Respiratory Sinus Arrhythmia on the ESA-short arm human centrifuge: a comparison of hypergravity vs microgravity influences on cardiorespiratory interactions.

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Abstract— **The European Space Agency (ESA) Short-Arm Centrifuge (SAHC) was used to generate 0.7, 1, and 1.2 Gz of artificial gravity at the level of the heart in 6 healthy male subjects. We investigated the hypothesis that the effects of hyper-gravity on Respiratory Sinus Arrhythmia (RSA) can mimic the effects observed after spaceflight cardiovascular deconditioning. Artificial gravity along the head-to-feet axis on a short-arm centrifuge induces gravity gradients. This physiological condition is new and with higher g at the feet than at heart level induces blood sequestration in the lower limbs. Astronauts are after spaceflight are in a condition of cardiovascular deconditioning where blood pooling in the legs or autonomic adaptation are factors contributing to orthostatic intolerance and changes in HRV. ECG and respiration were recorded during Imposed and Controlled Breathing (ICB) protocols which were repeated at different levels of artificial gravity as well as during supine and standing control measurements. RSA was studied with a time domain method suitable for the analysis of very short recordings. Results obtained on the centrifuge were compared to results from a previous study analyzing changes in HRV and RSA during similar ICB protocols during and after a short-duration (11 days) spaceflight mission.**

I. Introduction

Respiratory Sinus Arrhythmia (RSA), usually the high frequency (HF) component of heart rate variability (HRV), is a cardiorespiratory interaction mediated by the vagus nerve. RSA was thus considered a marker of the parasympathetic modulation of heart rate [1]. However, in the light of recent studies [2,3] care has to be taken for such a straight interpretation. Previous studies reported decrease in RSA and/or HF component of HRV after spaceflight [4]-[6]. Whether these changes can be interpreted as resulting from autonomic adaption following exposure to microgravity or only result from a decreased blood volemia is still a matter of debate. We measured respiration, heart rate, continuous blood pressure and RSA during imposed and controlled breathing (ICB) protocols performed during exposure to various gravity levels generated by the ESA Short-Arm Human Centrifuge (SAHC). It is hypothesized that hyper-gravity on the SAHC can generate blood pooling in the legs that will mimic the observed post-spaceflight autonomic response as the one observed through the analysis of RSA during ICB experiments [6]. Results from SAHC experiments are compared to results from similar ICB experiments performed before, during and after a short-duration (11 days) space mission [7].

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II. Methods

The ESA SAHC is a short-arm centrifuge (outer radius = 2.82m) that can generate up to 6g at the feet of the subject and contains 2 bed nacelles and 2 chairs that are radialy oriented. The bed nacelles can be oriented from -20 degrees (head down) to +50 degrees to generate different gravity gradients along the head to foot direction (Gz). When lying supine on the horizontally oriented bed, the heart was typically situated at 1.05 m from the center of rotation. Rotations were set at ~ 24, 29 and 32 rpm to obtain respectively 0.7Gz, 1Gz and 1.2 Gz at heart level. This yielded at the head values of approximately 0.47, 0.66 and 0.80 Gz and at the feet 1.5, 2.2 and 2.6 Gz respectively.

Ethical approval was obtained by the IRB of the Antwerp University Hospital and Informed Consent signed by the subjects. Electrocardiogram, continuous blood pressure and respiration were recorded from 6 healthy male control subjects. A series of 3 ICB protocols were repeated 5 times during 3 different G-load conditions. Imposed breathing was set at 6, 9 and 15 breaths per minute for at least 9 breaths. In between a series of 3 imposed breathing periods, a one minute break was inserted during which subjects were allowed to perform exercises with the lower limbs. Per Gz level, test time lasted approximately 20 minutes. Load conditions of 0.7 and 1 Gz were imposed without general stop of the centrifuge. Between 1 and 1.2 Gz however, a pause of 10 minutes was applied to unload the lower limbs. Controlled breathing was achieved by the display of a moving vertical bar on a flat screen situated in front of the subject in a dark environment canopy which was placed over the upper part of the body to ensure that the subjects had no cue of moving reference. Prior to rotation of the SAHC, control measurements were obtained in standing and supine position.

Similar ICB experiments were performed before during and after the 11 days Odissea mission to the international space station (ISS) on 3 male subjects. Recordings were performed on days 1, 2, 4, 9, 15, 19 and 25 after landing. Similar data recordings were performed with imposed breathing set at 6, 7.5, 9, 12 and 15 breaths per minute for 180s. The protocols were repeated in supine and standing position.

The parasympathetic response of the Autonomic Nervous System (ANS) to the orthostatic challenge induced by the different g-loads was assessed through the analysis of short-term HRV by means of a time domain algorithm, the "polar representation of the respiratory sinus arrhythmia" [8]. Briefly, this method is based on the modelisation of RR-intervals (RRI) oscillation in the breathing cycle and allows the determination of amplitude and phase of RSA on short recordings (3 breaths). It consists of a conversion of the time axis of heart-beats occurring at t_k^{rr} into their phase in the breath cycle. We define $\theta_{k,i}$ the phase of the heart beat k in the breath cycle i with onsets of inspiration at t_i^{in} and expiration at t_i^{ex} as $\theta_{k,i}^{in}$ or $\theta_{k,i}^{ex}$ depending whether the heart beat occur in the inspiration or expiration period:

$$\begin{aligned}\theta_{k,i}^{in} &= 0.5\left(t_k^{rr} - t_i^{in}\right)/\Delta_i^{in} \\ \theta_{k,i}^{ex} &= 0.5 + 0.5\left(t_k^{rr} - t_i^{ex}\right)/\Delta_i^{ex}\end{aligned} \qquad (1)$$

where $\Delta_i^{in} = t_i^{ex} - t_i^{in}$ and $\Delta_i^{ex} = t_{i+1}^{in} - t_i^{ex}$ are respectively the duration of the inspiration and expiration periods for the respiration cycle i. The total breathing period (Tresp) is $Tresp = \Delta_i^{in} + \Delta_i^{ex}$ and the inspiration starts at $\theta = 0\%$, the beginning of expiration is set to 50% and $\theta = 100\%$ corresponds to the end of expiration (i.e. the beginning of a new respiratory cycle). With such a change of coordinates, RRI from different respirations can be superimposed (Fig. 1). A large RSA appears then as a consistent oscillation in the breath cycle and can be modeled by a cosine curve:

$$RRI_{k,i} = R + \rho_c \cdot \cos\left[\left(\theta_{k,i} - \theta_c\right) \cdot 2\pi/100\right] \qquad (2)$$

where R is the mean RRI and ρ_c and θ_c are respectively the amplitude and phase of the cosine.

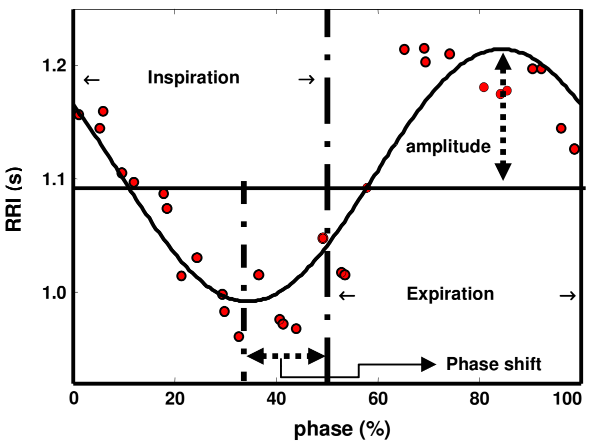

Fig. 1. Model of Respiratory Sinus Arrhythmia: (•) RRI vs. phase in the breath cycle, and (-) the cosine fitted curve (2).

The use of a cosine curve in the model corresponds to the analysis of the respiratory peak in the traditional Fourier spectral analysis. As the end of the cycle is physiologically equivalent to the beginning of a new cycle we take advantage of a polar coordinate representation, where the radial coordinate ρ is the RRI and the angular coordinate θ is the phase in breath cycle. In this representation the RSA is modelled by a circle with radius R and centre c with coordinates (ρ_c, θ_c), in which a large RSA appears as a large offset of the centre of the fitted circle whereas absence or very small RSA provides a centred circle on the origin (see [8]). This alleviates the issue of the fitting of a cosine with small amplitude and its consequent under-determination on the phase.

A regression analysis of RSA amplitude and phase as function of the imposed breathing period (Tresp) was applied to assess the parasympathetic dynamic range of response at the different g and gradients levels. Statistical significance of differences between regression parameters were analysed with the method of sum of squares for the comparison of two regressions [9].

III. Results

The results from the regression analysis of RSA performed on the recordings of the Odissea mission are presented in Fig. 2 and Fig 3, for supine and standing data, respectively.

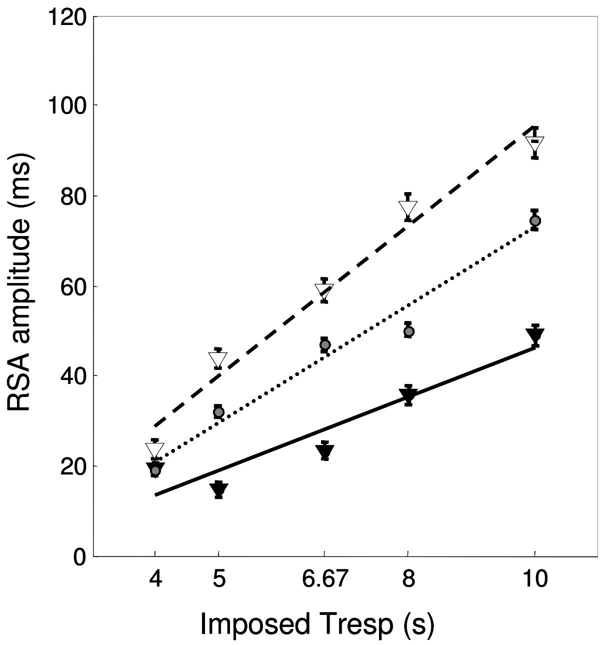

Fig. 2. Regression analysis of RSA amplitude vs. imposed breathing period (Tresp) for supine data from the short-duration spaceflight. Supine preflight values (∇--) are larger than in-flight (●…) and post-flight data (▼). Post-flight the slope (-) is significantly smaller and the intercept is larger than for preflight data ($p=0.015$). In-flight, the slope (…) is slightly lower than pre-flight ($0.05<p<0.1$).

Early postflight RRI (not shown here) and RSA amplitude are significantly decreased ($p<0.05$) at all Tresp, and the slope of the regression of RSA amplitude with Tresp is decreased

($p<0.05$). This suggests a state of parasympathetic withdrawal and decreased parasympathetic range of reactivity.

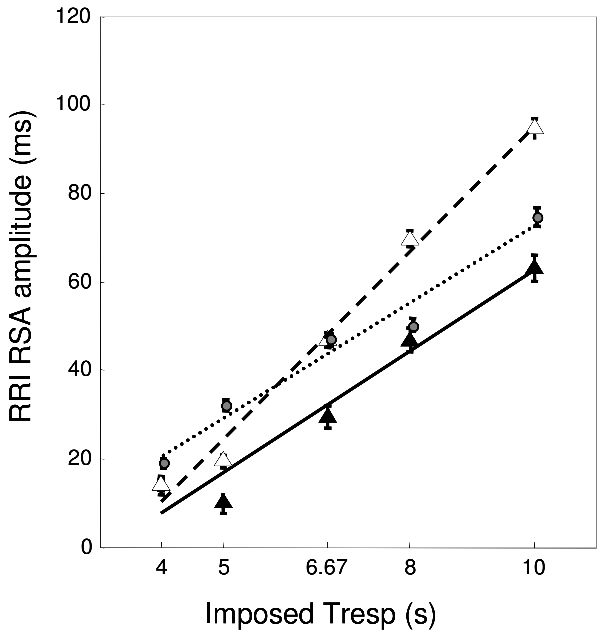

Fig. 3. Regression analysis of RSA amplitude vs. imposed breathing period (Tresp) for standing data from the short-duration spaceflight. Pre-flight standing (Δ--) and in-flight (o…) values of RSA are larger than post-flight data (▲-) at all imposed Tresp. Post-flight, the slope is lower than preflight ($p<0.05$) and similar to in-flight but with a decreased intercept ($p<0.05$). In-flight, the slope is significantly decreased compared to standing ($p<0.05$).

Baseline measurements from the SAHC experiments are presented in Fig. 4. Responses of RSA to the different imposed Tresp are in-line with previous experiments: baseline supine values are larger than standing values at all imposed Tresp, showing a parasympathetic predominant state, and RSA increases with Tresp.

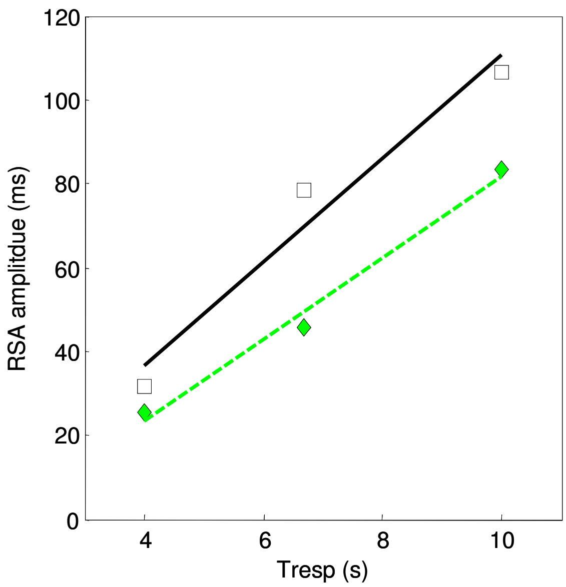

Fig. 4. Regression analysis of RSA amplitude vs. imposed breathing period (Tresp) for SAHC baseline supine and standing data. Supine data at rest (□) are larger than standing (♦) values at all Tresp.

The effects of different conditions are presented in Fig. 5. and 6. for RRI and RSA, respectively. As expected RRI decreases with the increase in Gz. In addition, there is a slope (RRI increasing with Tresp) which shows that RRI is significantly larger ($p<0.01$) for slow breathing (Tresp=10s) than for fast breathing (Tresp=4s) protocols. This suggests that slow breathing potentiates the parasympathetic effect of RSA on HR, possibly through a resonance with the low frequency component (0.1 Hz) of HRV.

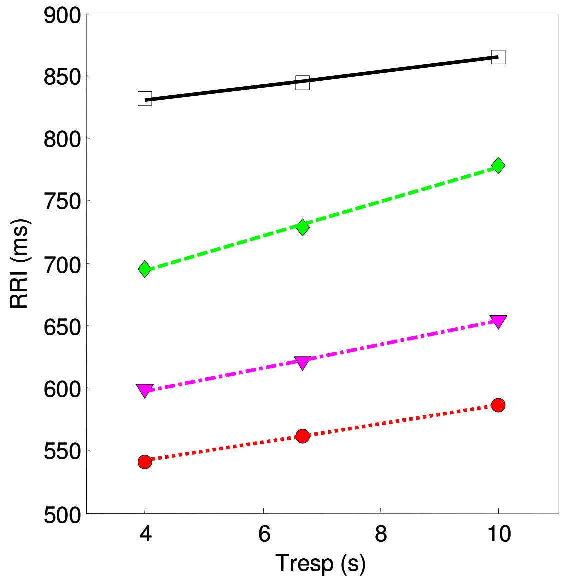

Fig. 5. RRI (ms) vs. imposed breathing period (Tresp) for the different g-load conditions on the SAHC. Measurements at rest supine (□) are larger at all Tresp than RRI in all artificial g-load conditions: 0.7g (♦--), 1g (▼-.), 1.2g (●…). For all g-load conditions RRI at the longer Tresp are significantly larger than that at the shortest Tresp. ($p<0.05$).

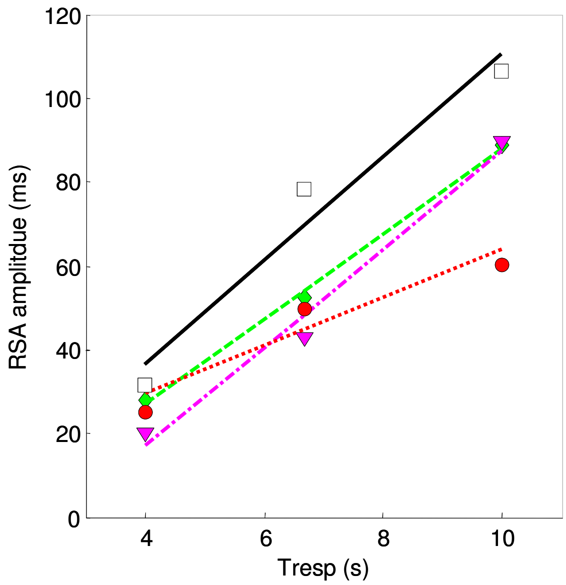

Fig. 6. Regression analysis for the different g-load conditions on the SAHC. Symbols as in fig. 5. The slope of the higher g-load condition is significantly lower ($p<0.05$) than all other slopes.

Fig. 6. presents the regression analysis of RSA amplitude with Tresp for the different conditions. The slope for the high

condition is the lowest. This suggests that the cardiovascular system is in a stated of reduced range of reactivity.
The influence of the repetition of the protocols during the higher Gz condition, thus the analysis of the duration of exposure to one particular orthostatic stress is presented in Fig. 7. Individual values of RSA tends to decrease with the duration of exposure to hyper-g and the slope shows also a tendency to decrease. The lowest slope is reached for the last repetition during the higher condition. This suggests that with the exposure to the orthostatic stress, and an expected pooling of blood in the lower limbs, there is a parasympathetic withdrawal and a decreased reserved for additional reactivity.
The results from the SAHC experiments shows that artificial gravity and gravity gradients can cause similar changes in HRV as the one seen in astronauts after a short duration space-flight.

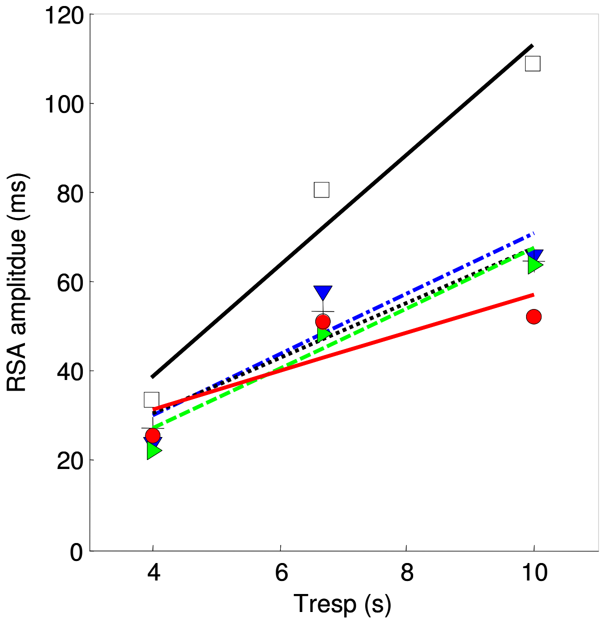

Fig. 7. Regression analysis of RSA vs. Tresp for the last 4 repetitions of the high-g load (1.2g) condition: (▼-.) rep.2, (+…) rep.3, (▶--) rep.4, (●-) rep.5. All repetitions at the higher g-load are lower than supine baseline data (□). The lowest slope is seen for the last repetition of the higher g-load condition.

The decrease of the slopes evidenced for the higher g-load on the SAHC and the post-spaceflight experiments shows a similarity of responses between these two situations. This suggests that blood pooling in the legs, mimicked by centrifugation of healthy subjects can be one factor explaining the HRV response observed after spaceflight.

IV. Conclusion

Our results on the SAHC show that the G-load induced blood pooling lead to increased HR and decreased RSA amplitude at all Tresp. The repetition of the protocol (or duration of exposure to a particular gravity level) accentuates these differences, thus evidencing a cumulative effect with a very short time constant. The response of the ANS to the orthostatic challenge was evidenced by a sympathetic activation and/or parasympathetic withdrawal (increased HR and decreased RSA amplitude) and decreased parasympathetic range of response (decreased slope of RSA amplitude with Tresp). The Gz-gradient seems to be an important factor of orthostatic challenge: even at a moderate 0.7 Gz at the heart, HR was significantly increased compared to supine and at 1.2 Gz this difference was even much more accentuated.
In addition, this study demonstrate that blood pooling in the legs achieved by centrifugation has a major influence on HRV and more particularly on RSA, and that this can partially reproduce the observed changes in RSA slope observed after a short-duration spaceflight. We can speculate that post-flight, due to the possibly decreased vascular stiffness, and therefore a more than normal blood pooling in the lower legs, a situation is generated where the heart is exposed to the terrestrial 1 G (as well as the legs), but in the lower limbs a pooling is present similar to a higher g-load at the legs. The net result is the same: an increased distensibility, experienced by the vascular bed in the lower legs while the heart is at 1 G. This is the physiological base for a similarity. By playing with the gradient (tilt of the SAHC nacelles), a dose response of this effect could be evaluated.

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