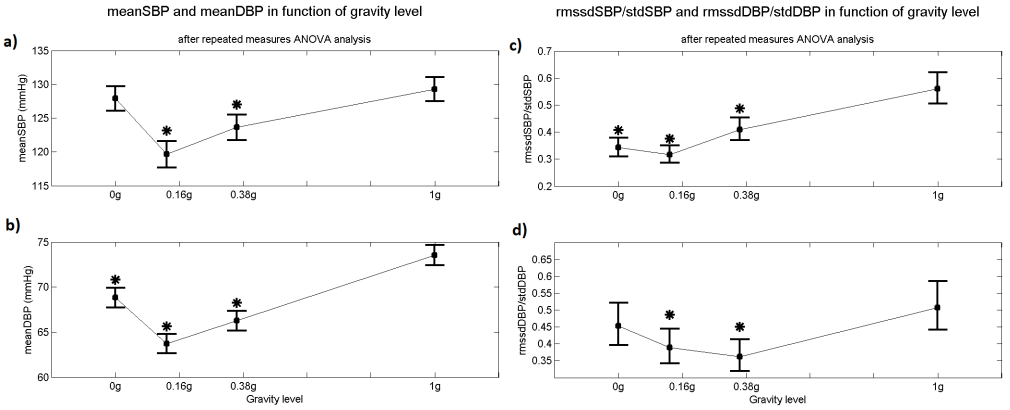

Figure 3. From a to d, statistical results for: meanSBP, meanDBP, rmssdSBP/stdSBP and rmssdDBP/stdDBP.

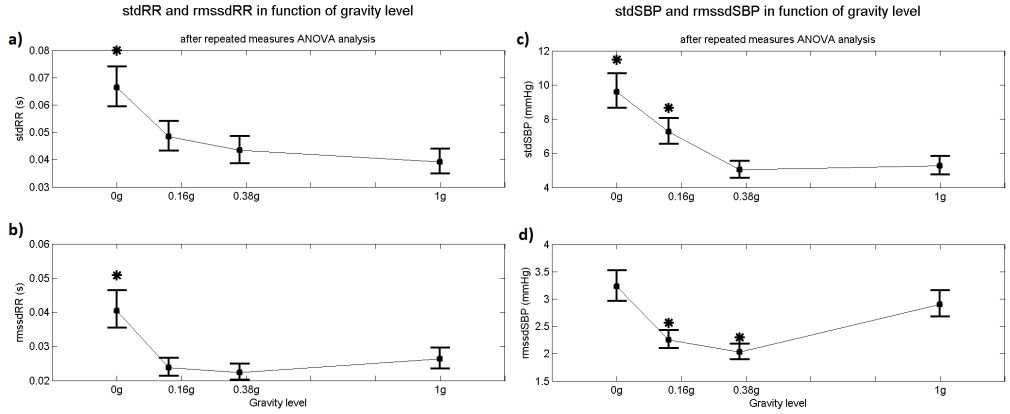

Figure 4. From a to d, statistical results for: stdRR, rmssdRR, stdSBP and rmssdSBP.

4. DISCUSSION AND CONCLUSION

The meanSBP and meanDBP are lower during microgravity compared to the normogravity, which can be explained by blood shift towards the head. One of the conditions associated with orthostatic intolerance is the orthostatic hypotension [6]. The correlation between the sympathovagal imbalance and the occurrence of orthostatic intolerance is found in several studies after performing head-up-tilt tests with subjects with vasovagal syncope [3, 13]. These studies found a significant increase of the LF and HF component of the mean arterial blood pressure in healthy subjects after a 60° tilt test, resulting in an increased parasympathetic predominance for higher gravities. This corresponds with the results found in this study.

Although it was hypothesized, a non-monotonic relation of meanRR was found. This shows that there are other factors influencing the heart rate, like the preceding hypergravity phases or mental stress of the subjects. In a study of Beckers et al. [4], subjects participated in at least two parabolic flights and a large inter-flight variation in meanRR was found. The higher heart rate during the Moon parabolas, can be explained by the sympathetic predominance, as shown via the LF/HF RR and rmssdRR/stdRR. Although there is no clear trend in the mean RR interval and sympathovagal balance, there is a decreasing relation in the power of the sympathetic and parasympathetic modulation, characterized via the stdRR and rmssdRR, as function of the gravity. This confirms the interaction between the parasympathetic and sympathetic modulation, as it was also found in a study by Malliani et al. [11]. Nevertheless, further research is needed to confirm these findings.

One serious limitation of parabolic flights is the short duration of the microgravity phases. The CVS is not able to reach a steady state during these short durations, meaning that only the transient behaviour of the cardiovascular response can be analyzed.

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