Effect of short-term microgravity and long-term hindlimb unloading on rat cardiac mass and function

CHESTER A. RAY,1 MARILYN VASQUES,2 TODD A. MILLER,3 M. KEITH WILKERSON,3 AND MICHAEL D. DELP3,4

1Departments of Medicine and Cellular and Molecular Physiology, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033; 2Life Sciences Division, National Aeronautics and Space Administration Ames Research Center, Moffett Field, California 94035; and 3Department of Health and Kinesiology, Texas A&M University, and 4Department of Medical Physiology, and the Cardiovascular Research Institute, Texas A&M Health Science Center, College Station, Texas 77843

Received 26 April 2001; accepted in final form 23 May 2001

Ray, Chester A., Marilyn Vasques, Todd A. Miller, M. Keith Wilkerson, and Michael D. Delp. Effect of short-term microgravity and long-term hindlimb unloading on rat cardiac mass and function. J Appl Physiol 91: 1207–1213, 2001.—The purpose of this study was to test the hypothesis that exposure to short-term microgravity or long-term hindlimb unloading induces cardiac atrophy in male Sprague-Dawley rats. For the microgravity study, rats were subdivided into four groups: preflight (PF, n = 12); flight (Fl, n = 7); flight cage simulation (Sim, n = 6), and vivarium control (Viv, n = 7). Animals in the Fl group were exposed to 7 days of microgravity during the Spacelab 3 mission. Animals in the hindlimb-unloading study were subdivided into three groups: control (Con, n = 20), 7-day hindlimb-unloaded (7HU, n = 10), and 28-day hindlimb-unloaded (28HU, n = 19). Heart mass was unchanged in adult animals exposed to 7 days of actual microgravity (PF 1.33 ± 0.03 g; Fl 1.32 ± 0.02 g; Sim 1.28 ± 0.04 g; Viv 1.35 ± 0.04 g). Similarly, heart mass was unaltered with hindlimb unloading (Con 1.40 ± 0.04 g; 7HU 1.35 ± 0.06 g; 28HU 1.42 ± 0.03 g). Hindlimb unloading also had no effect on the peak rate of rise in left ventricular pressure, an estimate of myocardial contractility (Con 8,055 ± 385 mmHg/s; 28HU 8,545 ± 755 mmHg/s). These data suggest that cardiac atrophy does not occur after short-term exposure to microgravity and that neither short- nor long-term simulated microgravity alters cardiac mass or function.

heart; deconditioning; cardiac atrophy

THE HUMAN BODY IS EXQUISITELY designed for maintaining an upright posture on Earth. However, when the force of gravity is removed during spaceflight, there is a cephalic fluid shift and an elimination of the head-to-foot hydrostatic pressure gradient (35, 36). This change in the fluid pressure distribution elicits adaptations within the cardiovascular system that are subsequently detrimental on return to the Earth’s gravitational environment (36). These microgravity-induced alterations of the cardiovascular system are primarily manifested as a diminished aerobic capacity (32, 36) and orthostatic intolerance (36). Several factors appear to contribute to the orthostatic intolerance after spaceflight (36). The first factor is the inability to elevate peripheral vascular resistance (4, 26). A second putative factor is the ability of the heart to maintain stroke volume and cardiac output. After spaceflight, stroke volume and cardiac output have been shown to be reduced (5, 6). Although it is generally believed that reductions in stroke volume and cardiac output result from decreased ventricular filling secondary to blood volume reductions and increased venous pooling (36), it has also been suggested that cardiac atrophy contributes to the diminished cardiac function after spaceflight (22). Cardiac atrophy would have greater adverse consequences than reductions in blood volume or venous pooling because immediate countermeasures could not be administered on return to the 1-G environment. Additionally, it is possible that cardiac atrophy would remain for sustained periods after return from microgravity and could conceivably elicit severe cardiac complications (i.e., heart failure).

To study physiological adaptations to microgravity on Earth, the tail-suspended, hindlimb-unloaded rat model has been used to simulate the effects of microgravity. This model induces the cephalic fluid shift (18, 24, 31) and postural muscle unloading (28) that are characteristic of exposure to microgravity. Specific adaptations occur in these rats that are similar to spaceflight, including postural muscle atrophy (28), hypovolemia (27, 33), a diminished capacity to elevate vascular resistance (25, 29, 38), orthostatic hypotension (23), and a reduced aerobic capacity (11, 30). Despite the extensive use of this animal model to infer physiological adaptations to microgravity, there is conflicting information on the effect of hindlimb unloading on cardiac adaptations in the rat. Moreover, little information has been obtained on cardiac adaptations in the rat while in space.

On the basis of this background, the purpose of the present study was to test the hypothesis that microgravity induces cardiac atrophy. To test this hypothesis, we carried out two separate experiments in rats. First, we measured heart mass after 7 days of space-
flight. Second, we measured heart mass (i.e., total, right and left ventricular, and septal) after 7 and 28 days of hindlimb unloading and left ventricular function after 28 days of hindlimb unloading. Contrary to our hypothesis, the results from both experimental models indicate that short-term microgravity and long-term simulated microgravity do not elicit cardiac atrophy or decreased function in healthy rats.

**METHODS**

The methods employed in this study were approved by the National Aeronautics and Space Administration Ames Research Center and Texas A&M University Institutional Animal Care and Use Committees. The investigations conformed to the National Institutes of Health (NIH) Guide for the Care and Use of Laboratory Animals (DHHS Publication No. (NIH) 85-23, Revised 1985, Office of Science and Health Reports, Bethesda, MD 20892).

**Study 1 (Spaceflight)**

*Experimental design.* Young (~200 g) and old (~400 g) male Sprague-Dawley rats (Taconic Farms, Germantown, NY) were studied under four conditions to examine the effects of microgravity on rats as previously described (12, 15). These conditions were preflight control, flight cage control (a ground-based cage simulation), vivarium control, and flight. All rats in these groups were individually housed in microisolator vivarium cages (Lab Product), the young rats for 7 days (beginning 20 days before launch) and the old rats for 14 days (beginning 27 days before launch). They received flight diet (food bars of Teklad 356 diet) and water ad libitum. The room temperature was 23 ± 1°C with a 12:12-h light-dark cycle. Thirteen days before launch of the National Aeronautics Space Administration's Spacelab 3 mission, animals in three of the groups (excluding vivarium controls) were transferred to flight-type cages (11 \( \times 11 \times 28 \) cm) where the rats were habituated to the flight feeders and Lixit water system. These cages were held in laminar flow hoods in the rodent animal housing facility to simulate the airflow present under flight conditions. Additionally, the light cycle and temperature were maintained to be comparable to actual flight conditions.

Twenty-four hours before flight, one group of animals was loaded into the shuttle space laboratory (flight) and a second group was returned from the launch pad and killed (preflight control). A third group was returned to the laboratory and housed in flight-type cages (flight cage control) and killed 2 days after the flight animals. The fourth group of rats from the vivarium was then killed 2 days later (vivarium control).

The flight animals were weighed and inspected on landing and then transported from California (Dryden Air Force Base) to Kennedy Space Center in Florida. The animals were then killed between 11 and 17 h after shuttle landing. All rats were anesthetized with halothane-oxygen gas mixture, weighed, and bled by cardiac puncture. The heart was dissected and weighed in all animals.

**Study 2 (Hindlimb Unloading)**

*Experimental design.* Forty-nine male Sprague-Dawley rats weighing 400–450 g (6–8 mo of age) were obtained (Harlan, Houston, TX) and housed in a temperature-controlled (23 ± 2°C) room with a 12:12-h light-dark cycle. Water and rat chow were provided ad libitum. One week after arrival from the breeder, the rats were randomly assigned to either a control (C; \( n = 20 \)), 7-day hindlimb-unloaded (7HU; \( n = 10 \)) or 28-day hindlimb-unloaded (28HU; \( n = 19 \)) group. Animals were inspected daily by laboratory personnel and weekly by a veterinarian to ensure proper health. The hindlimbs of the hindlimb-unloaded rats were partially elevated with a harness attached to the tail as previously described (8, 9). Briefly, the hindlimbs of the hindlimb-unloaded group were elevated to an approximate spinal angle of 40–45° via orthopedic traction tape placed around the proximal two-thirds of the tail. The height of hindlimb elevation was adjusted to prevent the hindlimbs from touching supportive surfaces while the forelimbs maintained contact with the cage floor. This allowed free range of movement around the cage while achieving the desired experimental results. The hindlimb unloading was maintained for 7 or 28 days. This time period has been shown sufficient to elicit cephalic fluid shifts (18, 23, 31), produce cardiovascular alterations in HU animals (8, 11, 23, 25, 27, 29, 30, 38), and induce skeletal muscle atrophy (7, 9, 10). After the unloading period, the animals were anesthetized with pentobarbital sodium (35 mg/kg ip) and weighed without allowing the hindlimbs to become weight bearing. The rats were then decapitated, and the heart was excised, dissected into the right and left ventricle and septum, and weighed. Finally, the soleus muscle was dissected from the hindlimb and weighed.

In two subsets of animals (C, \( n = 11 \); 7HU, \( n = 9 \); 28HU, \( n = 11 \)) cardiovascular hemodynamics were measured. In the first subset (C, \( n = 4 \); 7HU, \( n = 9 \); 28HU, \( n = 5 \)), a Silastic catheter (Dow Corning; ID 0.6 mm, OD 1.0 mm) filled with heparinized (200 U/ml) saline was advanced into the ascending aorta via the right carotid artery while under pentobarbital sodium anesthesia (35 mg/kg ip) 1 day before the end of the experimental period, as previously described (10). This catheter was used for the recording of arterial pressure pulse (MacLab data collection system), from which mean arterial pressure (electroponically averaged) and heart rate were determined. In the second subset of animals (C, \( n = 7 \); 28HU, \( n = 6 \)), a Silastic catheter (Dow Corning; ID 0.6 mm, OD 1.0 mm) filled with heparinized (200 U/ml) saline and connected to a pressure transducer (ADInstrument MLT0688 blood pressure transducer) and chart recorder was advanced into the left ventricle of the heart via the right carotid artery while under sodium pentobarbital anesthesia (35 mg/kg ip) 1 day before the end of the experimental period, as previously described (10). This catheter was subsequently used for the recording of left intraventricular arterial pressure, from which the peak rate of rise of left ventricular pressure \( (+dP/\) \( dt) \) was determined. A second polyurethane catheter (Braintree Scientific, Micro-renathane; ID 0.36 mm, OD 0.84 mm), used to record arterial pulse pressure, was implanted in the caudal artery of the tail and filled with heparinized saline as previously described (10). Both catheters were externalized and secured on the dorsal region. The animals were then returned to their cages. Hindlimb-unloaded animals from both subsets were placed prone in their cages during recovery. Once the animals began to stir, the tail harness was connected to the suspension apparatus of the cage and the hind feet elevated to just above the cage floor. Once the animals appeared to be fully conscious, the hindlimbs were elevated to the presurgery height. This procedure was followed to prevent the hindlimbs from becoming weight bearing during and after the surgical procedure.

The following day the catheters were connected to a pressure transducer and heart rate, mean arterial pressure and peak \( +dP/\) \( dt \) (second subset group only) were measured while the animals were standing. This necessitated that this subset of 7- and 28-day hindlimb-unloaded rats become weight bearing for ~5 min before euthanasia and tissue sampling.
Data Analysis

Data among the groups were compared using a one-way ANOVA. If the ANOVA indicated significant differences among groups, a Student-Newman-Keuls post hoc test was conducted to determine which groups were different from each other. A general linear models procedure was performed to determine the significance of relationships between body mass loss and heart mass loss and between body mass and heart mass. Significance was accepted at \( P < 0.05 \) for all analyses. All values are presented as means ± SE.

RESULTS

Study 1

Preliminary results of the Spacelab 3 mission have been previously reported in abstract form (12, 15). Heart masses were not different among groups of adult rats (Fig. 1). However, the heart-to-body mass ratio was lower in the vivarium control rats relative to the preflight control and flight animals. In the young rats, heart masses of the flight, flight cage control, and vivarium control rats were greater than that of the preflight control rats (Fig. 2). It should be noted that preflight control rats were 7 days younger than the flight animals, 9 days younger than the flight cage control rats, and 11 days younger than vivarium controls. Vivarium control rats also had greater heart mass than the flight and flight cage control rats. Conversely, heart-to-body mass ratio was lower in the flight, flight cage control, and vivarium control rats compared with preflight control rats. Vivarium control rats also had a lower heart-to-body mass ratio relative to flight rats.

Study 2

Neither total heart mass nor heart-to-body mass ratio was different among control, 7-day hindlimb-unloaded, or 28-day hindlimb-unloaded animals (Table 1). Similarly, 7 and 28 days of unloading did not affect right and left ventricular and septal masses.

Soleus muscle mass was 17 and 48% lower in the 7- and 28-day unloaded rats relative to control animals (Table 1). Similarly, unloading resulted in a 12 and 44% reduction in the soleus muscle-to-body mass ratio. Soleus muscle atrophy, which is characteristic of reduced skeletal muscle weight-bearing activity (28), confirmed the efficacy of the hindlimb unloading treatment.

Hindlimb unloading did not alter mean arterial pressure during 5 min of post-suspension standing (Table 2). However, 28-day hindlimb-unloaded rats exhibited a relative tachycardia during the standing period. Despite having a higher heart rate, neither the heart rate-pressure product (Table 2) nor peak \(+dP/dt\) during standing was different between control and unloaded rats (Fig. 3).

DISCUSSION

The major findings of this study were that 1) 7 days of spaceflight did not reduce heart mass or heart-to-body mass ratio in adult rats and 2) 7 and 28 days of hindlimb unloading, which elicited significant atrophy of the soleus muscle, did not alter cardiac mass, heart-to-body mass ratio, or left ventricular function. These findings suggest that neither short-term microgravity...
nor short- and long-term simulations of microgravity induce cardiac atrophy in the rat.

A major cardiovascular challenge with spaceflight is overcoming orthostatic intolerance or hypotension after spaceflight. Maintaining arterial pressure in the upright posture is dependent on both cardiac output and total peripheral resistance. It has been generally assumed that, when cardiac output is diminished after spaceflight, it is due to decreased stroke volume secondary to a decreased filling volume (36). However, human and animal studies have suggested that cardiac atrophy may contribute to decreased cardiac function after spaceflight. Using echocardiography to estimate cardiac mass of astronauts, Henry et al. (20) reported a reduction in left ventricular mass without a change in wall thickness after spaceflight. To our knowledge, these are the only human data to support the occurrence of cardiac atrophy in microgravity. In the rat, Goldstein et al. (14) reported cross-sectional fiber atrophy of left ventricular papillary muscle bundles after 14 days of spaceflight. More importantly, however, spaceflight did not elicit reductions in the cross-sectional area of left ventricular myocytes in these animals. Although cardiac mass was not reported, this finding is consistent with the flight results of the present study and suggests cardiac atrophy does not occur with 1–2 wk of weightlessness in adult rodents. The effects of long-term microgravity on cardiac mass remain to be determined.

As a result of the paucity of opportunities to perform flight investigations with humans and animals, many scientists have used ground-based analogs to estimate the effects of microgravity on the body. To address the question of cardiac adaptation to microgravity, Levine and co-workers (22) estimated left ventricular mass in humans after a 14-day, 6° head-down-tilt bed rest treatment using two-dimensional echocardiography. They reported a 5% decline in cardiac mass, although this reduction did not reach statistical significance. In the rat, Bao et al. (2) also assessed left ventricular volumes and mass using echocardiographic imaging after 28 days of unloading. They reported decreased left ventricular end-systolic and end-diastolic dimensions, lower stroke volume, and a reduced left ventricular mass. A number of studies have directly measured cardiac mass after head-down hindlimb unloading in adult rats with varying results; some have reported no effect of 14–29 days of unloading on heart mass (present study; 37, 40), whereas others have shown diminished cardiac mass (3, 39, 41).

In an attempt to bring unity to these seemingly disparate results, one can identify factors that are known to affect heart mass, such as developmental stage, hormonal status (13), mechanical stress imposed by the arterial circulation (16), and metabolic status (17, 34), and consider how these factors might be influenced by the hindlimb-unloading treatment. To avoid the potentially confounding effects of a developmental factor, the present consideration of the effects of hindlimb unloading on cardiac mass has been limited to studies of adult rats past the rapid growth stage (i.e., 3 mo of age and older). A second factor that can diminish heart mass is hormonal status, in particular hypothyroidism (13). We are unaware of any data to suggest that hindlimb-unloaded rats become hypothyroid; on the contrary, both thyroxine and triiodothyronine levels appear to be maintained at control levels (37). A third factor that has been shown to affect cardiac mass is arterial pressure. For example, chronic reductions in arterial pressure result in ventricular atrophy, whereas chronic elevations in pressure lead to cardiac hypertrophy (16). In the hindlimb-unloaded rat, ascending aortic pressure is elevated when the animals are initially placed in the head-down position (7, 25). This elevation in pressure persists for ~1 wk and then returns to and remains at levels equivalent to

### Table 1. Body and tissue masses after 7 and 28 days of hindlimb unloading in rats

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 20)</th>
<th>7-Day HU (n = 10)</th>
<th>28-Day HU (n = 19)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body, g</td>
<td>484 ± 11</td>
<td>439 ± 15</td>
<td>455 ± 13</td>
<td>0.07</td>
</tr>
<tr>
<td>Heart, g</td>
<td>1.40 ± 0.04</td>
<td>1.35 ± 0.05</td>
<td>1.42 ± 0.03</td>
<td>0.56</td>
</tr>
<tr>
<td>Heart-to-body mass ratio, g/kg</td>
<td>2.94 ± 0.07</td>
<td>3.06 ± 0.12</td>
<td>3.12 ± 0.08</td>
<td>0.27</td>
</tr>
<tr>
<td>Right ventricle, mg</td>
<td>283 ± 13</td>
<td>246 ± 9</td>
<td>281 ± 9</td>
<td>0.11</td>
</tr>
<tr>
<td>Left ventricle, mg</td>
<td>753 ± 28</td>
<td>747 ± 45</td>
<td>766 ± 21</td>
<td>0.90</td>
</tr>
<tr>
<td>Septum, mg</td>
<td>365 ± 14</td>
<td>358 ± 19</td>
<td>372 ± 11</td>
<td>0.80</td>
</tr>
<tr>
<td>Soleus, mg</td>
<td>243 ± 7</td>
<td>201 ± 7</td>
<td>129 ± 8</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Soleus-to-body mass ratio, mg/kg</td>
<td>509 ± 12</td>
<td>446 ± 15</td>
<td>287 ± 18</td>
<td>0.0001*</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of rats. *Student-Newman-Keuls post hoc test indicates that each group was significantly different from the others.

### Table 2. Hemodynamic variables after 7 and 28 days of hindlimb unloading

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 11)</th>
<th>7-day HU (n = 9)</th>
<th>28-day HU (n = 11)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>432 ± 12</td>
<td>427 ± 7</td>
<td>466 ± 8*</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>127 ± 4</td>
<td>132 ± 2</td>
<td>127 ± 4</td>
<td>0.50</td>
</tr>
<tr>
<td>Heart rate-pressure product, mmHg × beats/min</td>
<td>54,655 ± 2,644</td>
<td>57,631 ± 1,119</td>
<td>59,820 ± 2,686</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of rats. *Significantly different from control and 7-day HU groups, P < 0.05.
that in a standing control rat (7). In addition, if one examines the heart rate-pressure product, an index of myocardial work, it is clear that the work of the heart is not diminished over the duration of the unloading period (Table 2) (7). Therefore, it does not appear that alterations in the mechanical stress imposed on the heart by the arterial circulation or myocardial work would provide a stimulus for cardiac atrophy with hindlimb unloading.

A fourth factor that can affect cardiac mass is the metabolic status of the rat. Previous work has demonstrated that a negative caloric balance results in ventricular atrophy (17, 34). This atrophy is manifest only as a decrease in absolute cardiac mass, because heart-to-body mass ratio either remains unchanged or increases. It is important to note that the decrease in absolute cardiac mass, rather than the lack of change in heart-to-body mass ratio, is the critical index of heart mass because the diminished absolute mass corresponds to the functional changes of the heart, such as decreased peak systolic pressure and diminished +dP/dt (17). In an attempt to determine whether cardiac atrophy in some studies of hindlimb unloading might be related to a negative caloric balance, we plotted the percent difference in heart mass (hindlimb-unloaded vs. control rats) as a function of the percent difference in body mass (Fig. 4) from values of the present study and those reported in the literature for adult rats (3, 37, 39–41). There was a significant relationship between these two variables, indicating that, when there are relatively small decreases in body mass (e.g., <10–12%), no change in cardiac mass occurs (present study; 37). However, when relatively large reductions in body mass occur in conjunction with the unloading treatment, heart mass is lower (3, 41). Although these data indicate that alterations in cardiac mass with hindlimb unloading are proportional to the changes in body mass, it is possible that the relationship between body mass and heart mass is different between control and unloaded rats. To address this possibility, we plotted cardiac mass as a function of body mass for control and hindlimb-unloaded rats (Fig. 5) (3, 37, 39–41). There was no difference in this relationship between control and unloaded animals (P > 0.05), suggesting that for a given body mass, cardiac mass will not be lower in hindlimb unloaded rats. This assertion is further supported by the fact that none of the studies reporting cardiac atrophy find a decrease in the heart-to-body mass ratio with unload-

Fig. 3. Rate of rise in peak left ventricular pressure (+dP/dt) during standing in control and 28-day hindlimb-unloaded rats. There were not differences in left ventricular contractility between groups.

Fig. 4. Scattergram showing linear relationship between the loss of body mass and the loss of heart mass in adult head-down, hindlimb-unloaded (HU) rats relative to cage control (C) animals. Data are from present study (●), Bigard et al. (3) (◇), Woodman et al. (39) (●), Woodman et al. (40) (▲), Woodman et al. (41) (◇), and Woodman et al. (37) (●). The duration of unloading was between 14 and 29 days.

Fig. 5. Scattergram showing linear relationship between body mass and heart mass in adult hindlimb-unloaded (solid line and filled symbols) and control (dashed line and open symbols) rats. Data are from present study (●), Bigard et al. (3) (◇), Woodman et al. (39) (●), Woodman et al. (40) (▲), Woodman et al. (41) (◇), and Woodman et al. (37) (●). There was a linear relationship between body mass and cardiac mass in hindlimb unloaded and control rats (P > 0.05), but this relationship was not different between groups (P > 0.05).
ing (3, 39, 41). Perhaps the best study to illustrate the importance of maintaining body mass and caloric balance with unloading is that of Woodman et al. (37). These authors monitored food and water intake throughout the hindlimb-unloading treatment and found that when normal unloaded rats consume the same amount of food as cage controls, there is no significant difference in body mass between the two groups and no difference in heart mass. The relationship between body mass and cardiac mass indicates that cardiac atrophy does not result from hindlimb unloading per se but that it occurs when the loss of body mass during unloading becomes disproportionately large. These findings have important implications for astronaut health and serve to emphasize the need to maintain caloric and fluid balance during spaceflight.

In addition to changes in cardiac mass, investigators have also reported hindlimb-unloading-induced alterations in cardiac function. Recent work has shown that with 28 days of hindlimb unloading there is a reduced contractility (i.e., lower peak isometric tension and greater time to peak tension) of isolated papillary muscle (42). Using the same duration of unloading as that of Yu et al. (42), we measured peak +dP/dt to estimate whether functional cardiac changes occur with simulated microgravity. We could not detect any difference in +dP/dt between the hindlimb unloaded and control rats (Fig. 3). These findings suggest that simulated microgravity may differentially affect cardiac papillary muscle and ventricular myocytes, which is consistent with the actual microgravity-induced atrophy of papillary fibers with no change in ventricular myocyte cross-sectional area (14). In addition, the finding of no difference in peak +dP/dt supports the contention that microgravity does not alter intrinsic ventricular function but rather that decreased ventricular filling mediates any decline in stroke volume and cardiac output after spaceflight. This conclusion is also consistent with the findings of several human studies. For example, Mulvagh et al. (26) reported that ejection fraction did not change after short-term spaceflight using two-dimensional M-mode echocardiography. Similarly, Atkov et al. (1), using echocardiographic data, reported no change in cardiac contractility after 237 days in space. Using the bed rest model, Hung et al. (21) also showed no decrease in cardiac contractility as measured by ejection fraction after 10 days of bed rest. Although other investigators have reported data to suggest a decline in cardiac function after bed rest (22), the rodent data of the present study are consistent with the preponderance of human studies indicating intrinsic cardiac function is not compromised by actual or simulated microgravity.

In addition to determining the effects of microgravity on adult rat cardiac mass, we sought to determine whether short-term spaceflight had a potentially greater adverse effect on cardiac mass of growing rats. Although the data are not as definitive as that for the adult animals, presumably due to the interactive effects of microgravity, cage conditions and growth, tentative conclusions can be made. It was observed that heart mass of young flight rats was lower than that of vivarium control animals but similar to that of flight cage control rats (Fig. 2). These data suggest that the lower heart mass in the flight rats cannot be ascribed to microgravity but rather that it is related to some specific aspect of the flight cage. For example, it is possible that the flight cages restricted physical activity to a greater degree or was less conducive to the animals maintaining a proper caloric balance. In addition to the present study showing no apparent cardiac atrophy in young rats after 7 days in microgravity, Henriksen et al. (19) also reported similar heart weights in juvenile female rats after 7 days of hindlimb unloading compared with cage controls. Collectively, these studies indicate that neither short-term actual nor simulated microgravity induces cardiac atrophy in young rats.

In summary, the present study demonstrates that exposure to short-term microgravity and long-term simulated microgravity (i.e., hindlimb unloading) does not elicit changes in heart mass. Additionally, simulated microgravity does not alter peak +dP/dt, an index of cardiac contractility, indicating cardiac function is not compromised. These results suggest that cardiac atrophy and dysfunction are not adverse consequences of microgravity when body mass is fairly well maintained. Therefore, results from this study are consistent with the conclusion of Buckey et al. (4) that the failure of humans to maintain arterial pressure after exposure to short-term spaceflight appears to be related to changes in the periphery and not to cardiac deterioration. However, in cases where large decrements in body mass occur, cardiac atrophy may result and lead to impaired cardiac function. This observation has important implications for astronaut health and highlights the need for more detailed nutritional studies to determine the impact of caloric and nutritional imbalance on general cardiovascular function during and after spaceflight.

We gratefully acknowledge the contributions of Dr. Richard E. Grindeland, Project Scientist for the National Aeronautics and Space Administration (NASA) Spacelab 3 mission, in obtaining heart mass data from the flight experiments and review of this manuscript. This study was supported by NASA Grants NAG9-1034 (to C. A. Ray) and NAG2-1340 and NCC2-1166 (to M. D. Delp); National Space and Biomedical Research Institute Grants NCC9-58-42 (to M. D. Delp) and NCC9-58-168 (to C. A. Ray); and National Heart, Lung, and Blood Institute Grant HL-58503 (to C. A. Ray).

REFERENCES


