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Effects of gravitational acceleration on cardiovascular autonomic control in resting humans

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Abstract

Purpose Previous studies of cardiovascular responses in hypergravity suggest increased sympathetic regulation. The analysis of spontaneous heart rate variability (HRV) parameters and spontaneous baroreflex sensitivity (BRS) informs on the reciprocal balance of parasympathetic and sympathetic regulations at rest. This paper was aimed at determining the effects of gravitational acceleration ($a_{\rm g}$) on HRV and BRS.

Methods Eleven healthy subjects (age 26.6 ± 6.1) were studied in a human centrifuge at four $a_{\rm g}$ levels (1, 1.5, 2 and 2.5 g) during 5-min sessions at rest. We evaluated spontaneous variability of R–R interval (RR), and of systolic and diastolic blood pressure (SAP and DAP, respectively), by

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power spectral analysis, and BRS by the sequence method, using the BRSanalysis® software.

Results At 2.5 g, compared to 1 g, (1) the total power $(P_{\rm TOT})$ and the powers of LF and HF components of HRV were lower, while the LF/HF ratio was higher; (2) normalized units for LF and HF did not changed significantly; (3) the $P_{\rm TOT}$, LF and HF powers of SAP were higher; (4) the $P_{\rm TOT}$ and LF power of DAP were higher; and (5) BRS was decreased.

Conclusions These results do not agree with the notion of sympathetic up-regulation supported by the increase in HR and DAP (tonic indices), and of SAP and DAP LF powers (oscillatory indices). The $P_{\rm TOT}$ reduction leads to speculate that only the sympathetic branch of the ANS might have been active during elevated $a_{\rm g}$ exposure. The vascular response occurred in a condition of massive baroreceptive unloading.

Keywords Heart rate variability · Arterial blood pressure · Baroreflexes · Human centrifuge

Abbreviations

Gravitational acceleration **ANOVA** Analysis of variance **ANS** Autonomic nervous system **BRS** Baroreflex sensitivity DAP Diastolic arterial pressure **FFT** Fast fourier transform G_{7} Vertical acceleration HR Heart rate HF High frequency

HFnu Normalized high frequency
HRV Heart rate variability

LF Low frequency

LFnu Normalized low frequency



LF/HF Low and high frequency ratio

MAP Mean arterial pressure

MSNA Muscle sympathetic nerve activity

 P_{TOT} Total power

R_P Total peripheral resistance SAP Systolic arterial pressure VLF Very low frequency

Introduction

A variety of studies have examined tolerance to high gravitational acceleration (a_g) , both at rest and during exercise. Several cardiopulmonary variables were investigated, such as cardiac output, blood pressure, stroke volume and pulmonary diffusing capacity or oxygen consumption (Bjurstedt et al. 1968; Bonjour et al. 2010, 2011; Burton and Smith 2011; Girardis et al. 1999; Linnarsson and Rosenhamer 1967, 1968; Pendergast et al. 2012; Rohdin and Linnarsson 2002). These studies showed that at rest, when a_g [vertical acceleration (G_z) to be more specific] was increased, heart rate (HR), total peripheral resistance (R_p) , mean arterial pressure (MAP) and ventilation increased linearly with it, whereas stroke volume and pulmonary diffusing capacity decreased in a linear fashion.

Tools for indirect non-invasive assessment of the autonomic nervous system (ANS) regulation, including the analysis of spontaneous heart rate variability (HRV) parameters and spontaneous baroreflex sensitivity (BRS), are thought to inform on the reciprocal balance of parasympathetic and sympathetic regulations at any given time, at rest (Drouin et al. 1997; Pagani et al. 1986; Rosenstock et al. 1999; Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). These tools were applied in microgravity (Ferretti et al. 2009; Fortrat et al. 2001; Hirayanagi et al. 2004; Hughson et al. 1995; Traon et al. 1998), along with the study of peripheral sympathetic nerve activity and catecholamine concentration (Arbeille et al. 2008; Barbe et al. 1999; Christensen et al. 2005; Eckberg and Neurolab Autonomic Nervous System Team 2003; Edgell et al. 2007; Ertl et al. 2002; Ferretti et al. 2009; Kamiya et al. 2004; Tanaka et al. 2013). In contrast, the studies carried out in hypergravity are scanty, and only stress hormones and the effects of beta-adrenergic blockade were analysed (Bjurstedt et al. 1974; Schneider et al. 2008; Strempel et al. 2008). These studies coherently suggest an increased regulation of the sympathetic system.

On this basis, we carried out the present study, the aim of which was to determine the effects of $a_{\rm g}$ on HRV and baroreflex sensitivity (BRS).



Methods

Subjects

Eleven young healthy subjects participated in the study. They were 26.6 ± 6.1 years old, their body mass was 76.5 ± 8.2 kg and they were 180 ± 5.1 cm tall. The aims, design, protocol and method of the study were thoroughly described to the volunteers who agreed by signing an informed consent form. They had no history of cardiopulmonary disease and were not taking medications at the time of the experiments. They had to abstain from coffee and from nicotine-containing products during 24 h before the experiment. The study was approved by the Regional Ethical Board, Stockholm, and it was conducted in accordance with the 1964 Declaration of Helsinki on experiments on human subjects.

Set-up

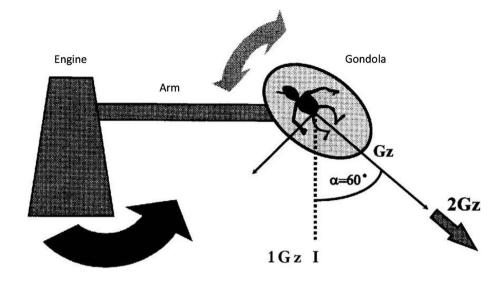
Experiments took place in the human centrifuge at the Karolinska Institute, Stockholm, Sweden. The subjects were located in the centrifuge gondola, sitting on a seat, which could be adjusted to be perpendicular to the resultant of the normal g vector and the centrifugal g vector. They were secured on the seat by a five-point safety belt, and their feet were fixed on an electrically braked cycle ergometer that was located in front of the seat. The rotational radius of the centrifuge was 7.2 m at the middle of the support surface. Slip rings at the centre of rotation allowed for audiovisual monitoring, power supply and transmission of physiological signals between the gondola and a control room.

Measurements

An electrocardiogram (ECG) was recorded and monitored throughout the experiments in order to look for abnormalities and to determine HR. Continuous recordings of arterial pulse pressure were obtained at a fingertip of the right arm by means of a non-invasive cuff pressure recorder (*Portapres*, TNO, Eindhoven, The Netherlands). The sensed fingertip was kept at the heart level. Systolic and diastolic blood pressure (SAP and DAP, respectively) values were obtained from each pulse pressure profile, using the Beatscope[®] software package (FMS, Amsterdam, The Netherlands). Beat-by-beat mean arterial pressure (MAP) was computed as the integral mean of each pressure profile, using the same software package.

It is noteworthy that the blood pressure profiles in this study were obtained from non-invasive recordings from a peripheral finger artery. The pulse wave characteristics of a peripheral artery are, in fact, remarkably different from

Fig. 1 Schematic illustration of subject's positioning in the spinning centrifuge. The subject seated in the centrifuge gondola is exposed to acceleration equal to $1/\cos\alpha$, α being the angle formed by the *vertical axis* and the *gondola axis*



those of a central artery (Remington and Wood 1956), and different absolute SAP and DAP values are obtained (Azabji-Kenfack et al. 2004). Possible vasoconstriction (see "Results") may blunt the pressure response as a_g is increased, although the growth of MAP with a_g was clearly demonstrated not only with the present method (Bonjour et al. 2011) but also with an invasive method (Linnarsson and Rosenhamer 1968).

Protocol

Experiments were conducted at four a_g levels, corresponding to 1, 1.5, 2 and 2.5 g. Control experiments at 1 g were also carried out in the gondola, using the same experimental set-up as for the hypergravity experiments. After having reached the appropriate spinning speed, 5 min at rest were allowed, during which all investigated parameters were continuously recorded. Then the protocol continued with an exercise session, which was carried out for other purposes (Bonjour et al. 2010). At the end of the exercise, the gondola was decelerated and parked. The reported values were obtained as the mean of all the beat-by-beat values determined during the last 2-3 min of the rest of each session with the centrifuge spinning. Overall, each subject underwent 16 experimental sessions as four different gravitational accelerations and four different workloads were used, which provided four repetitions of resting recordings at each investigated a_{o} for the sake of this study. A schematic drawing of the centrifuge arrangement during spinning, with indication of the gravitational vector, is shown in Fig. 1.

Data treatment

Examples at 1 and 2.5 g of the recordings and relevant analysis carried out in this study are presented in Fig. 2

for HRV and Fig. 3 for arterial pressure variability. After construction of the time series of R-wave to R-wave interval (RR), SAP and DAP from the continuous recordings of ECG and pulse pressure profiles, Fast Fourier transform (FFT) was used to evaluate spontaneous variability of RR, SAP and DAP (Pagani et al. 1986). The total power (P_{TOT}) of RR, SAP and DAP variabilities, corresponding to variance, was initially obtained. Subsequently, the powers of the low (0.03–0.14 Hz)- and the high (0.15–0.5 Hz)-frequency spectral components (low frequency, LF, and high frequency, HF, respectively) were computed and expressed in absolute units (ms²), and their ratio (LF/HF ratio) was calculated. The very low frequency (VLF) component was neglected, as they are known to reflect the long-term regulatory mechanisms which are not relevant in our study. Moreover, our data were obtained during 5-min sessions, a condition in which the analysis of the very low frequency component provides dubious results (Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). Normalized LF and HF (LFnu and HFnu, respectively) were also computed as

$$\frac{\text{LF} \times 100}{P_{\text{TOT}} - \text{VLF}} \tag{1}$$

and expressed in normalized units (nu) (Malliani et al. 1991; Pagani and Malliani 2000). The LF and HF central frequencies were also computed as the frequencies corresponding to the peak power value within the LF and HF bands of the HRV spectra.

The spontaneous baroreflex sensitivity (BRS, expressed in ms per mmHg) was estimated from SAP and RR by means of the sequence method (Bertinieri et al. 1988). In practice, we selected intermittent short sequences of



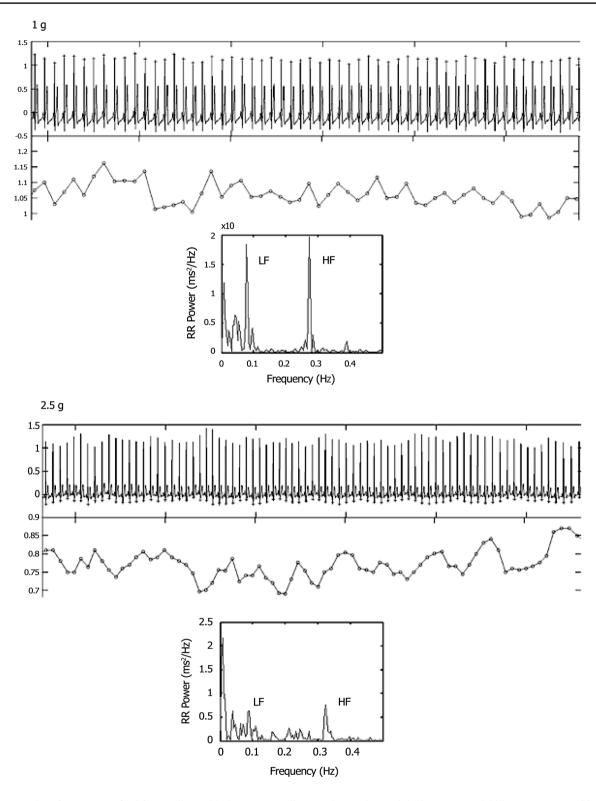


Fig. 2 Examples of a segment of ECG recording, with the corresponding RR time series, and the heart rate variability spectrum resulting from the experiment which the shown ECG segment belongs to *top* 1 g, *bottom* 2.5 g



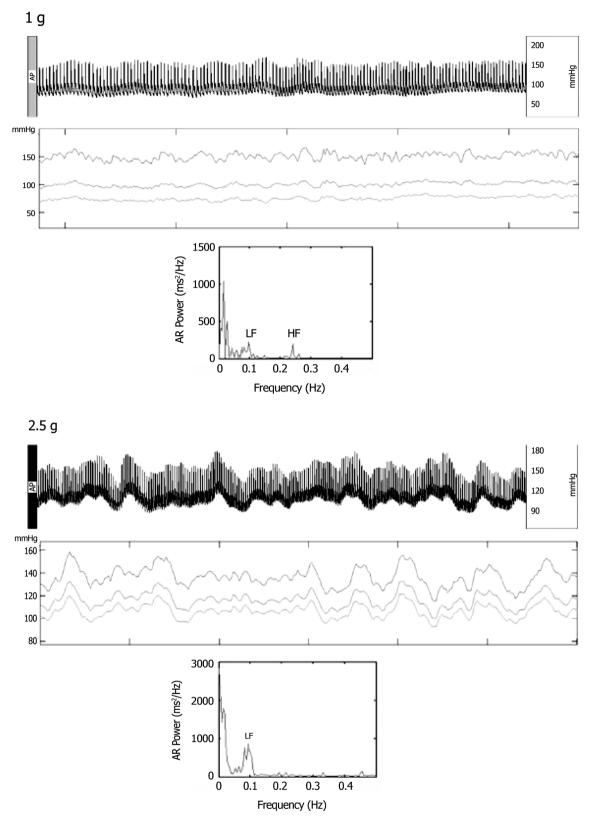


Fig. 3 Examples of a segment of arterial pressure recording, with the corresponding temporal series with SAP, MAP and DAP, and the SAP variability spectrum resulting from the experiment which the shown arterial pressure segment belongs to top 1 g, bottom 2.5 g



Table 1 Mean values measured at steady state and at each level of gravity acceleration (a_v)

Measured variables	1G	1.5G	2G	2.5G
HR (bpm)	70.20 ± 9.10	$79.52 \pm 6.19*$	$90.22 \pm 13.64*$	102.58 ± 15.25 *
SAP (mmHg)	132.19 ± 12.46	127.98 ± 25.75	127.87 ± 16.41	132.59 ± 14.39
DAP (mmHg)	68.73 ± 7.01	75.03 ± 11.51	76.59 ± 10.87	$82.04 \pm 12.55*$
MAP (mmHg)	89.88 ± 8.12	92.67 ± 15.62	93.69 ± 12.05	$98.88 \pm 12.05*$

Data are given as means and standard deviations of all measured variables at steady state at each level of $a_{\rm g}$

HR heart rate, SAP systolic arterial pressure, DAP diastolic arterial pressure, MAP mean arterial pressure

Table 2 Means and standard deviations of all calculated variables at steady state at each level of gravitational acceleration (a_{θ})

Measured variables	1G	1.5G	2G	2.5G
RR (ms)	870.34 ± 114.29	$762.88 \pm 59.03*$	$680.04 \pm 89.74*$	598.75 ± 89.49*
$f_{\rm LF} {\rm RR} ({\rm Hz})$	0.096 ± 0.015	0.099 ± 0.014	0.094 ± 0.023	0.088 ± 0.015
$f_{\rm HF}$ RR (Hz)	0.294 ± 0.049	0.325 ± 0.057	0.302 ± 0.069	0.335 ± 0.090
BRS (ms mmHg ⁻¹)	11.57 ± 2.85	9.95 ± 6.19	$7.46 \pm 6.48*$	4.88 ± 2.15 *

Data are given as means and standard deviations of all calculated variables at steady state at each level of a_g

RR R-R interval, f_{LF} RR (Hz) central frequency of the LF component of heart rate variability, f_{HF} RR (Hz) central frequency of the LF component of heart rate variability, BRS Spontaneous baroreflex sensitivity

at least three heart beats during which SAP increased or decreased resulting in a change in RR interval going to the same direction, resulting from a cardiovascular reflex. The software calculated the linear regression slope for each sequence, and only those sequences in which the value of r^2 was more than 0.85 were accepted and the slope retained. Then, BRS was calculated as the mean of the slopes of all sequences of each subject.

Spectral analysis and spontaneous baroreflex sensitivity were both analysed by means of BRSanalysis, a purposely laboratory-made programme written with Matlab[®] software (Version 7.9.1 R2009b) and produced by the Autonomic Nervous System Team at the University Jean-Monnet, Saint-Etienne, France (Assoumou et al. 2012; Costes et al. 2004; Dauphinot et al. 2013).

Statistical analysis

Data are reported as mean \pm standard deviation for each experimental session. The effects of $a_{\rm g}$ on the investigated parameters were analysed by 2-way ANOVA for repeated measurements. Then, Tukey Post-hoc test has been applied to identify corresponding samples. $a_{\rm g}$ was fitted as parametric variable. All data were analysed with *Statview* 5©. (SAS Institute Inc., Cary, NC, USA) The results were considered significant if p < 0.05

Results

The mean values measured at steady state at each level of $a_{\rm g}$ are shown in Table 1. HR at 2.5 g was 47.1 \pm 20.7 % higher than that at 1 g. Consistently, RR at 2.5 g was 30.76 \pm 9.46 % lower than that at 1 g. No arrhythmic beats were observed, and in all cases a normal sinus beat was maintained. Differences were significant between each $a_{\rm g}$ level. SAP did not change with $a_{\rm g}$, whereas DAP increased, being at 2.5 g significantly higher than that at 1 g (+19.5 \pm 14.6 %). Consistently, MAP at 2.5 g was also significantly higher than that at 1 g (+10.2 \pm 10.81 %).

The mean values calculated at steady state at each level of $a_{\rm g}$ are shown in Table 2. The central frequency of the HF component of RR, that is known to well represent the breathing frequency, did not change significantly with $a_{\rm g}$. The same was the case for the central frequency of the LF component of RR. At 2.5 g, the BRS decrease attained 57.4 \pm 17.7 %. This progressive BRS decrease led to significant changes at 2 and 2.5 g as compared to 1 g. The BRS at 2.5 g was also significantly lower than that at 1.5 g.

Means and standard deviations of all data calculated by means of HRV spectral analysis are shown in Table 3. $P_{\rm TOT}$ decreased progressively with increasing $a_{\rm g}$ from 1 g to 2.5 g. The $P_{\rm TOT}$ value at 2.5 g was significantly lower than the corresponding values at 1 and 1.5 g. Although the LF



^{*} Significantly different from 1G

^{*} Significantly different from 1G

Table 3 Means and standard deviations of all parameters calculated by means of heart rate variability, systolic arterial pressure and diastolic arterial pressure

	1G	1.5G	2G	2.5G
HRV				
$P_{\rm TOT} ({\rm ms^2 Hz^{-1}})$	1984.1 ± 390.6	1745.0 ± 411.2	1421.9 ± 432.4	$657.0 \pm 157.8*^{\#}$
$LF (ms^2Hz^{-1})$	702.9 ± 147.4	744.7 ± 190.7	640.8 ± 213.9	$336.8 \pm 105.4^{\#}$
$HF (ms^2Hz^{-1})$	314.4 ± 57.4	289.0 ± 115.7	186.9 ± 68.9	$66.7 \pm 15.4*$
LF/HF	2.60 ± 0.38	3.84 ± 0.55	4.41 ± 0.91	$4.97 \pm 1.34*$
LFnu (%)	64.95 ± 3.42	73.35 ± 2.82	72.36 ± 4.18	69.17 ± 5.11
HFnu (%)	34.91 ± 3.42	26.21 ± 2.75	24.87 ± 3.42	24.34 ± 3.47
SAP				
$P_{\rm TOT} ({\rm ms^2 Hz^{-1}})$	24.77 ± 3.94	33.77 ± 3.71	$44.23 \pm 4.87*$	46.63 ± 5.81 *
$LF (ms^2Hz^{-1})$	9.04 ± 1.61	11.38 ± 2.17	$19.37 \pm 3.96*$	$24.18 \pm 5.02*$
$HF (ms^2Hz^{-1})$	2.80 ± 0.47	5.04 ± 1.18	$7.83 \pm 1.28*$	$8.24 \pm 1.73*$
LF/HF	4.99 ± 1.29	3.04 ± 0.40	3.28 ± 0.75	4.51 ± 1.00
DAP				
$P_{\rm TOT} ({\rm ms^2 Hz^{-1}})$	8.17 ± 1.28	11.76 ± 2.01	15.73 ± 2.59	$20.53 \pm 3.23^{*\#}$
$LF (ms^2Hz^{-1})$	3.41 ± 0.46	5.01 ± 1.05	8.15 ± 1.69	$11.9 \pm 2.33*$ #
$HF (ms^2Hz^{-1})$	1.25 ± 0.76	1.85 ± 0.86	2.69 ± 0.76	3.02 ± 0.64
LF/HF	9.45 ± 1.39	6.22 ± 0.95 *	5.17 ± 1.06 *	7.67 ± 1.2

Data are given as means and standard deviations of all parameters calculated at steady state at each level of a_{σ}

HRV heart rate variability, SAP systolic arterial pressure, DAP diastolic arterial pressure, P_{TOT} total power, LF low frequency, HF high frequency, LF/HF low and high frequency ratio

power at 1 g did not change with increasing $a_{\rm g}$ up to 2 g, the value at 2.5 g resulted remarkably reduced. This change was significantly different with respect to the value at 1.5 g. HF power decreased progressively and significantly with increasing $a_{\rm g}$, from 1 to 2.5 g. This last value was significantly lower than the corresponding values at 1 and 1.5 g. The LF/HF ratio thus increased significantly between 1 and 2.5 g, growing by 105.8 \pm 156.1 %. LFnu and HFnu did not change significantly with $a_{\rm g}$.

Means and standard deviations of all data calculated by means of SAP spectral analysis are shown in Table 3. $P_{\rm TOT}$ increased progressively and significantly from 1 to 2.5 g. The value at 2.5 g represented a 127.8 \pm 132.9 % increase with respect to the corresponding value at 1 g and was significantly higher than the corresponding value at 1 g. The same was the case for the value at 2 g. LF power increased progressively with increasing $a_{\rm g}$, to reach the maximum at 2.5 g. At this $a_{\rm g}$ level, LF power was 232.5 \pm 257.3 % higher than that at 1 g and significantly different from that observed at 1 and 1.5 g. Also the value at 2 g was significantly higher than the corresponding value at 1G. HF power increased progressively with increasing $a_{\rm g}$. Value at 2.5 g was 248.9 \pm 230.5 % higher than that at 1 g. Values at 2 and 2.5 g were significantly higher than the corresponding

value at 1 g. The LF/HF ratio, as well as LFnu and HFnu, did not change significantly with increasing a_g .

Means and standard deviations of all data calculated by means of DAP spectral analysis are shown in Table 3. $P_{\rm TOT}$ increased progressively and significantly with increasing $a_{\rm g}$ until 2.5 g. This last value was 190.6 ± 146.6 % higher than and significantly different from the corresponding value at 1 g. It was also significantly higher than the value at 1.5 g. The value at 2 g was significantly higher than that at 1 g. LF power increased progressively with increasing $a_{\rm g}$ and significantly at 2 and 2.5 g. This represented a 275 ± 224.8 % increase. HF power did not change significantly between 1 g and 2.5 g. LF/HF ratio decreased progressively and significantly until 2 g. The rebound observed at 2.5 g was such as to have no significant differences with respect to any other $a_{\rm g}$ level. LFnu and HFnu did not change significantly with $a_{\rm g}$.

Discussion

The absolute steady-state values of the measured variables conformed with previous observations (Bjurstedt et al. 1968; Bonjour et al. 2011; Burton and Smith 2011;



^{*} Significantly different from 1 g

^{*} Significantly different from 1.5 g

Pendergast et al. 2012; Rosenhamer 1967): as a_g was increased, HR and DAP grew and SAP did not change, which implied an increase in MAP. On the same subjects, in a previous study (Bonjour et al. 2011), a decrease in cardiac output and stroke volume as a function of a_{α} was found. The increase in DAP can be attributed to an increase in R_p , also reported by Bonjour et al. (2011), as a consequence of arteriolar vasoconstriction, possibly due to sympathetic stimulation of alpha-adrenergic receptors (Inagaki et al. 2011). We propose that the drop of venous return, as suggested by low stroke volume and cardiac output, induced a switch toward sympathetic up-regulation of the cardiovascular system at rest, leading to higher $R_{\rm p}$ and MAP (vascular regulation) and to higher HR (cardiac regulation). It was therefore logical to expect that HRV indexes in condition of high a_{g} change in the direction of sympathetic up-regulation.

We thus analysed for the first time the spontaneous variability of RR, SAP and DAP in hypergravity condition by means of power spectral analysis. The choice of FFT relied on two considerations: on one side, the implicit assumptions underlying the application of autoregressive methods are unwarranted at elevated a_g levels; on the other side, our study was carried out in steady-state conditions (Bonjour et al. 2011) and FFT is considered accurate when it is used during steady states (Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). We also comment a posteriori that the present results have shown a reduction of the total power with increasing a_g , a condition in which FFT was demonstrated to be a most reliable technique (Weippert et al. 2010). We nevertheless acknowledge that application of autoregressive analysis would have in principle allowed a more consistent and smoother spectral estimation, a spectral resolution independent of the number of samples and the possibility of avoiding windowing procedures (Pagani et al. 1986). Moreover, autoregressive models would have allowed decomposition of the autocorrelation function in single components, thus directly providing the individual centre frequency, which in this case had to be recalculated off-line.

The most common condition implying up-regulation of the sympathetic system is exercise. Already, the classical study of Robinson et al. (1966) demonstrated a progressively greater sympathetic activity as the power at which exercise was carried out increased. Moreover, a reduction of $P_{\rm TOT}$ of HRV typically occurs when only one branch of the ANS is active, as is the case during exercise. As soon as exercise starts, there is an immediate HR increase, which was attributed to sudden withdrawal of vagal regulation (Arai et al. 1989; Fagraeus and Linnarsson 1976; Lador et al. 2006; Perini et al. 1990). At 30 % of the maximal power, most of the decrease in $P_{\rm TOT}$ known to occur during

exercise has already taken place (Perini et al. 1990). The reduction of P_{TOT} that we found in hypergravity is thus in agreement with what is currently observed in exercise (Perini et al. 1990; Perini and Veicsteinas 2003). During exercise, there is also an increase of the power of the LF component of SAP variability (Perini and Veicsteinas 2003; Cottin et al. 2008), a finding that characterises also the present results and is coherent with the concept of an increased peripheral sympathetic activity. There is however a remarkable difference between exercise and hypergravity, namely that in the former case the up-regulation of the sympathetic system occurs at low R_p , while in the latter it occurs at elevated R_p . This entails differences in the peripheral (vascular) component of oscillatory regulation mechanisms. In fact, an exercising human undergoes a major increase in muscle blood flow with respect to rest, with consequent dramatic fall of R_n (Ferretti et al. 1995; Rådegran and Saltin 1998), whereas hypergravity at rest is characterised by strong peripheral vasoconstriction (Bonjour et al. 2011; Linnarsson and Rosenhamer 1968).

Respiratory rate is also a major difference between hypergravity and exercise. Previous work done with the same set-up and subjects showed that there were no significant changes of resting ventilation with increased a_{σ} (Bonjour et al. 2011). Coherently, neither the power of the HF component of HRV nor its central frequency varied with increasing $a_{\rm s}$. This is obviously not the case with exercise. Respiratory rate is well known to modulate HF component of HRV (Perini and Veicsteinas 2003), the power of which increases at exercise intensities above the so-called ventilatory threshold (Cottin et al. 2008). Other conditions characterised by reduced P_{TOT} of HRV are exposure to acute hypoxia (Brown et al. 2013; Buchheit et al. 2004) and chronic heart failure (Lombardi and Mortara 1998; Rydlewska et al. 2011). Also, these conditions, however, entail physiological differences with respect to hypergravity, as far as cardiac output is concerned.

In this study, the reduction of the HF component of HRV, at least at 2 and 2.5 g, was associated with a smaller decrease in LF. As a consequence, (1) P_{TOT} , decreased significantly; and (2) the LF/HF ratio increased significantly. However, an increase of the LF/HF ratio should imply significant increases in LFnu and decreases in HFnu. This was not the case, although a tendency toward a decrease is evident for HFnu. These results reveal dissociation between oscillatory (HRV parameters) and tonic (steady-state physiological variables) indices of cardiovascular regulation, as long as the latter, but not the former, are varied at elevated a_{σ} levels (Bonjour et al. 2011). A similar dissociation was observed also after prolonged bed rest (Ferretti et al. 2009) and was related to the different meaning of these indices. The occurrence of changes in LFnu and HFnu is a crucial issue for the evaluation of the sympatho-vagal balance



concept (Pagani and Malliani 2000). These results rather suggest that the sympatho-vagal balance is not a key issue under elevated $a_{\rm g}$ conditions, considering also that in the present study the control condition was sitting instead of supine, in which case LFnu is already elevated.

In order to clarify the origin of the LF decrease for HRV, we analysed the spontaneous variability of SAP and DAP. Contrary to the LF component of HRV, the LF powers of both SAP and DAP increased progressively and significantly with increasing a_{g} , whereas the corresponding HF powers also significantly increased. This revealed the dissociation between the peripheral (arterial pressure control) and the cardiac (HRV) oscillatory components under the present circumstances. The increase in LF is coherent with the hypothesis that LF may have some links with the peripheral sympathetic activity (Pagani et al. 1997). Peripheral sympathetic activity can be investigated by analysing the muscle sympathetic nerve activity (MSNA). MSNA is increased in exercise (Victor et al. 1995) and head-down bed rest (Tanaka et al. 2013), all conditions that are generally associated with an increase in SAP LF power. Unfortunately, measuring MSNA was an impossible task in a spinning gondola due to space limitation and the exerted forces. The only data we are aware of, supporting these notions, were obtained during centrifugation at 3g and showed that both adrenaline and noradrenaline were increased (Schneider et al. 2008).

Mean BRS at 1 g was similar to the values reported with the same method in previous studies (Kardos et al. 2001). As long as a_g was increased, BRS decreased progressively and significantly. When MAP is artificially increased, e.g. by means of a bolus of phenylephrine (La Rovere et al. 2008), the ensuing MAP correction by arterial baroreflexes is mediated by increased cardiac parasympathetic outflow to the sinoatrial node. In a condition where the vagal branch of the ANS is inhibited, one would expect an impairment of such a MAP correction, as evidenced by a decrease in BRS. The hydrostatic force that is generated, e.g. by doubling a_g , unloads carotid baroreceptors remarkably—the exact amount depends in fact also on the position of the indifferent hydrostatic point in hypergravity, which is unknown in the present subjects so that the subjects may move toward the functional limits of arterial baroreflexes, a fact which per se would imply an acute reduction of BRS. In fact, age, among many factors, is known to be a major determinant of BRS impairment (Kardos et al. 2001; Laitinen et al. 1998; Piccirillo et al. 2001). Lower BRS values than the present ones were found on older subjects than the present subjects (Parati et al. 1988; Tank et al. 2000). Similar effects on BRS were found also during head-up-tilt after 6 h of water immersion (Florian et al. 2013) or at the end of prolonged headdown bed rest (Ferretti et al. 2009; Sigaudo et al. 1998).

All these conditions entail an increased sympathetic regulation (Kamiya et al. 1999; O'Leary et al. 2003). The low BRS values represent an intriguing aspect of this study, as long as they are associated with higher LF values and elevated DAP values. In more general terms, the reduction of BRS in association with an increased vascular regulation response reveals the complexity of the autonomic regulation in conditions of acute a_g elevation, which would require joint perusal of several indices simultaneously.

Conclusion

The decrease in the power of the LF component of HRV, as well as in $P_{\rm TOT}$, was associated, on one side, with a lack of significant changes in LFnu and HFnu and, on the other side, with significant changes in the LF/HF ratio. These results do not agree with the notion of sympathetic up-regulation, suggested by the increase in HR and DAP (tonic indices) and the increase in both SAP and DAP LF powers (oscillatory indices). Yet the $P_{\rm TOT}$ reduction leads us to speculate that only the sympathetic branch of the ANS might have been active during elevated $a_{\rm g}$ exposure. The finding that the vascular response, as revealed by the higher LF power of arterial pressure variability, occurred in a condition of massive baroreceptive unloading may indicate new tracks for the study of vascular regulation and, possibly, vascular to central interactions.

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