Cardiovascular and Valsalva responses during parabolic flight

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1Autonomic Reflex Laboratory, Mayo Foundation, Rochester, Minnesota 55905; 2Autonomic Reflex Laboratory, Mayo Foundation, Rochester, Minnesota 55905; 3Life Sciences Research Laboratories, National Aeronautics and Space Administration, Johnson Space Center, and 2Wyle Laboratories, Houston, Texas 77058; 4Autonomic Reflex Laboratory, Mayo Foundation, Rochester, Minnesota 55905

Schlegel, Todd T., Edgar W. Benavides, Donald C. Barker, Troy E. Brown, Deborah L. Harm, Suresh J. DeSilva and Phillip A. Low. Cardiovascular and Valsalva responses during parabolic flight. J. Appl. Physiol. 85(5): 1957–1965, 1998.—We investigated the integrated cardiovascular responses of 15 human subjects to the acute gravitational changes (micro- and hypergravity portions) of parabolic flight. Measurements were made with subjects quietly seated and while subjects performed controlled Valsalva maneuvers. During quiet, seated, parabolic flight, mean arterial pressure increased during the transition into microgravity but decreased as microgravity was sustained. The decrease in mean arterial pressure was accompanied by immediate reflexive increases in heart rate but by absent (or later-than-expected) reflexive increases in total vascular resistance. Mean arterial pressure responses in Valsalva phases II, III, and IV were accentuated in hypergravity relative to microgravity (P < 0.01, P < 0.01, and P < 0.05, respectively), but accentuations differed qualitatively and quantitatively from those induced by a supine-to-seated postural change in 1 G. This study is the first systematic evaluation of temporal and Valsalva-related changes in cardiovascular parameters during parabolic flight. Results suggest that arterial baroreflex control of vascular resistance may be modified by alterations of cardiopulmonary, vestibular, and/or other receptor activity.

Valsalva maneuver; baroreflex; microgravity; hypergravity

PARABOLIC FLIGHT provides an accessible means of investigating human cardiovascular responses to the acute onset phase of microgravity (5, 16, 25, 28–31). Abrupt changes in mean arterial pressure (MAP), for example, have been reported during and after entry into parabolic microgravity (5), as have abrupt changes in heart rate (HR) (5, 25, 28, 29), stroke volume (SV) (25, 28), central venous pressure (16, 30), cardiac index (25, 28, 29), cerebral blood flow (5), and intra-esophageal and intra-abdominal pressures (31). Recently, two aspects of cardiovascular changes during parabolic flight have been stressed: 1) their heavy dependence on posture (5, 16, 28, 29, 31), and 2) their association with unanticipated temporal separations, such as those observed by Bondar et al. (5) between changes in MAP, HR, and cerebral blood flow during parabolic microgravity. Although the posture-dependent changes are interesting in light of their implications for alterations in cardiac pressure-flow relationships during spaceflight (16, 31), the temporal separations might have unique relevance for the study of human baroreflex interactions. The temporal separations, however, have not been systematically investigated (to our knowledge), nor have cardiovascular responses to the Valsalva maneuver during parabolic micro- or hypergravity.

The Valsalva maneuver, a uniquely human clinical and research tool used to assess the integrity of autonomic cardiovascular control mechanisms, consists of voluntary elevation of intrathoracic and intra-abdominal pressures provoked by blowing (“straining”) against pneumo-resistance. During the maneuver, venous return to the heart is impeded, setting off a well-characterized sequence of positive and negative arterial pressure changes heavily influenced by the autonomic nervous system (24, 35, 41). As shown in Fig. 1, cardiovascular responses to a Valsalva maneuver in 1 G are traditionally divided into four phases (24, 35, 45, 46). Phase I consists of a transient mechanical increase in MAP and a decrease in HR immediately after the commencement of straining. Phase II is characterized by an acceleration in HR and a decrease [early phase II (IIa)] and later recovery [late phase II (IIl)] in MAP during the period of straining. Phase III consists of a sudden brief mechanical reduction in MAP and an increase in HR immediately after the release of straining. Phase IV is characterized by an elevation of MAP above baseline levels (“overshoot”) and a reduction in HR.

On Earth, cardiovascular responses to Valsalva maneuvers are predictably altered by changes in posture (23, 43, 45, 46). This has led to the suggestion that Valsalva responses be investigated during spaceflight to help characterize cephalad fluid-shifting associated with weightlessness (43). Recently, changes in cardiovascular responses to Valsalva maneuvers have been identified in astronauts after several weeks in orbit (T. E. Brown, personal communication) and after return to Earth (17). However, the underlying effects of acute exposure to microgravity on such responses are not known, in part because operational considerations often prohibit the collection of physiological data during the earliest portions of spaceflight.

A principal objective of this study, therefore, was to simply describe cardiovascular responses to seated Valsalva maneuvers in acute (i.e., parabolic) micro- and hypergravity. A second, related objective was to document, from a detailed temporal perspective, changes in cardiovascular parameters during “quiet, seated, para-

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SUBJECTS AND METHODS

Those elicited by postural transitions in 1 G.

rabolas would elicit cardiovascular responses similar to seated flight and for seated Valsalva maneuvers, we might be contextually understood. For both quiet, bolic flight," such that responses to the Valsalva maneuvers might be contextually understood. For both quiet, seated flight and for seated Valsalva maneuvers, we hypothesized that gravitational transitions during parabol as would elicit cardiovascular responses similar to those elicited by postural transitions in 1 G.

SUBJECTS AND METHODS

Subjects. Fifteen healthy test subjects (10 men and 5 nonpregnant women; mean age, 32 yr; range, 22–45 yr) participated in the study, which was approved by the Johnson Space Center Institutional Review Board. All subjects were free of cardiopulmonary, renal, or other systemic disease, and each gave written, informed consent after passing a US Air Force Class III physical examination. In addition, all subjects were normotensive nonsmokers who had normal creatinine levels, electrolytes, hemoglobin-hematocrits, liver function tests, urinalyses, drug screens, and electrocardiograms. Caffeine, alcohol, heavy exercise, and all medications (including antimotion sickness medications) were strictly prohibited beginning 24 h before any testing, which was commenced in the morning hours after subjects had eaten a light breakfast. Parabolic flights. While loosely restrained at the waist, unmedicated subjects flew four sets of 10 parabolas in the seated position aboard NASA's KC-135 aircraft, a Boeing 707 specifically modified for parabolic flight. During their flights, subjects were instructed to avoid unnecessary head movements and to look forward at a computer monitor placed immediately in front of them. As verified by an accelerometer mounted inside the aircraft, single parabolas consisted of the following three phases, each lasting approximately 20–25 s: 1) “pull up,” with increased G-load of up to 1.8 Gz. Because the pull-out and pull-up phases are contiguous during consecutive parabolas, these two phases together constituted one single hypergravity (-Gz) period. Transitions between all three phases, however, are known to vary slightly in quality (5, 25, 28, 29).

General protocol. Subjects performed controlled Valsalva maneuvers under the following four conditions: 1) preflight in the supine position; 2) preflight in the seated position; 3) in flight during the microgravity condition (seated); and 4) in flight during the hypergravity condition (seated). Preflight supine Valsalva measurements were performed in triplicate before flight in a hangar facility at Ellington Air Field, Pasadena, TX. All seated Valsalva measurements were performed in the airplane, immediately before flight (condition 2, also in triplicate) and during flight (conditions 3 and 4), respectively. During the 40-parabola inflight period, subjects performed Valsalva maneuvers every fourth parabola, at the beginning of alternating microgravity and hypergravity parabol ic phases, for a maximum of 10 total maneuvers (5 each in microgravity and hypergravity). The inflight protocol therefore called for the performance of a Valsalva maneuver: 1) during the microgravity portion of the first parabola; 2) during the hypergravity portion of the fifth parabola; 3) during the microgravity portion of the ninth parabola; and 4) during the hypergravity portion of the thirteenth parabola (and so on in a similar alternating manner for the rest of the flight).

When not performing Valsalva maneuvers, subjects rested during the parabolas for quiet, seated (i.e., non-Valsalva-maneuver-related) data collection, breathing regularly to a 0.25-Hz tone in preparation for the next Valsalva maneuver. Every 5 min during flight, subjects were evaluated for signs and symptoms of motion sickness by using a standard Graybiel scale (20). Graybiel notations in flight (as well as answers to a postflight questionnaire) were then utilized to exclude from the ultimate analyses any data collected during motion sickness equal to or exceeding epigastric awareness (20). For two subjects, inflight data collection was mostly unsuccessful: one because of the early onset of severe motion sickness, and one because of mechanical difficulties with a data collection device.

Cardiovascular measurements. Throughout the study, beat-to-beat MAP was estimated using a noninvasive finger-photoplethysmographic device (Portapres, TNO Industrial Research, Amsterdam, The Netherlands) referenced to the level of the heart. Excellent estimates of directly measured intra-arterial pressure changes have been demonstrated with these devices during controlled Valsalva maneuvers (21, 32). Beat-to-beat SV was estimated by using impedance cardiography (BoMed, Irvine, CA). Although impedance cardiography may not give accurate information pertaining to absolute SV, it does provide useful data pertaining to changes in SV (14, 18, 39). Impedance devices have also been utilized during prior parabolic flight investigations (25, 28, 29). Changes in beat-to-beat total vascular resistance ([VR] = MAP/cardiac output) were derived in real time from the MAP, HR, and SV data by using a special software program developed specifically for this purpose (P. A. Low, Mayo Clinic, Rochester, MN).

Valsalva technique. Before the performance of a Valsalva maneuver, subjects had at least a 15-min resting period in the assigned postural configuration (i.e., supine or seated). Each maneuver was performed at an expiratory pressure of 30 mmHg for 15 s and was preceded and followed by at least 1 min of controlled frequency breathing (8) at 0.25 Hz. During Valsalva strains, subjects blew into a mouthpiece connected by a short plastic tube to a calibrated pressure gauge.
Electrocardiogram, impedance cardiogram, respiratory rate, and arterial and expiratory pressures were measured continuously, as was the acceleration of the aircraft during the inflight period.

Analysis of cardiovascular responses during quiet, seated, parabolic flight. For quiet, seated, parabolic flight, baseline cardiovascular values for a micro- or hypergravity period were defined as those values obtained during the first heart beat after stabilization of the concomitant Gz accelerometer recording. Stabilization of the accelerometer recording was defined as that moment when the Gz digital readout became \( \pm 5\% \) of its average value during the subsequent micro- or hypergravity period. Maximal and minimal cardiovascular values were then noted, together with their times of occurrence relative to the first beat of the respective period. For the purposes of calculating group means, only quiet, seated responses collected during the first 10 parabolas of any given flight were considered for incorporation into the overall data set. This was done to minimize the physiologically confounding effects of both unrecognized motion sickness and fatigue.

To minimize the effects of prior Valsalva maneuvers on measurements during quiet, seated flight, we ignored the data from quiet, seated flight that were obtained in any gravitational period immediately after the specific period in which a Valsalva maneuver had just been performed. For example, we ignored the 45 s of data from the hypergravity portion of quiet seated flight that immediately followed the microgravity Valsalva maneuver of parabola 1. For most subjects, therefore, the measurements made while they were quietly seated actually represent uninterrupted data collected from the microgravity portion of parabola 2 through the hypergravity portion of parabola 5 (i.e., four uninterrupted microgravity periods punctuated by three uninterrupted hypergravity periods). In a few cases, equipment problems compromised data collection during the first few parabolas of a flight, so that the first Valsalva maneuver in microgravity and the subsequent determinations for quiet, seated flight were delayed until later parabolas. In all cases, determinations for quiet, seated flight were derived by averaging the responses from the three earliest uninterrupted and noncorrupted parabolas commencing at least 45 s after a Valsalva maneuver in nonsick subjects during the first 10 parabolas.

Analysis of cardiovascular responses during Valsalva maneuvers. For each of the four Valsalva-related testing conditions, all Valsalva responses obtained outside of the context of motion sickness as defined above were averaged together to obtain an individual’s mean result for that condition. Individual means were then averaged to obtain the group mean for each condition.

For individual Valsalva maneuvers in normogravity and hypergravity, baseline cardiovascular readings were derived by averaging the values from the four beats immediately before the beginning of the Valsalva strain. For individual Valsalva maneuvers in microgravity, baseline cardiovascular readings were derived by averaging values from only 1 to 3 microgravity beats before the beginning of the Valsalva strain. This was necessary because of the time constraints encountered when using a 15-s strain within a 20- to 25-s microgravity period and the need to define a phase IV MAP peak in microgravity before the beginning of the next hypergravity period. Because cardiovascular responses are constantly changing during parabolic flight, we used intraphase (17, 41, 46) rather than baseline-referenced (4, 35, 45) calculations for Valsalva phases II through IV. Phasic changes in cardiovascular parameters during Valsalva maneuvers were therefore identified as follows. 1) \( \Delta \) Phase I is the change in the given parameter occurring between the maximal MAP value during phase I and the baseline MAP value (as defined above). 2) \( \Delta \) Phase II is the change in the given parameter occurring between the maximal MAP value during phase II and the minimal MAP value during phase II. 3) \( \Delta \) Phase III is the change in the given parameter occurring between the minimal MAP value during phase III and the maximal MAP value during phase IV. 4) \( \Delta \) Phase III is the change in the given parameter occurring between the maximal MAP value during phase I and the minimal MAP value during phase II. 5) \( \Delta \) Phase IV is the change in the given parameter occurring between the minimal MAP value during phase III and the maximal MAP value during phase IV. For the decrease in MAP during phase I, and for the increase in MAP during phase IV, estimates of baroreflex responsiveness (i.e., \( \Delta R-R \) interval/\( \Delta MAP \)) were also calculated by using the general method of Fritsch-Yelle et al. (17).

Statistics. Paired t-tests were utilized to examine the effect of posture (in normogravity) on mean cardiovascular responses during Valsalva maneuvers. The effect of \( G_z \) on seated cardiovascular responses during Valsalva maneuvers was tested by using a repeated measures ANOVA specific to the experimental design. Differences in means contributing to significant results were then identified by using a follow-up Scheffé multiple comparison procedure (38). For all determinations, statistical significance was accepted at \( P < 0.05 \).

RESULTS

Cardiovascular responses during quiet, seated, parabolic flight. One representative subject’s beat-to-beat cardiovascular responses, averaged over three consecutive parabolas during quiet, seated flight, are shown in Fig. 2. At the beginning of the microgravity phases, MAP levels were relatively high, in part because of increases in MAP during the previous hypergravity phases and in part because of further increases in MAP during the just-completed, 4- to 5-s hypergravity-to-microgravity transition periods (shaded T1 areas). As true microgravity began, however, both MAP and HR decreased, with HR reaching its lowest levels within a few seconds (points labeled B). As MAP then continued to decrease, not reaching its lowest levels until after microgravity had ended (A), HR partially recovered. Simultaneous impedance cardiographic recordings for this subject demonstrated that LV increased during microgravity, reaching peak levels toward the end of the microgravity period (C). VR, on the other hand, decreased to trough levels shortly after microgravity (D), often after increasing briefly in the earliest portions of microgravity. As shown in Fig. 2, for this subject, SV reached peak levels ~20 s after the commencement of microgravity, whereas MAP, VR, and HR reached trough levels ~26, 24, and 2 s, respectively, after the commencement of microgravity. The average times of occurrence of microgravity-related peaks and troughs for all subjects (first 10 parabolas) are shown in Table 1.

In the representative subject shown in Fig. 2, during the microgravity-to-hypergravity transition period [open bar (T2)], MAP and SV decreased, while HR increased. In the earliest portions of true hypergravity, SV decreased further, while MAP, HR, and VR all increased. During the mid-to-late portions of hypergravity, HR
then stabilized (i.e., oscillated) to some degree as MAP and VR trended principally upward. The average times of occurrence of the respective peaks and troughs for all subjects in hypergravity (first 10 parabolas) are also shown in Table 1.

Responses to Valsalva maneuvers: effects of posture and gravity. Valsalva-related changes in MAP across the two postural conditions in 1 G, and across the three gravitational conditions with subjects seated in the aircraft are summarized for all subjects in Table 2. In the seated (vs. the supine) position in 1 G, mean MAP responses were significantly accentuated during phases IIe and IIl. However, mean MAP responses during phases I, III, and IV were not significantly influenced by the supine-to-seated postural change in 1 G. Across the three gravitational conditions in the seated position, mean MAP increases during phase I and mean MAP decreases during phase IIe were not significantly changed. However, mean MAP increases during phase IIl, decreases during phase III, and increases during phase IV varied across gravitational conditions. Specifically, during phase IIl, mean MAP increases in hypergravity were significantly greater than those in either microgravity or normogravity, and mean MAP increases in normogravity were also significantly greater than those in microgravity. During phase III, on the other hand, mean MAP decreases in hypergravity were significantly greater than those in either microgravity or normogravity, but mean MAP decreases in normogravity did not differ from those in microgravity. During phase IV, the only notable change was that mean MAP increases in hypergravity were greater than those in microgravity.

Trends in one representative subject’s beat-to-beat cardiovascular responses during seated Valsalva maneuvers in micro- and hypergravity are shown in Fig. 3. This is the same subject whose seated MAP and HR responses to a Valsalva maneuver in 1 G are shown in Fig. 1. As already described for the overall group (Table 2), this subject’s phase IIl MAP response in microgravity was significantly attenuated (Fig. 3A), whereas his phase IIl MAP response in hypergravity was significantly accentuated (Fig. 3B). These changes held true not only in terms of the absolute magnitude (in mmHg) of his phase IIl MAP responses, but also in terms of the temporal duration (in s) of his responses. Moreover, the magnitude of the subject’s MAP responses during Valsalva phase IIl closely paralleled the magnitude of his VR responses during that same phase (diagonal arrows, Fig. 3). For the group as a whole, there was a significant linear relationship, consistent across all three gravitational conditions, between the magnitude

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Microgravity</th>
<th>Hypergravity</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Average Absolute Change vs. First-beat Baseline</td>
<td>-26.8±12.3 mmHg</td>
<td>30.4±11.9 mmHg</td>
</tr>
<tr>
<td>Mean Time of Occurrence vs. First-beat Baseline</td>
<td>24.8±3.7 s</td>
<td>29.4±9.7 s</td>
</tr>
<tr>
<td>HR trough (B)</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Average Absolute Change vs. First-beat Baseline</td>
<td>-24.4±13.6 beats/min</td>
<td>14.7±7.1 beats/min</td>
</tr>
<tr>
<td>Mean Time of Occurrence vs. First-beat Baseline</td>
<td>5.2±2.9 s</td>
<td>18.1±11.5 s</td>
</tr>
<tr>
<td>SV peak (C)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Average Absolute Change vs. First-beat Baseline</td>
<td>43.5±25.3 ml</td>
<td>32.8±20.9 ml</td>
</tr>
<tr>
<td>Mean Time of Occurrence vs. First-beat Baseline</td>
<td>16.8±5.6 s</td>
<td>27.1±8.9 s</td>
</tr>
<tr>
<td>VR trough (D)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Average Absolute Change vs. First-beat Baseline</td>
<td>-4.8±3.5 units</td>
<td>6.6±3.9 units</td>
</tr>
<tr>
<td>Mean Time of Occurrence vs. First-beat Baseline</td>
<td>21.2±7.0 s</td>
<td>27.7±7.6 s</td>
</tr>
</tbody>
</table>

Values are means ± SD as obtained during quiet, seated flight within the first set of 10 parabolas; n, no. of subjects; MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; VR, calculated total vascular resistance. A–D, peaks and troughs for the group that correspond to those labeled for the individual in Fig. 2.
of changes in MAP and the magnitude of changes in VR during Valsalva phase II (R = 0.80, and P < 0.001 by repeated measures regression).

Actual changes (increases) in VR during Valsalva phase II for the group as a whole were 2.4 ± 1.8 U in supine normogravity, 3.3 ± 2.3 U in seated normogravity, 1.4 ± 1.5 U in seated microgravity and 5.9 ± 2.5 U in seated hypergravity. Significance levels (i.e., P values) associated with these changes were practically indistinguishable from those associated with the phase II changes in MAP across the testing conditions (see Table 2). Decreases in SV across the postural and gravitational conditions during the whole of phase II (i.e., phase II + phase II) were unchanged.

### Table 2. MAP responses to Valsalva maneuvers: effects of posture and gravity

<table>
<thead>
<tr>
<th>Condition</th>
<th>ΔPhase I</th>
<th>ΔPhase II</th>
<th>ΔPhase III</th>
<th>ΔPhase IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine normogravity</td>
<td>17.19 ± 6.39</td>
<td>-15.01 ± 8.57a</td>
<td>10.42 ± 4.98b</td>
<td>-17.60 ± 8.46</td>
</tr>
<tr>
<td>Seated normogravity</td>
<td>17.45 ± 5.76</td>
<td>-22.34 ± 9.99</td>
<td>21.39 ± 11.07</td>
<td>-19.10 ± 5.00</td>
</tr>
<tr>
<td>Seated hypergravity</td>
<td>18.95 ± 6.00</td>
<td>-22.66 ± 13.19</td>
<td>33.35 ± 12.15d</td>
<td>-26.23 ± 10.92d</td>
</tr>
</tbody>
</table>

Values are means ± SD in mmHg. Phases I, IIa, IIb, III, and IV as defined in text. Effect of posture (paired t-test, n = 15): a P < 0.05 vs. seated normogravity; b P < 0.01 vs. seated normogravity. Effect of gravity (repeated measures ANOVA followed by Scheffé multiple comparison test, n = 13): c P < 0.01 vs. seated normogravity and vs. seated hypergravity; d P < 0.01 vs. seated normogravity and vs. seated microgravity; e P < 0.05 vs. seated microgravity.

Fig. 3. Integrated, beat-to-beat trends in cardiovascular responses during seated Valsalva maneuvers (strain, top, to 30 mmHg) in microgravity (micro-G; A) and hypergravity (hyper-G; B) in the same subject whose responses to a Valsalva strain in 1 G are shown in Fig. 1. Terminal peaks and troughs in MAP during and after Valsalva strains are indicated as I, II, II, III, and IV (see Fig. 1 for definitions). The II increase in MAP during straining is clearly attenuated in microgravity and clearly accentuated in hypergravity. The pattern of the HR response and the magnitude and temporal duration of the vascular resistance response during straining also vary with gravitational condition. Specifically, during the microgravity strain (A), HR peaks just once (p) during phase III after a small increase in VR during phase II (small diagonal arrow). During the hypergravity strain (B), HR peaks once during phase II (p1), troughs shortly thereafter in same phase after a substantial increase in VR (large diagonal arrow), and then peaks again during phase III (p2).
with the following exception: decreases in SV during phase II in the seated position in microgravity (−18.3 ± 28.8 ml) were significantly less than decreases in SV during phase II in the seated position in normogravity (−41.3 ± 34.9 ml; P < 0.05).

In hypergravity, the HR response during Valsalva phase II was often biphasic (Fig. 3B). Thus comparisons of the net increase in HR during this phase (i.e., across the gravitational conditions) were not meaningful. Sustained increases in HR did occur, however, during Valsalva phase II regardless of the testing condition (Figs. 1 and 3). Nonetheless, for the group as a whole, neither posture nor gravity significantly influenced the magnitude of the mean increase in HR during phase II (13.7 ± 10.9 beats/min in supine normogravity, 15.5 ± 6.1 beats/min in seated normogravity, 14.4 ± 13.5 beats/min in seated microgravity, and 11.3 ± 6.2 beats/min in seated hypergravity; P > 0.05 for all comparisons). “Baroreflex responsiveness” (i.e., ΔR-R interval/ΔMAP) during phase II was also statistically unchanged across the postural and gravitational conditions, although there was a trend toward decreased responsiveness in the seated (vs. the supine) position and in the hypergravity (vs. the normogravity and microgravity) conditions (Table 3). During phase IV, these overall trends were similar in direction, with the difference between responsiveness in hypergravity and normogravity reaching statistical significance (Table 3).

Changes in the temporal duration of intrastrain phases II and II were summarized for the group in Table 4. During Valsalva maneuvers in the seated (vs. the supine) posture in 1 G, II decreases in MAP were temporally attenuated while II increases in MAP were temporally accentuated. Across the gravitational conditions in the seated position, directionally similar but larger changes occurred when Valsalva maneuvers were performed in hypergravity as opposed to in either normo- or microgravity. When Valsalva maneuvers were performed in microgravity, opposite directional changes occurred, i.e., phase II decreases in MAP were temporally accentuated, while II increases in MAP were temporally attenuated.

### Table 4. Temporal duration of early and late phase II MAP responses during Valsalva strains: effects of posture and gravity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Phase II Duration</th>
<th>Phase II Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine normogravity</td>
<td>5.64 ± 1.28</td>
<td>5.12 ± 1.74</td>
</tr>
<tr>
<td>Seated normogravity</td>
<td>6.12 ± 1.41</td>
<td>6.2 ± 1.47</td>
</tr>
<tr>
<td>Seated microgravity</td>
<td>9.31 ± 1.69†</td>
<td>3.7 ± 2.01‡</td>
</tr>
<tr>
<td>Seated hypergravity</td>
<td>4.88 ± 1.34</td>
<td>8.59 ± 1.50‡</td>
</tr>
</tbody>
</table>

Values are means ± SD (in s). Effect of posture (paired t-test, n = 15): *P < 0.05 vs. seated normogravity. Effect of gravity (repeated measures ANOVA followed by Scheffé multiple comparisons test, n = 13): †P < 0.01 vs. seated normogravity and vs. seated hypergravity; ‡P < 0.05 vs. seated normogravity and P < 0.01 vs. seated microgravity.

### DISCUSSION

This study is the first to describe cardiovascular responses to Valsalva maneuvers during parabolic micro- and hypergravity. It is also the first to document, from a detailed temporal perspective, integrated changes in MAP, HR, SV, and VR during parabolic flight. Novel findings and findings relevant to the hypothesis are discussed below.

Quiet, seated flight. During quiet, seated flight, the gravitational transitions did elicit cardiovascular responses similar to those elicited by postural transitions (i.e., tilt) in 1 G. Specifically, the hypergravity-to-microgravity transitions (1 bars, Fig. 2) elicited cardiovascular responses (increases in MAP and SV) similar to those elicited by upright-to-supine postural transitions in 1 G (47), whereas the microgravity-to-hypergravity transitions (2 bars, Fig. 2) elicited cardiovascular responses (decreases in MAP and SV and increases in HR) similar to those elicited by supine-to-upright postural transitions in 1 G (7).

A more interesting finding during quiet, seated flight, however, occurred during the sustained portion of microgravity, when MAP decreased (Fig. 2, left). Presumably, the hypotensive response during this period was mediated purely through vasodilation, because VR was dramatically reduced and MAP continued to decrease in the face of elevations of HR and SV. One possible explanation for these findings is that during the decrease in MAP, the arterial baroreceptors became dynamically unloaded (prompting the recovery in HR), while the cardiopulmonary (CP) baroreceptors remained loaded (i.e., as witnessed by the upward trend in SV). If so, then as MAP decreased, the loaded CP baroreceptors may have been able to modulate (i.e., prevent) arterial baroreflex-mediated increases in VR but not HR. This concept would be in accord with the findings of other investigators (1, 2, 44), as summarized by Mancia and Mark (26). In the current study, however, reductions in sympathetic activity associated with vestibular (i.e., otolith) “destimulation” might also have contributed to the sustained decrease in VR during microgravity (15, 33, 34, 36, 40, 48, 49).

During quiet flight in hypergravity, the most prominent changes (i.e., increased MAP, HR, and VR; decreased SV; see Fig. 2) are consistent with unloading of
both CP and arterial baroreceptors, which would lead to a decrease in efferent cardiovagal activity and an increase in efferent sympathetic activity (13, 22, 26). Gravity-related “stimulation” of vestibular-sympathetic reflexes, however, may have contributed to the presumptive vasoconstriction during this period (15, 34, 36, 40, 48, 49). In both micro- and hypergravity, autonomic reflexes originating in certain extraversatile graviceptors, such as the trunk and kidneys, might also have contributed to cardiovascular responses (27). The fact that we asked subjects to maintain head position to the best of their abilities during flight may have helped minimize any potential effect of semicircular canal input on vagal modulation (11, 33).

Responses to Valsalva maneuvers, effects of posture. The assumption of the seated upright posture in normogravity significantly altered absolute MAP responses to Valsalva maneuvers (Table 2). The supine-to-seated changes in absolute MAP responses that we observed resemble those observed in systolic pressure by Ten Harkel et al. (46), who used a slightly different Valsalva analysis method. Ten Harkel et al. also measured Valsalva responses in the standing position, where they found additional exaggerative effects on arterial pressure responses during Valsalva phases Ile and IV. They concluded that a smaller intrathoracic blood pool in subjects in the upright position is not able to compensate for the decrease in venous return induced by straining.

Responses to Valsalva maneuvers, effects of gravity. Changes in $G_z$ in the seated position significantly influenced absolute MAP responses during Valsalva phases Ile, III, and IV but not during Valsalva phases I and IIe (Table 2 and Figs. 1 and 3). During Valsalva phase IIe in microgravity (Fig. 3A), the decrease in MAP may have been largely due to the contextual vasodilation noted in microgravity during quiet, seated flight (Fig. 2). This contextual vasodilation could also explain why Valsalva maneuver responses were not typically square-wave during microgravity, as might have been expected given the square-wave responses commonly observed in supine congestive heart failure patients (23, 37), acutely volume-loaded patients (23), and some supine healthy subjects (17, 46). In contrast, during Valsalva phase IIe in hypergravity, the temporal abrogation of the decrease in MAP (Table 4 and Fig. 3B) is consistent with the contextual vasoconstriction noted during quiet flight in that condition (Fig. 2).

During Valsalva phase IIe, the magnitude of the increase in MAP always correlated strongly with the magnitude of the increase in VR, regardless of the gravitational condition. This finding supports the notion that increases in MAP during phase IIe of Valsalva maneuvers principally represent reflexive vasoconstriction (3, 35). In microgravity, the weak MAP response during Valsalva phase IIe may have been related to lesser stimulatory unloading of “volume-sensitive” CP baroreceptors during microgravity strains, because the decrease in SV during those strains was relatively attenuated. If so, then arterial baroreceptor control of VR may have been modulated by CP baroreceptor input during Valsalva strains as well, because this modulation (1, 2, 4, 26, 44) could explain the weak VR but preserved HR response to the intrastrian decrease in MAP in microgravity (Fig. 3A). The potentially confounding effects of vestibulosympathetic (and other) reflexes on VR, however, must again be kept in mind.

During Valsalva phase III, absolute decreases in MAP in microgravity ($-18.17$ mmHg) did not statistically differ from those in normogravity ($-19.10$ mmHg), suggesting that the relatively large absolute decreases in MAP in phase III in hypergravity ($-26.23$ mmHg) may have accounted for all of the phase III-related differences (Table 2). These relatively large decreases in MAP after strains in hypergravity may have been related to the more pronounced phase IIe MAP responses found during that condition. In addition, for many individuals, both reflexive decreases in HR at the end of phase IIe in hypergravity (Fig. 3B), and irregularities (decreases) in the external $G_z$ level during the middle portions of some hypergravity periods (see * in Fig. 3, A and B) may have contributed to large decreases in MAP during hypergravity phase III.

During Valsalva phase IV, the directional changes in MAP across the gravitational conditions tended to mirror those found during Valsalva phase IIe (Table 2). This finding is in accord with the high correlation that has been found between arterial pressure elevations during phase IV and increases in muscle-sympathetic nerve activity during the strain itself (41). Average changes in $\Delta$MAP, however, were less significant across the testing conditions in phase IV than in phase IIe, possibly reflecting the complex, multifactorial nature of phase IV (35).

The reduction in baroreflex sensitivity ($\Delta$R-R interval/ $\Delta$MAP) during Valsalva phase IV in hypergravity in this study (Table 3) is consistent with the attenuated baroreflex responsiveness known to occur after redistributions of blood to the lower extremities (12, 45). Our findings should be interpreted cautiously, however, inasmuch as we found that large changes could be introduced into the phase IV results by relatively small manipulations in the method of analysis, in accord with the findings of Smith et al. (42). Measurements of baroreflex sensitivity during Valsalva phase IIe (i.e., those determined from the terminus a quo and terminus ad quem of the phase) (Table 3; see also Ref. 17) were also not wholly trustworthy in this study, because they were possibly more prone to reflect changes in the duration of the phase rather than changes in vagal efferent responsiveness per se across the testing conditions. More specifically, the temporal duration of phase IIe in microgravity was nearly twice as long as it was in hypergravity (Table 4, Fig. 3); thus HR had a much longer period of time to respond directionally to the decrease in MAP during phase IIe in microgravity than in hypergravity. Given the differences in the latencies and time constants of the cardiac parasympathetic and sympathetic branches (6), this finding gives credence to the notion that the calculation of linear regression slopes (19) may be required if changes in “vagal” efferent responsiveness across conditions are
to be inferred from changes in the value of ΔR-R
interval/blood pressure during Valsalva phase II_e.
Differential effects of posture and gravity on cardiovas-
cular responses to Valsalva maneuvers. Note that the
magnitude of the decrease in MAP during Valsalva
phase II_e was influenced by posture but not by gravity
(Table 2). In this study, the limited effect of gravity on
absolute MAP responses during Valsalva phase II_e may
have been related to contextual (i.e., temporal) factors.
Specifically, during parabolic flight, subjects necessar-
ily performed Valsalva maneuvers seconds after grav-
tional transitions, whereas after postural adjustments in
norgavity, they performed Valsalva maneuvers minutes
after postural equilibration. Thus the non-Valsalva-
related trends in MAP noted during quiet, seated,
parabolic flight (Fig. 2) may have served to enhance
(microgravity) or to buffer (hypergravity) Valsalva-
related decreases in MAP during phase II_e such that
net II_e MAP decreases in seated normogravity. A
similar phenomenon may have contributed to the pres-
ence of the (lack of) notable differences between the effects of
posture and gravity on the other Valsalva phases.

Limitations. In addition to the limitations already
described, environmental factors such as temperature
and humidity were not within our immediate control in
the aircraft, and variations in these factors may have
influenced our overall results. In addition, fatigue may
have contributed to an underestimation of the signifi-
cant differences that we found between Valsalva re-
sponses in hypergravity and Valsalva responses in the
other gravitational conditions because, in few individu-
als, the responses in hypergravity tended to become
less hypersinusoidal as flights progressed. Order-
related differences in hypergravity constituted only a
threat, however, and we did not find any comparable (or
opposite) trends in microgravity as flights progressed.
Finally, it is important to note that we obtained inflight
data only in the seated posture, reserving the semi-su-
pine and other postures for future KC-135 investiga-
tions. This limitation is important, because directional
hemodynamic responses during parabolic flight are
known to depend greatly on the initial posture of the
test subject (5, 16, 25, 28–31). Recently, Foldager et al.
(16) have extended this finding by reporting that
central venous pressure always moves to the same
ultimate value in a given subject during parabolic
microgravity, regardless of the subject’s antecedent
posture, but that the direction of movement of that
pressure (and therefore also the starting pressure)
depends completely upon the subject’s antecedent (i.e.,
1 G) posture. In terms of the current study, this means
that we would not expect the directional hemodynamic
responses of our seated test subjects to necessarily
resemble those of shuttle crewmembers, who currently
enter microgravity in the semisupine (i.e., feet up)
posture. Semisupine shuttle crewmembers are known to
have decreases in central venous pressure after inser-
tion into orbit (9, 10, 16), whereas seated test
subjects entering parabolic microgravity are known to
have increases in this same parameter (16, 30).

Conclusion. In conclusion, we documented, from a
detailed temporal perspective, the integrated, beat-to-
beat, cardiovascular responses of healthy human test
subjects during parabolic flight. We found that during
quiet, seated flight, transitions into parabolic micro-
gravity and into parabolic hypergravity elicited initial au-
tonomic cardiovascular responses similar to those elic-
ted by acute downward tilt and by acute upward tilt,
respectively, in normogravity. In addition, during the
sustained portion of parabolic microgravity, as MAP
decreased and SV increased, we found persistent vaso-
dilation even after a prolonged (>16 s) period of hypo-
tension-induced cardioacceleration, possibly support-
ing the notion of Mancia and Mark (26) and others (1, 2,
44) that alterations of human cardiopulmonary barore-
ceptor activity are able to modulate arterial baroreflex
control of VR but not HR. A confounding effect in the
present study of vestibulosympathetic (and other) re-
flexes on VR (15, 27, 34, 40, 48, 49), however, could not
be excluded as having contributed to these results.
With respect to seated Valsalva maneuvers, we found
that parabolic gravitational transitions significantly
influenced cardiovascular responses during Valsalva
phases II, III, and IV. Specific changes in these re-
sponses, however, differed qualitatively and quantita-
ively from those occurring after a postural transition
in normogravity, probably because of differences in the
temporal nature of the respective stimuli.

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