

Dysrhythmias in Laypersons During Centrifuge-Simulated Suborbital Spaceflight

Rahul Suresh; Rebecca S. Blue; Charles H. Mathers; Tarah L. Castleberry; James M. Vanderploeg

- INTRODUCTION:** There are limited data on cardiac dysrhythmias in laypersons during hypergravity exposure. We report layperson electrocardiograph (ECG) findings and tolerance of dysrhythmias during centrifuge-simulated suborbital spaceflight.
- METHODS:** Volunteers participated in varied-length centrifuge training programs of 2–7 centrifuge runs over 0.5–2 d, culminating in two simulated suborbital spaceflights of combined $+G_z$ and $+G_x$ (peak $+4.0 G_z$, $+6.0 G_x$, duration 5 s). Monitors recorded pre- and post-run mean arterial blood pressure (MAP), 6-s average heart rate (HR) collected at prespecified points during exposures, documented dysrhythmias observed on continuous 3-lead ECG, self-reported symptoms, and objective signs of intolerance on real-time video monitoring.
- RESULTS:** Participating in the study were 148 subjects (43 women). Documented dysrhythmias included sinus pause ($N = 5$), couplet premature ventricular contractions ($N = 4$), bigeminy ($N = 3$), accelerated idioventricular rhythm ($N = 1$), and relative bradycardia (RB, defined as a transient HR drop of >20 bpm; $N = 63$). None were associated with subjective symptoms or objective signs of acceleration intolerance. Episodes of RB occurred only during $+G_x$ exposures. Subjects had a higher post-run vs. pre-run MAP after all exposures, but demonstrated no difference in pre- and post-run HR. RB was more common in men, younger individuals, and subjects experiencing more centrifuge runs.
- DISCUSSION:** Dysrhythmias in laypersons undergoing simulated suborbital spaceflight were well tolerated, though RB was frequently noted during short-duration $+G_x$ exposure. No subjects demonstrated associated symptoms or objective hemodynamic sequelae from these events. Even so, heightened caution remains warranted when monitoring dysrhythmias in laypersons with significant cardiopulmonary disease or taking medications that modulate cardiac conduction.
- KEYWORDS:** dysrhythmia, commercial spaceflight, electrocardiogram, tolerance, bradycardia, vagal, $+G_z$, $+G_x$.

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To date, space travel has been limited to a highly select population of test-pilot-astronauts, scientists (both full-time astronauts and one-flight experimenters), and rare paying passengers. Soon, self-selected, volunteer, paying passengers will experience suborbital travel provided by any one of several commercial spaceflight companies. Understanding of the physiological response and tolerance to hypergravity exposures anticipated on such spaceflights among individuals of a range of ages and with preexisting medical conditions is limited. Recent studies have attempted to bridge this knowledge gap with the use of centrifuge-simulated suborbital acceleration profiles.^{2,3} These studies have demonstrated that, in general, individuals of a wide age range and controlled medical conditions are likely to tolerate suborbital spaceflight well.^{2,3}

The primary G exposures anticipated during commercial spaceflight under nominal conditions include $+G_z$ (head-to-toe)

and $+G_x$ (chest-to-back) acceleration. Cardiovascular response to $+G_z$ has been well studied in aviators and other military personnel undergoing centrifuge-simulated hypergravity exposures or performing aerobatic flight, establishing thresholds for acceleration tolerance and demonstrating that electrocardiographic (ECG) abnormalities are common.^{8,16,17} Positive G_z exposures up to $+9 G_z$ with slow- and rapid-onset rates have been shown

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to induce primarily single or couplet premature ventricular complexes (PVCs) and, less frequently, premature atrial complexes (PACs), bigeminy, or trigeminy.^{8,16} In a small percentage of individuals, other rhythms have been observed, including ventricular tachycardia, atrial fibrillation, supraventricular tachycardia, and anomalous sinus bradycardia.^{5,8} In one study, 47% of individuals experiencing hypergravity developed dysrhythmias, but only 4.5% of these aberrant rhythms resulted in termination of the centrifuge run by the medical monitor.⁸ Nearly half of run-terminating dysrhythmias were due to ventricular tachycardia, but in all cases, these resolved immediately after resolution of G exposure or shortly thereafter. Although specific hemodynamic values were not presented, none of the reported cases appeared to demonstrate clinical decompensation requiring intervention.⁸ While rare conditions may cause clinical concern, prompting termination of training, sufficient accumulated data and observations regarding the incidence of these rhythms during $+G_z$ exposures have accrued to recognize that most aberrant rhythms associated with $+G_z$ are benign and self-limited.⁵

Unlike $+G_z$ exposure, characterization of the cardiovascular responses to positive and negative G_x is more limited. In 1955, Duane et al. reported on the tolerance of short-duration $+G_x$ and $-G_x$ exposures up to $+15 G_x$ lasting between 1–15 s.⁴ While limited by poor ECG signal acquisition, the authors report witnessing episodes of “slight bradycardia” during $+G_x$ and sinus dysrhythmias post-run for both $+G_x$ and $-G_x$.⁴ Torphy et al. explored the incidence of dysrhythmias during isolated, single-direction $+G_z$ and $+G_x$ in U.S. Air Force pilots during various training runs.¹⁵ They found that 12–68% of subjects developed PACs and premature contractions with aberrant conduction during primarily $+G_x$, with lower incidence of ectopy that favored PVCs during $+G_z$.¹⁵ Rogge et al. subsequently compared the ECG response during $+G_x$, treadmill stress testing, and tilt-table testing.¹⁰ In contrast to treadmill stress testing and tilt-table testing, which induced mostly PVCs, they found that isolated $+5.5$ – $8.0 G_x$ provoked primarily PACs and rare PVCs, with an overall incidence of dysrhythmias during centrifugation in 47.4% of subjects.¹⁰ These studies established the physiological and operational tolerance limits for $+G_x$ exposures and the prominent ECG findings in healthy and primarily young airmen. However, studies to date do not address the effects of combined $+G_z$ and $+G_x$ exposure, as would be expected during commercial suborbital spaceflight. Moreover, they do not provide a clear understanding of the ECG responses to $+G_x$ and $+G_z$ in laypersons, particularly those of a wide age range, with chronic medical conditions, or who have limited prior experience with acceleration exposure.

A recent study attempted to characterize layperson responses to highly varied training programs for centrifuge-simulated suborbital spaceflight, including combined $+G_z$ and $+G_x$ exposures.¹ During this study, hemodynamic and ECG data were collected on study subjects undergoing G exposure, but have not been previously analyzed or reported. We describe here the incidence, tolerance, and factors associated with documented dysrhythmias observed during this study.

METHODS

Subjects

Study data were collected during a previous study¹ in which voluntary layperson subjects were solicited to participate in human centrifuge research at the National Aerospace Training and Research (NASTAR) Center in Philadelphia, PA. The methods of the study are briefly summarized here; study protocols were approved by the Institutional Review Board of the University of Texas Medical Branch. Medical documentation required for study subjects included a self-reported medical history questionnaire, a physical exam completed by their personal physician, and a resting ECG, with documentation of effective control of any pre-existing medical conditions. This process and the forms used were similar to the guidance and materials provided for Federal Aviation Administration approved exams performed by aviation medical examiners. Based on review by a study physician, subjects could be approved directly, be required to undergo further tests or provide more documentation, or be excluded altogether depending upon their medical status, history, and physical findings. All subjects provided informed consent before participating in the study protocol. Subjects were advised to take any home medication throughout their participation in the study as per their usual schedule, with the exception of alpha-adrenergic antagonists and peripheral vasodilators, which were held a minimum of 24 h prior to centrifugation.

Equipment

The ATFS-400 simulator, a centrifuge-based, wide field-of-view flight simulator able to impose the actual combined $+G_x/+G_z$ of a typical spaceflight launch profile, was used to provide a highly realistic simulation of suborbital spaceflight. High-fidelity audiovisual simulation was provided during simulated spaceflight exposures described below to help create a suborbital spaceflight experience and enhance the realism of the experience.

Procedure

Prior to centrifuge runs, subjects were trained on how to perform an anti-G straining maneuver consisting of continuous and maximum contraction of lower extremity skeletal muscles as well as the “hook” (L-1 closed-glottis variant) respiratory maneuver. They were advised to use muscular strain alone during $+G_z$ exposure, but to add the hook maneuver only in the event of grayout or light-headedness.

Subjects participated in varied length training programs of 0.5 d, 1 d, or 2 d in length, all of which culminated in the same final two centrifuge-simulated spaceflight experiences [described as “Combined Profile 1 (CP1)” and “Combined Profile 2 (CP2)” below]. The 2-d training program included four centrifuge runs on day 1, the first two providing stepwise familiarization with $+G_z$ acceleration and the subsequent two providing stepwise familiarization with $+G_x$ acceleration. Runs 1–4 on Day 1 were each 2 min in duration and peaked at $+2.15 G_z$, $+3.5 G_z$, $+3 G_x$, and $+6 G_x$ for 15 s each (Table I). Subjects remained in the gondola for the <1 min between runs 1 and 2 and between runs 3 and 4. Day 2 profiles included CP1, performed first at 50% of

Table I. G-Exposure Profiles Included in Training for 2-d, 1-d, and 0.5-d Cohorts.

G EXPOSURE TRAINING	G EXPOSURE RUN	G EXPOSURE DIRECTION	TOTAL G	PEAK G	MAX PEAK G		G ONSET RATE ($G \cdot s^{-1}$)		2-D COHORT	1-D COHORT	0.5-D COHORT
			EXPOSURE DURATION (s)	EXPOSURE DURATION (s)	+G _z	+G _x	+G _z	+G _x			
Single direction +G exposure	+2.15 G _z	+G _z	120	15	2.15	-	0.5	-	√		
	+3.5 G _z	+G _z	120	15	3.5	-	0.5	-	√		
	+3 G _x	+G _x	120	15	-	3	-	1.5	√		
	+6 G _x	+G _x	120	15	-	6	-	1.5	√		
50% CP1	50% CP1	+G _z & +G _x	240	5	1.65	3	0.5	1.5	√	√	
100% CP1	100% CP1	+G _z & +G _x	240	5	3.8	6	0.5	1.5	√	√	√
100% CP2	CP2	+G _z & +G _x	240	5	4	4.5	0.5	1.5	√	√	√

CP: combined profile (simulated spaceflight); +G_z: head-to-toe acceleration; +G_x: chest-to-back acceleration.

acceleration exposure limits anticipated in suborbital spaceflight, then repeated at 100% acceleration, and CP2, performed only at 100% acceleration. Day 2 profiles were 4–7 min in duration, with peak G sustained for 5 s of +3.8 G_z and +6.0 G_x for CP1 and +4.0 G_z and +4.5 G_x (maximum resultant vector 6.1 G) for CP2. Subjects remained in the gondola for an approximately 5-min break between the 50% CP1 and 100% CP1 experiences. The 1-d training program consisted of 50% CP1, 100% CP1, and 100% CP2. The 0.5-d training program included only the 100% profiles of CP1 and CP2. A summary of centrifuge exposures included in each training group, as well as G onset rates, peak G exposures, and time at peak G is provided in Table I.

Subjects were monitored in the gondola by video at all times during centrifugation and both the subjects and the medical monitors could access two-way voice communication as needed. Medical monitors documented any objective signs of acceleration intolerance on real-time video monitoring, including objective signs of confusion or altered mentation. Resting heart rate (HR) and blood pressure (BP) were measured at the time subjects arrived at the facility on Day 1 and Day 2 and repeated immediately prior to entering and after exiting the gondola. A study physician monitored continuous 3-lead ECG and beat-to-beat HR in real time throughout all centrifuge runs. However, because the original study was not designed to specifically assess heart rate variability during G exposure, HR was only recorded as 6-s averages at prespecified points during dynamic phases of flight and during idling. All identified dysrhythmias were recorded by the monitor, including episodes of bigeminy, trigeminy, couplet PVCs, and transient relative bradycardia (RB), defined by 1) an abrupt drop in HR by greater than 20 bpm based on real-time beat-to-beat HR, as provided by monitoring equipment, following onset of peak G exposure; and 2) resolution of RB by the completion of peak G exposure. The study physician documented the presence of RB as well as the run and exposure during which it occurred. Single, isolated atrial or ventricular premature beats were not documented. Following each centrifuge run, subjects completed subjective data collection forms regarding the occurrence of motion sickness, spatial disequilibrium, greyout, vertigo, or any other centrifuge-related symptoms. Pre- and post-run BP, 6-s average HR, incidence of dysrhythmias identified by continuous ECG, objective signs of acceleration intolerance noted by monitors, and subjective

symptoms noted on post-run data collection forms were abstracted for statistical analysis.

Statistical Analysis

Summary statistics for demographic and clinical factors are reported as mean \pm SD for continuous variables and count (%) for categorical variables. Hypothesis testing was performed using *t*-test, Chi-squared test, Fisher's exact test, and McNemar's test. Logistic regression was used to test whether self-reported weekly exercise was associated with dysrhythmia incidence. A significance level of 0.05 or lower was considered statistically significant. All tests were performed on SPSS® Statistical Software, version 23.

RESULTS

A total of 148 subjects (43 women and 105 men) underwent 0.5-d, 1-d, or 2-d centrifuge training programs. A summary of the clinical and demographic characteristics of the entire cohort and by training group is summarized in Table II. The three cohorts did not differ in any demographic or clinical characteristics except for sex: the 2-d cohort had significantly more men than the other two cohorts (79.7% of men participated in a 2-d cohort vs. 62.1% of women, $P = 0.019$). One subject reported use of a beta-blocker; there were no subjects reporting use of alpha-adrenergic blockers or other peripheral dilators.

Dysrhythmias observed included sinus pause ($N = 5$), couplet PVCs ($N = 4$), bigeminy ($N = 3$), accelerated idioventricular rhythm ($N = 1$), and RB ($N = 63$). None of the affected subjects reported any motion sickness, spatial disequilibrium, greyout, vertigo, palpitations, or any other centrifuge-related symptoms correlated with occurrence of any dysrhythmia. In addition, monitors noted no objective signs of acceleration intolerance, such as confusion, or altered mentation, during or after episodes of dysrhythmias.

Three individuals experienced brief episodes (less than 10 s each) of bigeminy; one occurred during +6 G_x single-direction exposure, the other two immediately following completion of the launch phase of CP2. Four subjects demonstrated couplet PVCs; one during +6 G_x single-direction exposure, one during the entry (+6 G_x) phase of the 100% CP1 run, and two during

Table II. Baseline Clinical Characteristics of All Subjects and By Cohort.

	TOTAL (N = 148)	2-d (N = 74)	1-d (N = 35)	0.5-d (N = 39)
Age (mean ± SD)	39.5 ± 13.1	38.5 ± 12.5	39.0 ± 13.2	41.7 ± 14.3
Men (N, %)	105 (70.9)	59 (79.7)*	22 (62.9)	24 (61.5)
BMI (mean ± SD)	25.1 ± 3.4	24.9 ± 3.4	25.4 ± 3.2	25.1 ± 3.6
History of hypertension (N, %)	8 (5.4)	5 (6.8)	1 (2.9)	2 (5.1)
History of cardiac pathology** or vasovagal syncope (N, %)	6 (4.1)	3 (4.1)	1 (2.9)	2 (5.1)
Stimulant† use (N, %)	4 (2.7)	0 (0)	1 (2.9)	3 (7.7)
Beta-blocker use (N, %)	1 (0.7)	1 (1.4)	0 (0)	0 (0)
Opted-out or reduced experience (N, %)	10 (6.8)	4 (5.4)	3 (8.6)	3 (7.7)
Identified as concerning (N, %)	29 (19.6)	15 (20.3)	6 (17.1)	8 (20.5)

* 2-d vs 0.5-1-d: $P = 0.019$.

** Includes supraventricular tachycardia and mitral valve prolapse.

† Includes armodafinil, atomoxetine, amphetamine, methylphenidate.

BMI: body mass index.

the launch phase of CP2. One individual, a 30-yr-old man, developed an episode of wide-complex ectopic ventricular rhythm at a rate of 91–95 bpm immediately following CP2 that was consistent with an accelerated idioventricular rhythm (AIVR). This rhythm was sustained for 2 m, 24 s before reversion to normal sinus. This event has been reported at length in a previous publication.¹³

The most common dysrhythmia noted during centrifuge exposure was RB, with 63 episodes identified in 42 individuals (28% of subjects). Subjects who experienced RB demonstrated significantly lower average HR during peak G exposure than those that did not [comparison of delta HR, +3 G_x: RB −16.0 ± 17.8 bpm, no RB 7.7 ± 20.0, $t(72) = -3.0$, $P = 0.01$; +6 G_x: RB −26.3 ± 18.8, no RB 10.0 ± 36.2, $t(72) = -5.2$, $P < 0.001$; 50% CP1: RB −14.0 ± 3.5, no RB 15.9 ± 12.3, $t(107) = 4.2$, $P = 0.003$; 100% CP1: RB −10.6 ± 17.4, no RB 20.3 ± 17.5, $t(143) = -7.3$, $P < 0.001$]. When comparing those with RB events to those without, no significant differences in pre- and post-run HR were noted. Overall, subjects demonstrated higher post-run mean arterial blood pressure (MAP) compared to pre-run MAP during all runs [+G_z: pre = 99.0 ± 10.5, post = 103.3 ± 10.5, $t(73) = 3.48$, $P < 0.001$; +G_x: pre = 98.2 ± 10.7, post = 103.4 ± 10.4, $t(73) = 4.28$, $P < 0.001$; CP1: pre = 97.9 ± 13.5, post = 102.6 ± 18.4, $t(144) = 6.77$, $P < 0.001$; CP2: pre = 99.5 ± 10.5, post = 104.1 ± 11.5, $t(133) = 4.68$, $P < 0.001$]; there was no significant difference in pre- vs post-run delta MAP during any run when comparing those that experienced RB and those that did not. A representative HR tracing of one subject who experienced RB during 100% CP1 and without evidence of RB during CP2, graphed against the acceleration profiles of each exposure, is provided in Fig. 1. Five individuals experienced sinus pause; of these, two individuals experienced sinus pause and RB concurrently, during +3 G_x and 6 G_x, respectively.

The 2-d cohort was the only cohort to experience all seven centrifuge runs. In this cohort, there were significantly more episodes of RB during single-directional +6-G_x exposure than any other centrifuge run (Fig. 2), including the entry phase of 50% CP1 ($\chi^2 = 25.3$, $df = 1$, $P < 0.001$), the entry phase of 100% CP1 ($\chi^2 = 9.38$, $df = 1$, $P = 0.002$), the entry phase of CP2 ($\chi^2 = 29.03$, $df = 1$, $P < 0.001$), and single-directional +3-G_x exposure ($\chi^2 = 18.58$, $df = 1$, $P < 0.001$). RB was more common

during the entry phase of 100% CP1 than the entry phase of 50% CP1 ($\chi^2 = 8.47$, $df = 1$, $P = 0.003$) or the entry phase of CP2 ($\chi^2 = 11.53$, $df = 1$, $P < 0.001$). There was no difference in incidence of RB between single-direction +3 G_x, the entry phase of 50% CP1, and the entry phase of CP2. A significantly higher proportion of the 2-d cohort had RB than in the other two cohorts (50% of 2-d subjects vs. 6.8% of non-2-d subjects; $\chi^2 = 34.04$, $df = 1$, $P < 0.001$). After stratifying by sex to account for any associated differences given the significantly higher participation of men in the 2-d cohorts than women, the 2-d cohort still demonstrated significantly more events than the other two cohorts among either sex (55.9% of men in the 2-d cohort vs. 8.9% of men in the non-2-d cohorts; $\chi^2 = 25.27$, $df = 1$, $P < 0.001$; 26.7% of women in the 2-d cohort vs. 3.8% of women in the non-2-d cohorts; $\chi^2 = 5.07$, $df = 1$, $P = 0.024$).

Subjects who developed RB were younger than those who did not (41.3 ± 13.8 yr vs. 34.9 ± 10.2 yr, $df = 147$, $P = 0.017$). Men were more likely to exhibit RB than women (35.2% of all men vs. 11.6% of all women; $\chi^2 = 8.36$, $df = 1$, $P = 0.004$). The stratified analysis of the 2-d cohort demonstrated that men remained more likely to exhibit RB than women (55.9% of men vs. 26.7% of women; $\chi^2 = 4.0972$, $df = 1$, $P = 0.043$). There were no statistical differences in any other clinical characteristics between those that developed RB and those that did not, including body mass index, history of hypertension, history of cardiac abnormality (including atrial tachycardia, atrioventricular nodal reentry tachycardia, or mitral valve prolapse), vasovagal syncope, stimulant use (including armodafinil, atomoxetine, amphetamine, methylphenidate), or self-reported daily exercise. There were 13 individuals who had RB on more than 1 exposure. There were no differences in any demographic or clinical characteristics between those with multiple RB episodes compared to those with a single RB episode.

Overall, 29 subjects were identified by monitors as having evidence of poor psychological tolerance of the centrifuge experience (including anxiety, panic, or other concerning behavior). In these subjects, seven episodes of RB in four individuals and one episode of sinus pause (occurring concurrently with RB) were noted. There was no statistically significant association between incidence of RB and identification of poor tolerance by

DISCUSSION

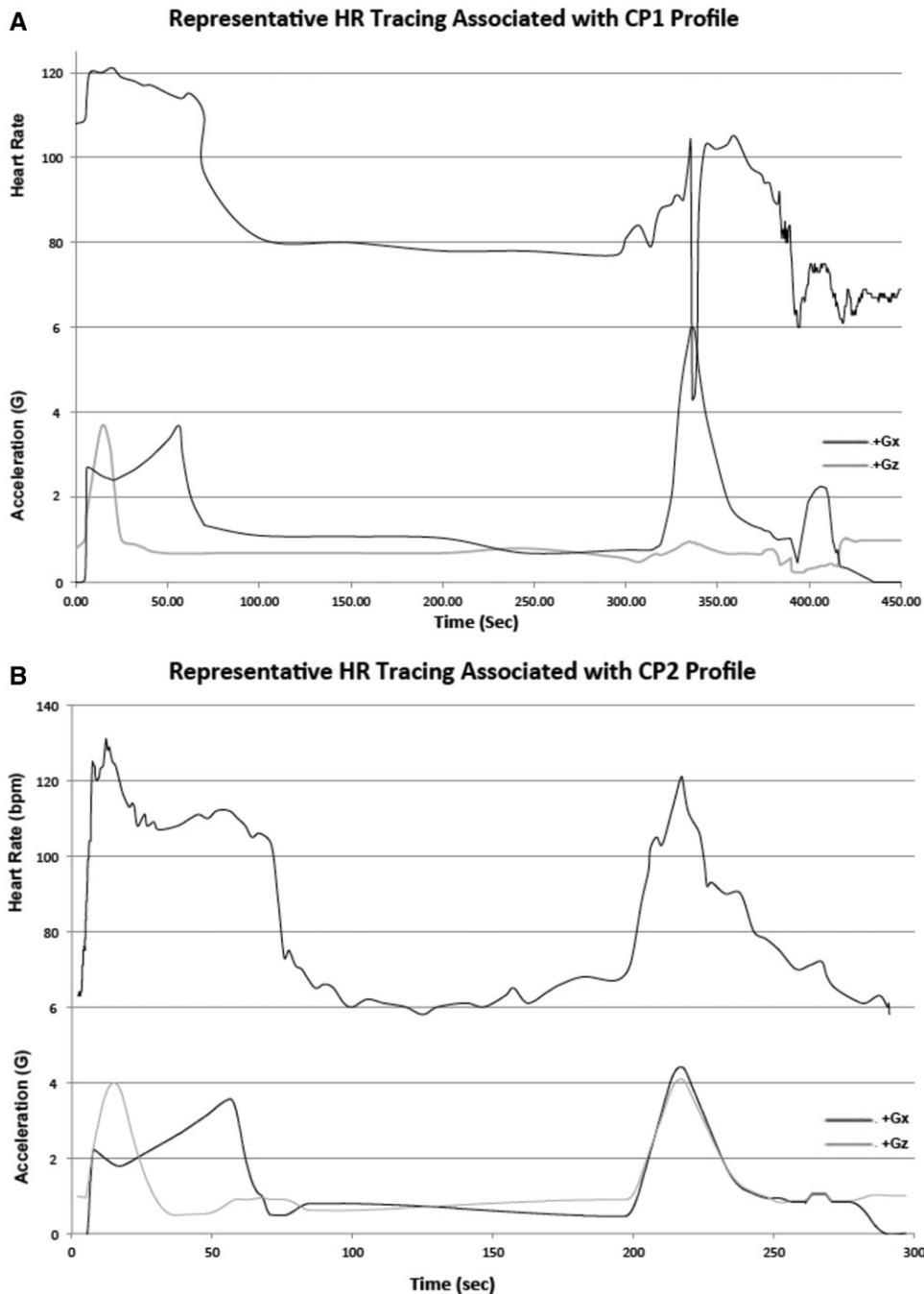


Fig. 1. Representative heart rate tracing associated with combined spaceflight profiles. Continuous HR from one subject is graphed against the acceleration profiles of the simulated spaceflight profiles, CP1 and CP2. Note the transient incident of relative bradycardia that occurs during entry (+6 G_x) in CP1 and the lack of such an event during the combined entry (+ G_x and + G_z , resultant 6.1 G) of CP2. HR: heart rate; CP: combined profile (simulated spaceflight); + G_z : head-to-toe acceleration; + G_x : chest-to-back acceleration.

study monitors. A total of eight subjects opted out of one or more centrifuge exposures and two reduced their experience for one or more runs (voluntarily requesting 50% G exposure where a 100% run was scheduled). Among these subjects, one experienced RB during +6- G_x single-directional exposure, but completed an additional centrifuge run without RB before discontinuing study participation. No other dysrhythmias were documented in any of these 10 subjects.

Clinically, severe bradycardia can lead to hemodynamic instability or potentiate other dysrhythmias. Infrequently, bradycardia has also been reported as sufficient criteria for termination in previous centrifugation studies in the military population.⁸ However, several features of RB in our results suggest this is a benign finding, including incidence most commonly in younger individuals without baseline ECG abnormalities, abrupt onset and resolution associated with peak G exposure,

Dysrhythmias observed during this study included sinus pause, couplet PVCs, bigeminy, AIVR, and RB. There was no objective evidence of physiological acceleration intolerance associated with any dysrhythmias or conduction abnormalities. While 29 subjects displayed behavior concerning for psychological intolerance and 10 individuals voluntarily opted out of one or more centrifuge runs, there was no temporal association in any of these subjects with incidence of dysrhythmias or conduction abnormalities.

Transient RB was the most common ECG finding. This dysrhythmia has been infrequently reported in previous studies as a sequela of acceleration exposure. One Russian study reported a cosmonaut with RB during entry after long-duration spaceflight.⁶ The authors of that study observed that such an event did not occur in those who used anti-G countermeasures and postulated that RB was evidence of intolerance to hypergravity exposure. However, the report did not provide any hemodynamic data or specific signs or symptoms as objective evidence of acceleration intolerance.⁶ Interestingly, a similar phenomenon has also been documented in parachutists immediately after exiting the plane, during which they experience transient exposure to typically less than +1 G_x .¹⁴ In this study, three of the seven parachutists developed considerable HR slowing and two converted to a slow atrial rhythm, but no subjects reported any associated symptoms.¹⁴

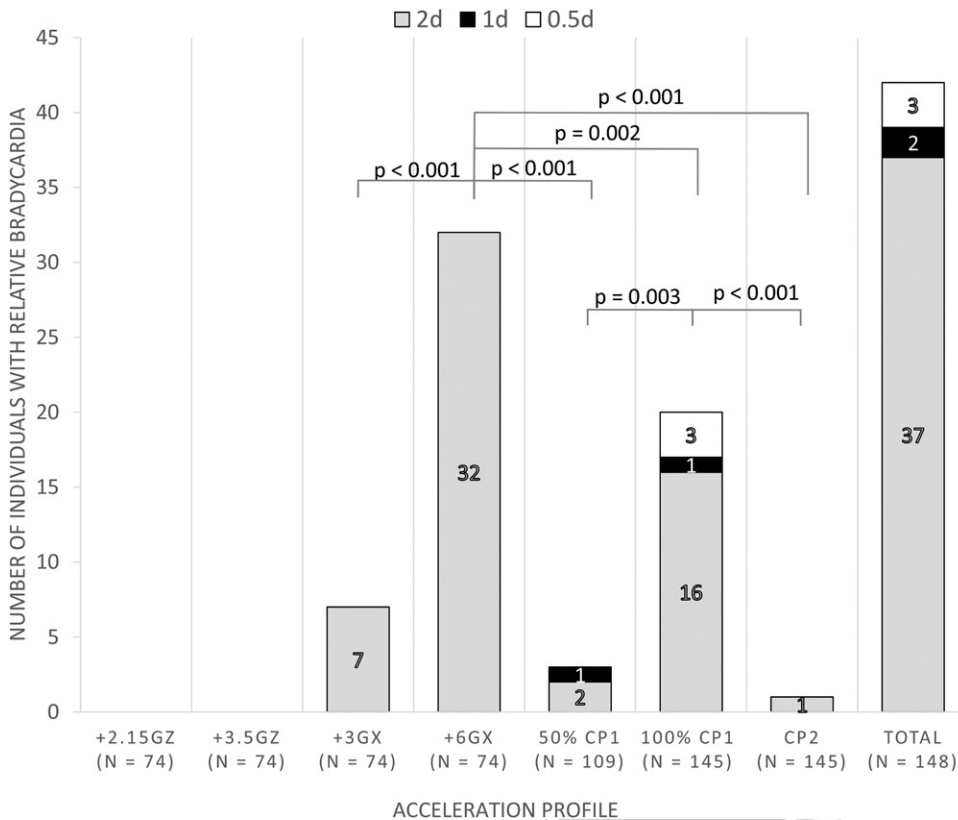


Fig. 2. Incidence of relative bradycardia by acceleration profile. The number of individuals undergoing each exposure is shown below the label for each acceleration profile. Significance of $P \leq 0.05$ between exposure profiles is indicated above the bars.

lack of objective signs of acceleration intolerance, absence of association with other significant dysrhythmias, and lack of post-event sequelae. Only one subject was on a beta-blocker; while this subject did demonstrate RB events, there was no clinically significant evidence of inappropriate hemodynamic response that might suggest that the beta-blockade altered that subject's response or tolerance of acceleration.

Autonomic tone is an important modulator of HR variability; in the absence of underlying cardiovascular disease or conduction system abnormalities, we postulate that RB represents a physiological response to autonomic feedback resulting from cardiovascular disturbances during G exposure. RB occurred only during $+G_x$ exposures, was completely absent during isolated $+G_z$ exposures, and occurred more often at higher magnitude $+G_x$ exposures. Chest-to-back compression of the thorax during $+G_x$ can lead to compression of the heart and the aorta¹¹ and produce increased aortic, central venous, and right atrial pressures.^{7,9} This in turn may trigger the baroreceptor reflex, increasing vagal tone, and predisposing to RB. Unlike $+G_z$, which primarily elicits PVCs, $+G_x$ provokes ectopy originating primarily in the atria.^{8,10,15} In this regard, increased parasympathetic tone can cause suppression of ventricular ectopy while promoting atrial ectopy and atrial dysrhythmias.¹²

Our observations regarding the types of G exposures during which RB was observed fit within the paradigm of an autonomic-mediated event. Given that $+G_z$ exposure provokes a strong

sympathetic response, it is not surprising that RB was rarely observed when $+G_x$ and $+G_z$ occurred simultaneously. Attenuation of the incidence of RB was seen even when $+G_z$ and $+G_x$ occurred serially during the same run, possibly due to residual sympathetic drive from initial $+G_z$ exposure. The novelty of the experience and prior G exposure may also play a role in modulating the adrenergic response to G exposure. For example, the 2-d cohort had a higher incidence of these rhythms during the 50% and 100% CP1 runs on day 2, after experiencing single-directional exposures on day 1, than the 1-d or 0.5-d groups. It is also worth noting that the single-direction exposures on the first day, during which most of these events were identified, were not equipped with the high-fidelity audio-visual simulation of the simulated spaceflight experiences. Lower-fidelity $+G_x$ exposure may not have elicited the same novelty or excitement, potentially attenuating the sympathetic response and predisposing to RB during these low-fidelity runs. Interestingly, specific underlying conditions, including prior history of hypertension, supraventricular tachycardia, mitral valve prolapse, and vasovagal syncope were not associated with events, nor was a documented history of the use of stimulants. However, the prevalence of these factors was low, limiting the power to detect subtle effects on RB incidence.

Control of cardiac autonomic tone is complex and can be modulated by other mechanisms than those discussed here. For example, the Valsalva maneuver can cause transient bradycardia. Subjects were not instructed to perform a Valsalva maneuver during $+G_x$ exposure (where most episodes of RB occurred), nor were they observed to be performing the maneuver during these exposures. However, subjects were taught anti-G straining maneuver techniques, including the hook maneuver, which includes physiological actions that are similar to the Valsalva technique. While our intent was for subjects to use such techniques only during symptomatic $+G_z$ exposure, it is possible that some subjects may have inadvertently performed the maneuver during $+G_x$ exposure, contributing to the incidence of RB.

Although our findings suggest that RB is likely a benign physiological response to $+G_x$ exposure, caution is advised when monitoring individuals with other pre-existing cardiopulmonary conditions such as coronary artery disease, conduction abnormalities, dysrhythmias, pacemakers, defibrillators, heart failure, and chronic obstructive pulmonary disease. These factors

may predispose individuals to pathological bradycardias in the setting of $+G_x$, increasing their risk for decompensation. The one subject on a beta-blocker tolerated his experience well, but was also the only subject to develop RB during simultaneous $+G_z$ and $+G_x$ exposure in CP2. Previous reports of beta-blocker use during similar centrifuge exposures have been associated with good physiological tolerance of acceleration, though dysrhythmia incidence was not monitored in these studies.^{2,3} Further studies are needed to understand how individuals on beta-blockers and medications that interfere with cardiac conduction will tolerate these exposures and whether their use is associated with higher incidence or decreased tolerance for these events. Other observations that should merit further investigation include incidence of these rhythms outside of $+G_x$ exposures, sustained bradycardias that persist after resolution of $+G_x$ exposure, or sustained bradycardias associated with objective signs or symptoms of acceleration intolerance.

The findings in this study are pertinent to hypergravity exposures like those anticipated on commercial suborbital spaceflight. However, true suborbital spaceflight profiles will include several minutes of microgravity between acceleration peaks that could adversely affect the physiological response to acceleration-induced dysrhythmias; this duration of microgravity exposure cannot be simulated in a ground-based analog and remains a limitation to the conclusions discussed here. In addition, peak G_x exposures tested in this study lasted from 5 to 15 s. While previous studies in healthy military populations with exposures of $+15 G_x$ for brief periods and between $5-8 +G_x$ for up to several minutes did not reveal an association between dysrhythmias and objective signs of acceleration intolerance,^{4,10,15} it is possible that longer exposures could result in more severe or frequent episodes of RB or other dysrhythmias with possible clinical sequelae.

There were limitations to data collection that affected the results. While the monitor used beat-to-beat HR to identify episodes of RB, HR collection points were not designed to capture either the HR immediately before an RB event nor the lowest identified HR during an RB event. We have presented average HR based on 6-s intervals as described; however, these averages can be misleading as they do not express the extremes of HR maximums or minimums as experienced by subjects during RB episodes. In addition, HR recorded just prior to G exposure was averaged at a time of idle centrifuge motion before the voice-over countdown that prepared subjects for G exposure; thus, the HR recorded does not reflect any anticipatory adrenaline-mediated HR elevation that preceded G onset (and any RB event). As a result, the reported mean delta HR generally underestimates the true delta HR witnessed during RB episodes. Real-time BP was not monitored during G exposures and was therefore not an available parameter for the assessment of any hemodynamic compromise. Instead, hemodynamic compromise was assessed by the absence of objective signs of acceleration intolerance (such as confusion or altered mental status on video monitoring) during dysrhythmias and the absence of a statistically significant drop in MAP following G exposures.

Dysrhythmias observed during ECG monitoring of layerpersons during isolated and combined $+G_z$ and $+G_x$ acceleration exposures similar to those anticipated during commercial suborbital spaceflight included sinus pause, bigeminy, couplet PVCs, AIVR, and RB. These were well tolerated and were not associated with objective signs of physiological or psychological intolerance. Short-duration $+G_x$ exposure was particularly associated with episodes of RB that resolved with discontinuation of $+G_x$ acceleration. RB was most common in young men, was absent during $+G_z$ exposure, and was not associated with post-spin sequelae. These events were common and well tolerated; we suspect that similar events are unlikely to necessitate termination of an acceleration experience (centrifuge- or spaceflight-associated) when identified. Caution is warranted when monitoring individuals with or at high risk for cardiopulmonary disease or on medications modulating cardiac conduction that could lower tolerance of these rhythms or predispose them to clinical decompensation.

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