Quantitative Analysis of T-Wave Amplitude during Parabolic Flight

EG Caiani[1], C Vimercati[1], TD Tu[1], A Capderou[2], S Cerutti[1], P Vaida[3]

[1]Dipartimento di Bioingegneria, Politecnico di Milano, Italy
[2]Université Paris Sud, UPRES EA 2397, CCML, Physiologie, Le Plessis Robinson, France;
[3]Université Bordeaux 2, Médecine Aérospatiale, UPRES EA 518, Bordeaux, France

Abstract

Our goal was to develop a method for the analysis of T-wave maximum amplitude (Tmax), to quantify its changes with gravity (G^z) during parabolic flight, and test the hypothesis that microgravity ($0G^z$) induces alteration in ventricular repolarization. ECG was obtained in 12 normal male subjects in upright position during consecutive parabolas with lower-body negative pressure (LBNP) randomly activated at $0G^z$. The X, Y and Z leads were used to compute vector V. Each QQ was classified according to G^z ($1G^z$, $1.8G^z$, $0G^z$, $1G^z$ recovery) at its time occurrence and used to obtain a template, from which Tmax was computed. At $0G^z$, Tmax showed a significant increase (15%±4%), compared to $1G^z$. With LBNP, the Tmax increase at $0G^z$ was only 8%±4%. At $1G^z$ recovery, Tmax was increased by 5%±2%. Microgravity influences ventricular repolarization by increasing T wave amplitude.

1. Introduction

The human cardiovascular system undergoes profound changes when exposed to spaceflight, including alterations in cardiovascular autonomic regulation which may adversely influence cardiac repolarization and induce cardiac rhythm disturbances. While it is well known that weightlessness leads to cardiovascular deconditioning, as evidenced by post-spaceflight orthostatic intolerance and decreased exercise capacity, only anecdotal data exist regarding the possible increased risk of cardiac dysrhythmias during spaceflight [1-7].

In the attempt to better understand the origin of these cardiac dysrhythmias, in order to prevent the issue of their insurgence during long term space missions, several studies were recently performed by retrospectively analyzing ECG data obtained in previous space missions. In particular, significant differences in cardiac conduction and repolarization between short- and long-duration space flights were reported by manually analyzing 24-hour Holter recordings. Long duration space flight was found to prolongue QT interval, corrected by the Bazett's formula ($QTc=QT/(RR)^{1/2}$), thus increasing the arrhythmia susceptibility [8].

Therefore, while there is some evidence suggesting that spaceflight may be associated with an increased susceptibility to ventricular dysrhythmias, few systematic studies have been conducted and no causal relationship has been established. In addition, during previous space flights no investigation has been focused on the evaluation of T wave morphologic changes.

In particular, as regards the relationship between the T wave amplitude and the increased risk of developing arrythmias, recently Di Bernardo and Murray showed, using a mathematical model, that an increase in the T wave amplitude is related to an increase in dispersion of repolarization [9]. Also, during the recovery phase following stress-test, when an increase in vagal tone is known to be present, an increase in Twave amplitude has been observed and related to an increase in the action potential duration heterogeneity, which contributes to the increased dispersion of repolarization [10].

Basing on these considerations, and on previous findings that changes in gravity during parabolic flight affect the ECG R-wave amplitude [11], we hypothesized that the evaluation of changes in T wave amplitude elicited by changes in gravity during parabolic flight could allow to study the physiologic mechanisms involved, to better understand the effects of short-term exposure to microgravity on ventricular repolarization. Our goal was then to develop an automated technique for the analysis of the ECG signal acquired during parabolic flight in order to evaluate the T-wave peak amplitude changes, and possibly disentangle among the contributes of the different acting physiologic mechanisms.

2. Methods

We retrospectively analyzed the ECG tracings (Cardionics, 12 leads, 500 Hz) acquired during six previous ESA and CNES parabolic flight campaigns

(2001-2005) performed onboard the Airbus A-300 Zero-G (Novespace, CNES-ESA, Bordeaux, France).

The ECG signals obtained from 12 normal unmedicated male subjects (age 41±11 yrs) in upright position, during 12 consecutive parabolas (Airbus A-300 Zero-G, CNES-ESA), and the corresponding gravity signal (G^z) acquired from the airplane accelerometer, were selected for analysis. In 4 of the 12 parabolas considered for each subject, lower-body negative pressure (LBNP) at –50 mmHg was activated during $0G^z$, to study the effects of this countermeasure, which reduces venous return, on the cardiac rhythm.

2.1. Data pre-processing

Using the G^z signal as a reference, after low-pass filtering (order 20, cut-off frequency 10 Hz), the following phases were identified in each parabola: I) normogravity ($1G^z$), before the parabola starts; II) hypergravity ($1.8G^z$), for about 20 sec; III) microgravity ($0G^z$), at the top of the trajectory, lasting about 24 sec; IV) hypergravity ($1.8G^z$), for other 20 sec; V) recovery ($1G^z$rec), for 24 sec after the end of the parabola.

From the ECG, the Q-wave was automatically identified from the V1 lead by commercial software (Cardionics). Moreover, the leads corresponding to the X, Y and Z orthogonal projections, were extracted and low-pass filtered (order 20, cut-off frequency 15 Hz).

2.2. Selective beat averaging procedure

Each QQ interval was labeled as $1G^z$, $1.8G^z$, $0G^z$, $0G^z_{LBNP}$, $1G^z$rec, according to the G^z value at its time occurrence, and to the application of the LBNP in the considered parabola. Then, for each label, a QQ duration histogram (10 ms bin amplitude) was calculated; thus generating QQ duration classes C (400 msec÷1400 msec), each including beats which differ by a maximum of 5 samples.

For each class C(n), the beats with the corresponding QQ duration were located on the ECG signal corresponding to the X, Y and Z orthogonal leads, and extracted. After beats realignment according to the R wave peak [12], a simple averaging operation was then applied, thus obtaining a mean template T(n), representative of all the beats owing to the class C(n), for X, Y and Z separately.

To avoid inclusion of beats affected by noise or artifacts in the averaging operation, a cross-correlation operation was computed between each beat and the corresponding T(n): beats with cross-correlation $<7*10^7$ were excluded and T(n) recalculated.

The isoelectric line, defined as the straight line connecting the J point (flex located between S wave and T wave) to the mean of the 5 samples preceding the P wave upslope, was then identified for each T(n), and subtracted to T(n).

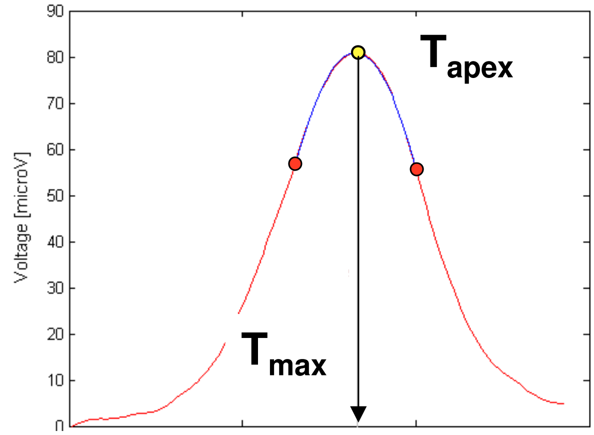

Figure 1.Schematization of the detection strategy applied to identify the T_{start} and T_{end} points (see text for details).

Finally, the template V(n), corresponding to the modulus vector, was computed as the modulus of the templates obtained for the X, Y, and Z leads separately.

2.3. Parameters extraction

For each n in the range 580÷940 msec, the templates T(n) obtained from X, Y and Z leads and their modulus V(n) were analyzed as follows.

The fiducial points corresponding to the apex (T_{apex}) of the T wave was automatically detected as the maximum of the parabolic interpolation of the T wave, from the point of maximum upslope to the point of minimum downslope (Figure 1).

From this point, the T wave peak maximum amplitude (Tmax) was computed as its value in respect to the isoelectric line.

For each subject, the curves representing the relation between the QQ duration and Tmax were computed for each gravity phase.

Once analyzed all the subjects, the cumulative mean curves for each phase in the parabola were computed: the mean value $\overline{T}max(n)$ for each QQ duration class C(n) was computed as the mean of the values obtained from each subject, weighted by the corresponding number of beats w(n) whose generated the template M(n):

$$\overline{T}max(n) = \frac{\sum_{1}^{X} {}_i Tmax_i(n) * w_i(n)}{\sum_{1}^{X} {}_i w_i(n)} \quad (1)$$

To define a normality range of ±2SD (95% confidence interval) around the mean value, the corresponding SD was computed as:

$$\sigma_T(n) = \sqrt{\frac{\sum_{1}^{X}{}_i(\overline{T}max(n) - Tmax_i(n))^2 * w_i(n)}{\sum_{1}^{X}{}_i w_i(n) * (X-1)}} \qquad (2)$$

Also, normalized curves useful for comparison between gravity phases were obtained by dividing Tmax, for every C(n), by the corresponding 1Gz value before the application of (1) and (2).

3. Results

In total, we analyzed 47631 heart cycles, subdivided as follows: 31851 at $1G^z$, 5981 at $1.8G^z$, 2883 at $0G^z$, 1624 at $0G^z_{LBNP}$, 4399 at $1G^z$rec. The selective beat averaging procedure appeared able to highly improve the SNR, resulting in templates on which the automated fiducial point detection was feasible and reliable (Figure 2).

The proposed method was able to quantify T_{max} in each G^z, despite the short duration of each gravity phase (about 20 sec). Observing the results obtained separately for the X, Y, and Z orthogonal leads, we observed that the value of Tmax extracted from the templates was lead-dependent, with higher values in X lead and smaller values in Z lead (Figure 3).

By averaging the values obtained from the templates in the range QQ=580÷940 msec, significant changes in Tmax with gravity were noted (Table 1). In particular, a decrease at $1.8G^z$ in X, Y and Z, in respect to $1G^z$, and an increase at $0G^z$ in X and Y can be observed. At $1G^z$rec, a slight increase in Y and a decrease in Z were reported, while X did not change significantly. The application of LBNP during $0G^z$ resulted in an increase in Tmax in X and Y, and in a reduction in Z, compared to $1G^z$.

When the analysis was performed on the modulus V(n), at $0G^z$, Tmax showed a significant increase (15%±4%) compared to $1G^z$, while at $1G^z$rec, Tmax was increased by 5%±2% only. With the application of LBNP during $0G^z$, the increase in Tmax was 8% ±4%. No reliable results were available at $1.8G^z$, due to the reduced number of templates obtained from X, Y and Z in correspondence to the same C(n).

Table 1. Mean ± st.dev. of Tmax (in μV) computed from the template T(n) in the three orthogonal leads, for each gravity phase (cumulative mean for QQ=580÷940 msec)

	Der X	Der Y	Der Z
$1G^z$	183.4±12.1	142.2±17.7	94.6±18.3
$1.8G^z$	154.8±12.0*	123.5±11.3*	90.5±13.8*
$0G^z$	207.6±17.0*	148.5±17.6*	94.4±15.4
$0G^z$LBNP	204.1±13.5*	160.6±19.4*	82.6±12.5*
$1G^z$rec	186.5±14.7	148.9±13.7*	89.8±12.4*

*:p<0.05 paired t-test vs relevant$1G^z$

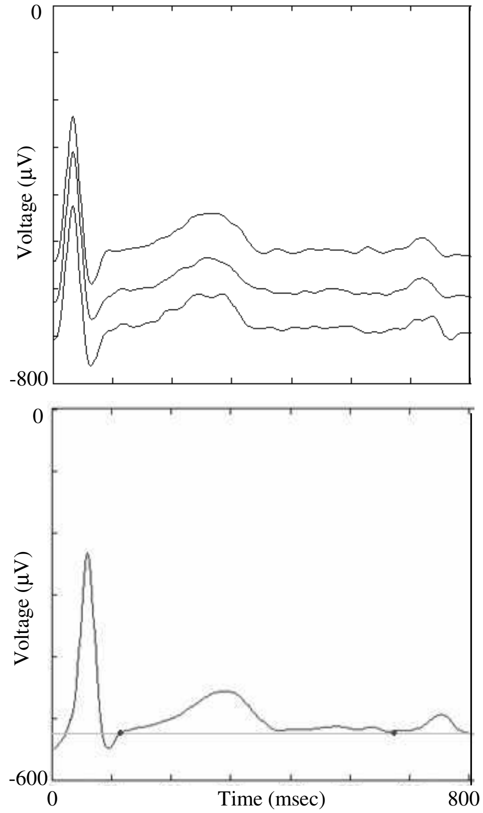

Figure 2. Example of noise reduction and improvement in morphologic shape definition. Beats of the same duration class QQ (top) were averaged in order to obtain the relevant template T(n), from which the isoelectric line (in light gray) was identified as the intersection of isoelectric points (black dots) (bottom panel, see text for details).

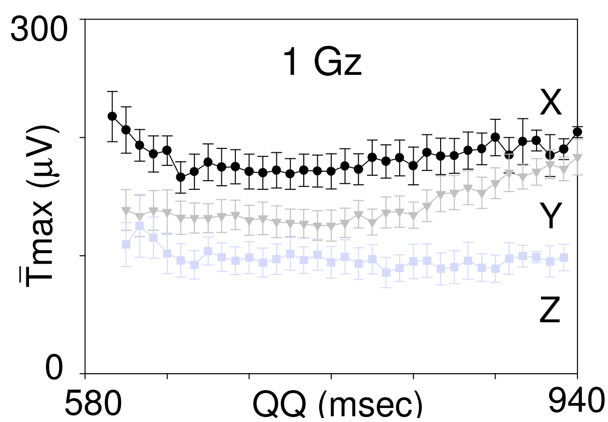

Figure 3. Results obtained from the X, Y and Z orthogonal leads relevant to Tmax at 1 G^z.

4. Discussion and conclusions

Parabolic flight presents an unique opportunity to study the immediate physiological adaptations of the cardiovascular system to different gravity conditions. In particular, we used this experimental protocol to induce abrupt changes in fluid distribution to study potential effects on ventricular repolarization phenomena, focusing on Tmax.

Our results showed that microgravity during parabolic flight influences ventricular repolarization by increasing T wave amplitude. Our experimental protocol allowed to elicit the different mechanisms which could contribute to this fact: 1) augmented parasympathetic activation, which increases action potential dispersion in myocardial cells, and is also present in the $1G^{z}$rec phase; 2) increased venous return, which causes cardiac dilation and increased conductibility in the thorax; 3) changes in heart position.

At $0G^{z}$ the application of the LBNP countermeasure resulted in smaller variation in Tmax, as a result of the reduced increase in venous return during the microgravity phase. Without LBNP, the upward fluid shift generates an increase in thorax conductivity. Also, the cardiac volume increases by about 20% [13], which results in stretching of the myocardial fibers and probably in a higher variability in the length of the paths that the repolarization wave front has to take. Also, by our evidences at 0Gz, T wave amplitude appears to be preload dependent.

In conclusion, the method we developed and applied allowed the quantification of the T wave amplitude, and its relationship with the cardiac cycle duration during parabolic flight. Significant changes in T wave amplitude with gravity were observed. In particular, an increase in Tmax was found with microgravity, as a result of increased vagal tone, upward blood shift and cardiac deformation. If confirmed by future investigations on data acquired during space flight, this fact could represent the first quantitative evidence of increased risk in developing cardiac dysrhythmias during spaceflight.

Acknowledgements

We want to acknowledge Pierre Vaida, Andre Capderou, Suzel Bussieres, Christian Kays, André Technouyers from the Parabolic Flight Team of the University of Bourdeaux 2 “Victor Segalen” for their support and help in the organization of the data acquisition session. Also, Pierre Vaida was the recepient of grant 02/CNES/4800000039 from the CNES.

References

[1] Charles JB, Bungo MW, Fortner W. Cardiopulmonary function. In: Nicogossian A, Huntoon C, Pool S, editors. Space Physiology and Medicine, 3rd Edition. Philadelphia: Lea & Febiger, 1994: 286-304.

[2] Hawkins WR, Zieglschmid JF. Clinical aspects of crew health. In: Johnston R, Dietlein LD, Berry CA, editors. Biomedical results of Apollo (NASA SP-368). Washington, DC: Government printing office, 1975.

[3] Dietlein LD. Summary and conclusions. In: Johnston R, Dietlein LD, Berry CA, editors. Biomedical results of Apollo (NASA SP-368). Washington, DC: Government Printing Office, 1975.

[4] Douglas WR. Current status of space medicine and exobiology. Aviat Space Environ Med. 1978;49:902-904.

[5] Smith R, Stanton K, Stoop D, et al. Vectorcardiographic changes during extended space flight (M093): Observations at rest and during exercise. In: Johnson RS, Dietlein LF, editors. Biomedical results of Skylab (NASA SP-377). Washington, DC: 1977.

[6] Bungo MW, Johnson PC. Cardiovascular Examinations and Observations of Deconditioning During the Space-Shuttle Orbital Flight Test Program. Aviat Space Environ Med 1983;54:1001-1004.

[7] Fritsch-Yelle JM, Leuenberger UA, D'Aunno DS, et al. An episode of ventricular tachycardia during long-duration spaceflight. Am J Cardiol 1998;81:1391-1392.

[8] D'Aunno DS, Dougherty AH, DeBlock HF, et al. Effect of short- and long-duration spaceflight on QTc intervals in healthy astronauts. Am J Cardiol 2003;91:494-497.

[9] di Bernardo D, Murray A. Explaining the T-wave shape in the ECG. Nature. 2000 Jan 6;403(6765):40.

[10] Langley P, di Bernardo D, Murray A. Quantification of T wave shape changes following exercise. Pacing Clin Electrophysiol 2002;25(8):1230-4.

[11] Saltykova M, Capderou A, Atkov O, et al. Variations of intrathoracic amount of blood as a reason of ECG voltage changes. Ann Noninvasive Electrocardiol 2003;8:321-332.

[12] Badilini F, Maison- Blanche P, Childers R, Coumel P. QT interval analysis on ambulatory electrocardiogram recordings: a selective beat averaging approach. Med Biol Eng Comput 1999;37(1):71-9.

[13] Caiani EG, Sugeng L, Weinert L, Capderou A, Lang RM, Vaida P. Objective evaluation of changes in left ventricular and atrial volumes during parabolic flight using real-time three-dimensional echocardiography. J Appl Physiol 2006;101(2):460-8 (Epub 2006 Apr 6).

Address for correspondence

Enrico G Caiani
Dipartimento di Bioingegneria, Politecnico di Milano
Piazza L. da Vinci 32, 20133 Milano (Italy)
caiani@biomed.polimi.it