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Effect of Short- and Long-Duration Spaceflight on QTc Intervals in Healthy Astronauts

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The human cardiovascular system undergoes profound changes when exposed to spaceflight, including cardiac rhythm disturbances during long-term missions.[1–5] Underlying spaceflight-induced alterations in cardiovascular autonomic regulation may adversely influence cardiac repolarization and thus precipitate these rhythm disturbances.[6–8] Therefore, we analyzed electrocardiograms or Holter monitor tracings obtained from astronauts who experienced short- and long-duration space missions. Our findings reveal striking differences in cardiac conduction and repolarization between short- and long-duration spaceflight.

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Informed consent was obtained in accordance with the guidelines of the Committee for the Protection of Human Subjects at the Johnson Space Center. A retrospective analysis of electrocardiograms from 7 astronauts (6 men and 1 woman, average age 44 ± 5 years for short-duration flights and 47 ± 6 years for long-duration flights), who experienced both short-duration spaceflight onboard the space shuttle and long-duration spaceflight onboard Mir or the International Space Station, were used to measure PR, RR, and QT intervals. Three-lead electrocardiograms were recorded during 1 minute of supine rest on digital tape 10 days before flight, on landing day (within 2 hours of touchdown), and 3 days after landing for short- and long-duration missions. One minute of data at rest was analyzed from lead II and the results averaged.

Twenty-four-hour Holter monitoring recordings from 3 crew members (3 men, average age 45 ± 6 years) were obtained 60 days before launch, at 3 separate times during the mission (4-month flight), and 2 times after transfer to the space shuttle before re-entry on landing day (1 subject's Holter was recorded 2 days after landing) and at 11 or 39 days after landing. PR, RR, and QT intervals from lead V_2 were measured for 10 cardiac cycles at 1, 6, 11, and 16 hours. The results for each interval were averaged at each time period. Activity logs are not available.

The PR, RR, and QT intervals were measured manually, in random order, by 2 examiners blinded to flight duration or testing day. The beginning of the P wave and the beginning of the QRS complex defined the PR interval. The beginning of the Q (or R) wave and the end of the T wave at the isolectric point defined the QT interval. The QT interval was corrected for heart rate using Bazett's formula: $QTc = QT/(RR)^{0.5}$.

Electrocardiographic data from 1 long-duration astronaut were not collected 3 days after landing. Five of the 7 astronauts from long-duration spaceflights had complete electrocardiographic data sets available from previous short-duration spaceflights for comparison. Serum concentrations of potassium, calcium, and

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TABLE 1 Serum Electrolytes in Astronauts Before and After Spaceflight

	Short Duration (n = 5)			Long Duration (n = 7)		
	Before Flight	Landing	After Flight	Before Flight	Landing	After Flight
K^+ (mmol/L)	4.2 ± 0.10	4.2 ± 0.15	4.2 ± 0.09	4.2 ± 0.09	3.8 ± 0.09*	4.1 ± 0.11
Mg^{++} (mmol/L)	0.95 ± 0.05	0.95 ± 0.02	0.99 ± 0.03	1.1 ± 0.04	1.0 ± 0.03	1.0 ± 0.04
Ca^{++} (mmol/L)	2.3 ± 0.05	2.4 ± 0.05	2.3 ± 0.06	2.4 ± 0.03	2.4 ± 0.04	2.4 ± 0.04

*p <0.01.

Data are expressed as mean ± SEM.

Serum concentrations of total calcium (Ca^{++}) potassium (K^+), and magnesium (Mg^{++}) were obtained before flight, on landing day, and after flight (3 days after landing) for short- and long-duration spaceflight.

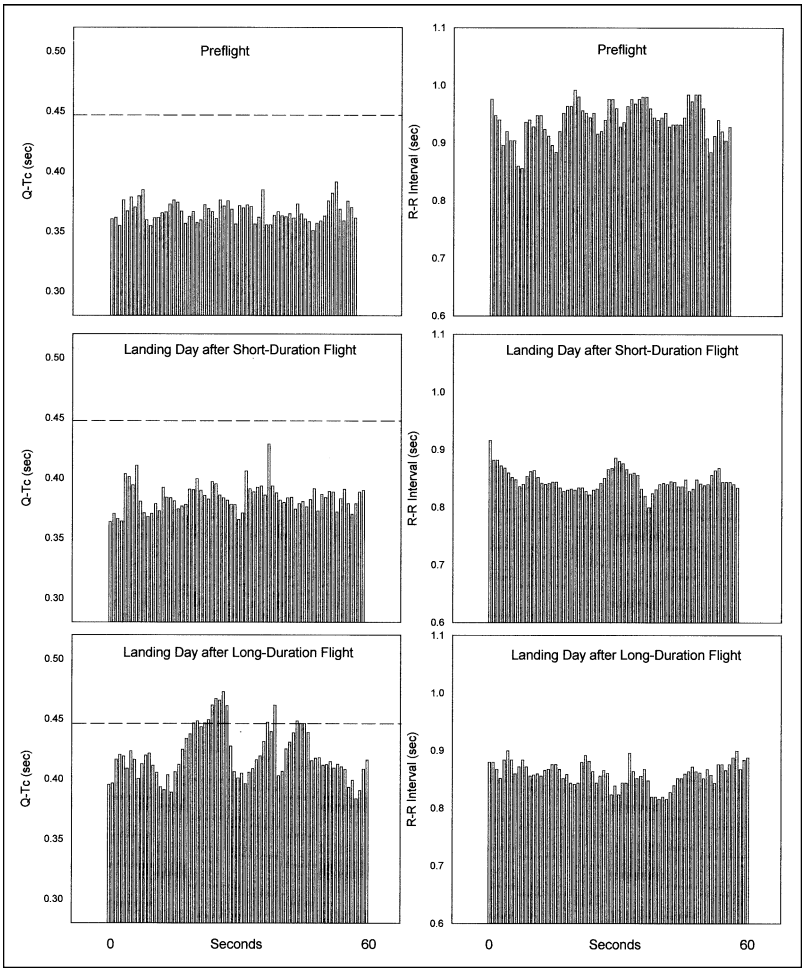

FIGURE 1. Individual QTc *(left)* and RR *(right)* intervals obtained from electrocardiograms recorded during 1 minute of supine rest, from a single male astronaut, before flight *(top)*, and on landing day after short- *(middle)* and long- *(bottom)* duration flights.

magnesium were measured before flight, on landing day, and 3 days after landing.

Data were checked for normalcy and are expressed as mean ± SEM. The coefficient of variation, a measure of relative variability, was calculated for RR and QTc intervals from 1 minute of electrocardiographic data obtained during supine rest before flight and on landing day, for short- and long-duration spaceflights. A 2-way analysis of variance with repeated measures was used to determine if flight duration had an affect on PR, RR, and QTc intervals, coefficient of variation, and serum concentrations of potassium, calcium, or magnesium. Paired *t* tests were used to document differences when there was a significant main effect due to spaceflight duration. A p value <0.05 was considered significant.

Table 1 lists serum concentrations for potassium, calcium, and magnesium. Although there was a statistically significant decrease in the concentration of potassium on landing day after long-duration spaceflight ($p = 0.002$), clinically there were no changes in electrolyte levels sufficient to affect cardiac conduction or repolarization.

Figure 1 represents 1 minute of supine individual QTc and RR interval data for a single male astronaut before flight, and on landing day after short- and long-duration flight. After a short-duration flight, QTc intervals were not prolonged. After a long-duration flight, 24% of the QTc intervals were ≥0.45 second. The degree of variability of the QTc interval was increased in this subject after short and long missions. This is consistent with group findings that revealed an increase in the variability of QTc intervals on landing day after short- and long-duration spaceflights ($p = 0.03$, $p = 0.04$). The coefficient of variation of the QTc intervals were 2.6 ± 0.2% before flight, and 6.9 ± 4.3% and 4.9 ± 2.6% on landing day after short- and long-duration flight, respectively.

This subject had shorter RR intervals than those before flight after short and long flights, with the greatest decrease after the shorter flight. There were

TABLE 2 Electrocardiographic Intervals Before Flight, on Landing Day, and Three Days After Landing for Short- and Long-duration Spaceflights*

		Before Flight		Landing Day		After Flight	
Subject	Interval	SD	LD	SD	LD	SD	LD
A	RR	1.36	1.17	1.07	1.30	1.04	0.79
	PR	0.15	0.15	0.13	0.17	0.13	0.13
	QT	0.40	0.43	0.43	0.43	0.39	0.36
	QTc	0.37	0.35	0.37	0.42	0.37	0.41
B	RR	1.10	1.03	0.68	1.07	1.04	0.83
	PR	0.16	0.15	0.13	0.18	0.14	0.13
	QT	0.36	0.36	0.32	0.41	0.37	0.36
	QTc	0.35	0.36	0.38	0.40	0.36	0.40
C	RR	NA	0.93	NA	0.93	NA	0.84
	PR	NA	0.17	NA	0.18	NA	0.18
	QT	NA	0.36	NA	0.38	NA	0.35
	QTc	NA	0.37	NA	0.39	NA	0.38
D	RR	NA	1.06	NA	0.97	NA	0.90
	PR	NA	0.17	NA	0.19	NA	0.16
	QT	NA	0.36	NA	0.38	NA	0.35
	QTc	NA	0.35	NA	0.39	NA	0.37
E	RR	0.87	0.88	0.73	1.07	1.05	NA
	PR	0.17	0.17	0.14	0.19	0.17	NA
	QT	0.36	0.36	0.33	0.41	0.39	NA
	QTc	0.38	0.38	0.39	0.40	0.38	NA
F	RR	0.96	0.94	0.85	0.88	0.92	0.80
	PR	0.19	0.20	0.18	0.21	0.17	0.19
	QT	0.38	0.37	0.35	0.38	0.37	0.36
	QTc	0.39	0.37	0.37	0.41	0.39	0.40
G	RR	0.99	1.01	0.80	0.87	1.12	0.85
	PR	0.18	0.17	0.17	0.21	0.19	0.14
	QT	0.37	0.36	0.32	0.35	0.38	0.35
	QTc	0.38	0.35	0.36	0.39	0.36	0.38

*PR, RR, QT, and QTc intervals (in seconds) from electrocardiograms recorded during 1 minute of supine rest before and after both short- and long-duration spaceflights.

LD = long-duration spaceflight; NA = no data available; SD = short-duration spaceflight.

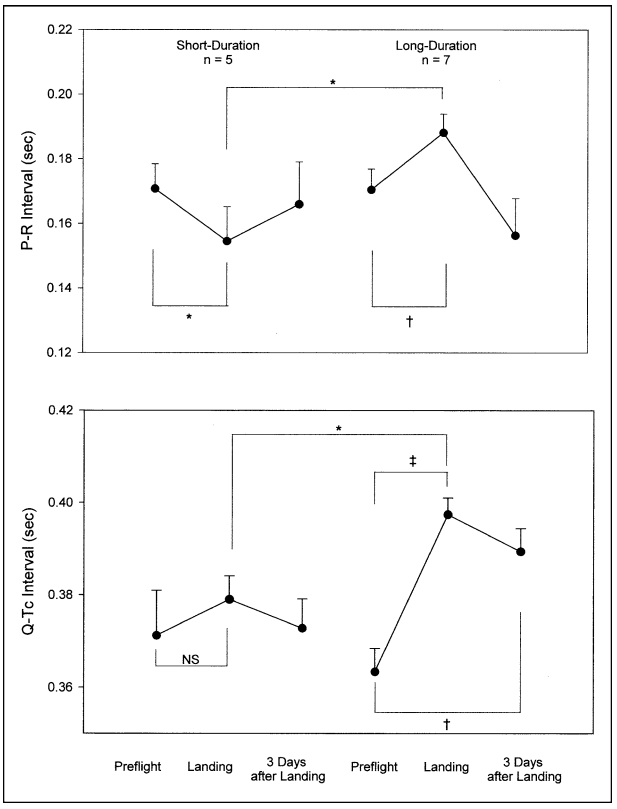

FIGURE 2. PR *(top)* and QTc *(bottom)* intervals (mean ± SEM) from electrocardiograms obtained during 1 minute of supine rest before flight, on landing day, and 3 days after landing for short- *(left)* and long- *(right)* duration spaceflight. *p <0.05; †p <0.01; ‡p <0.001.

consistent intervals in the group. There was a trend toward greater RR interval variability after spaceflight, which was consistent with group findings. The degree of variability of the RR intervals obtained from 1 minute of supine rest before flight and on landing day showed a tendency toward an increase after short- and long-duration spaceflights ($p = 0.05$, $p = 0.09$).

Table 2 shows PR, RR, QT, and QTc intervals, and Figure 2 shows mean PR and QTc intervals measured from electrocardiograms obtained during 1 minute of supine rest before flight, on landing day, and 3 days after landing for short- and long-duration spaceflights. Preflight PR, RR, and QTc intervals were similar for short- and long-duration spaceflights. PR intervals were decreased on landing day after short-duration spaceflight ($p < 0.05$, Figure 2). After a long-duration flight, PR and QTc intervals were significantly increased ($p = 0.014$, $p = 0.012$; Figure 2). The decrease in RR intervals observed on landing day after short-duration spaceflight was not present after long-duration spaceflight ($p = 0.034$).

Figure 3 shows mean PR, RR, and QTc intervals measured from Holter monitoring recordings obtained before, during, and after long-duration spaceflight. Data were analyzed 4 times (at 5-hour intervals) for each 24-hour Holter recording. PR and QTc intervals were significantly increased during and after long-duration flight ($p < 0.001$, $p < 0.001$). This was consistent within each time period. Transfer from Mir to shuttle revealed a decrease in PR and QTc intervals (both were still greater than preflight values, $p < 0.001$), with little change in the RR interval. Onboard the shuttle, the PR and QTc intervals increased and were prolonged on landing day ($p < 0.001$). The normal circadian variability in RR intervals was attenuated during shuttle day 1 and immediately after landing, but was present during all other test days.

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The major finding of this study is that long-, but not short-, duration spaceflight prolongs cardiac conduction and repolarization. Shifts in sympathovagal balance and primary cardiac changes may be responsible. Long-duration flight is associated with QTc interval prolongation and may increase arrhythmia susceptibility. Medications that prolong

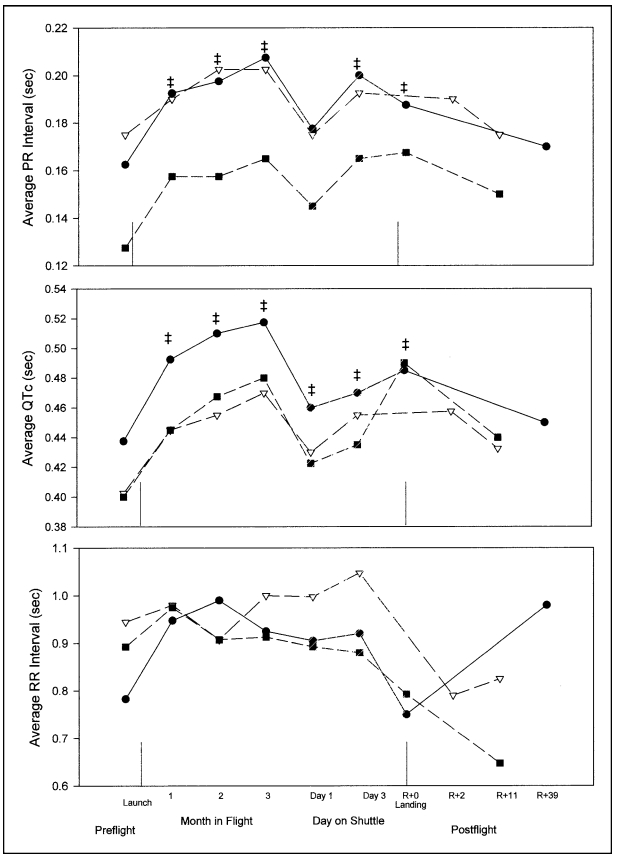

FIGURE 3. Mean PR, RR, and QTc intervals from 24-hour Holter recordings for 3 crew members before flight, during a 4-month space mission, after transfer to the space shuttle, on landing day, and 11 and/or 39 days after landing. ‡p <0.001.

the QT interval should be administered with caution during and after long-duration spaceflight.

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Endothelial Dysfunction and Reduced Myocardial Perfusion Reserve in Heart Failure Secondary to Coronary Artery Disease

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Diminished myocardial perfusion reserve[1–6] and endothelial dysfunction[7,8] have been observed in patients with chronic heart failure. The aim of the present study was to examine a possible relation between severity of heart failure and perfusion and endothelial dysfunction in patients with left ventricular dysfunction. B-type natriuretic peptide (BNP) was measured as an objective measure of heart failure. Myocardial perfusion was assessed at rest during cold pressor testing (CPT) to assess endothelial function and during maximal vasodilation to assess perfusion reserve.

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Patients satisfied the following inclusion criteria: men or women, 20 to 80 years old; left ventricular ejection fraction of <0.5, an old (>3 months) myocardial infarction, and no complaints of angina pectoris. Exclusion criteria were: hyper- or hypotension, hemodynamically significant valvular disease, pacemaker treatment, other serious illnesses, diabetes mel-

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