Effects of Microgravity: Cardiovascular Baroreflex Adaptation in Space Flight

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May 4, 2009

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1 Introduction

Weightlessness is the most important factor affecting the health of astronauts during space flight. Whether we realized it or not, the mankind has evolved a number of structures, mechanisms, controls and reactions that are adapted to the constant stress of gravities. Exposure to zero- or micro-gravity conditions during space flights induces drastic changes in the human body that may threaten the safety of astronauts and inhibit their activities. While humans have little difficulty surviving in space for short periods in time, it is still unknown whether long-term exposure to microgravity may be detrimental to human health. For the health of astronauts, as well as better utilization of their precious time in space, it is critical to understand the effects of microgravity...
on human bodies and the corresponding physiological mechanisms, so that scientists may develop countermeasures to facilitate the adaptation process. Similarly, any long-distance manned space mission (e.g., journey to Mars) would be impossible before the effect of long-term exposure to microgravity is well understood.

Microgravity influences a variety of systems in the human body, and some effects are illustrated in Figure 2. The direct and indirect effects of weightlessness consists of a cascade of interrelated adaptations that begin in three types of responses: the redistribution of fluid, the change of weight-bearing structures, and the dysfunction of gravity receptors.

Fluid redistribution means the body fluids shifts from the lower body to the upper body as they are no longer subject to gravitational forces. Fluid redistribution is coupled with fluid loss, because the brain interprets the increase volume of fluid in the upper body as an increase of total volume and responds by triggering fluid excretion.

The removal of gravity also deteriorates weight-bearing structures like bones and muscles. Bones are dimineralized because its density is stimulated by the stress in the presence of gravity. Similarily, muscles used for antigravity movements on the ground atrophy because of disuse in weightless conditions. Some other muscles change their structure from slow-twitch fibers that are useful for antigravity support to contractile fibers useful for rapid response.

Weightlessness disables human receptors responsible for sensing mass, direction and balance. Balancing receptors in ears no longer perceive correct cues. Touching receptors in the feet and ankels no longer receive the signals of down direction. The failures of these receptors lead to hand-eye disorientation, poor self-balancing and motion sickness, inhibiting astronauts’ activities in space.

These effects in turn give rise to adaptations in other physiological systems, ranging from anemia, immunity system weakening to flatulency in digestive systems. Among them the cardiovascular system have shown the most significant adaptations and plays a critical role in astronauts’ health. This paper aims to explore how the cardiovascular structures and functions are adapted under the microgravity condition. More specifically, we investigate the effect of weightlessness on baroreceptor
reflex (or baroreflex), one of the body’s homeostatic mechanisms for maintaining blood pressure.

The rest of the paper is organized as follows. Section II introduces the general cardiovascular response to microgravity exposure and brings out the remaining questions concerning the baroreflex sensitivity. Section III presents the methodology used to study the baroreflex. Section IV shows the results, which are then discussed in Section V.

2 Background

The cardiovascular system is heavily dependent on the gravity. The gravitational field, the body posture, and the characteristics of blood vessels jointly determine the distribution of blood and consequently a number of cardiac pumping factors, including heart rate, heart size, stroke volume, blood pressure, oxygen uptake, blood volume, etc.

The primary stimulus for the adaptation of cardiovascular systems is the shift of intravascular and interstitial fluid from the lower to the upper part of the body, particularly to the central circulation. An initial increase of fluid in the thoracic area increases the left ventricular volume and cardiac output. As the brain senses the increase of fluid, the intravascular fluid was excreted, making the ventricles shrink and cardiac output decrease.

Under microgravity conditions, the heart no longer needs to sustain blood flow against gravitational stresses, causing the reduction of heart rate and cardiac output according to decreased demands. The decrease of cardiac output is also manifested in terms of maximal oxygen uptake. Because pulmonary function does not limit oxygen uptake, cardiac pumping function is probably the limiting step, hence the maximal oxygen uptake reflects the cardiac output.

The adaptation to microgravity also reduces the heart size and stroke volumes. The total heart size was reported to decrease according to studies in both simulated microgravity environment and real space flights. Stroke volumes of both ventricles have been observed to decrease by 20%-30% in either supine and upright postures, according to results from the US space station Skylab. The reduction of stroke volumes are attributed to two factors. First, the loss of plasma volume due to fluid redistribution results in smaller filling volumes, which in turn reduces the stroke volume. Second, intrinsic myocardium contractilities are depressed under microgravity.

Although space flights over the past forty years have accumulated large amounts of data for scientists to understand the cardiovascular adaptations to zero-gravity, a number of questions still remain to be solved. One of the unknown questions concerns the regulation of blood pressures. Blood pressures, including central venous pressure, diastolic pressure, systolic pressure and arterial pressure, are important variables that help scientists understand the dynamics of fluid shirt under microgravity. Blood pressures are regulated by baroreflex, a homeostatic mechanism that relies on neurons to monitor blood pressure and relay feedback to the brainstem mediating the blood
pressure. A yet-unsolved question is the dynamic adaptation of the baroreflex sensitivity under microgravity.

The adaptation of baroreflex is of interest for the astronauts’ health. Without gravitational effects, blood pressures is virtually the same throughout the systemic arteries. A possible impairment of baroreflex control during space flight may lead to hypertension in cerebral arteries in astronauts.

Investigations of baroreflex activities have been limited by technical and logistic challenges. Most studies of baroreflex activity were conducted in the conditions of simulated microgravity via prolonged head-down bed rest, or in the post-spaceflight time, or under short-term changes of gravity during parabolic flights. These experiments however did not directly measure baroreflex function during real space flights, and the results were inconsistent. Since 1996, direct assessments of baroreflex and other cardiovascular variables during space flights have been available but still lack comprehensiveness and thoroughness. Both the direct and indirect measurements have been limited to static before-and-after comparisons, and little is known about the dynamic adaption of baroreflex functions under microgravity. In early studies, the earliest evaluation of baroreflex was obtained 12 days after launch. Only in the STS 107 Columbia Space Shuttle mission have scientists been able to study the complete time course of the baroreflex adaption from the first day to the end of the mission. On the other hand, the effects of long-term exposure to microgravity is also a great research interest. Scientists have studied cardiovascular responses during a 9-month space mission aboard the Russian space station Mir.

In the rest of the paper, I will describe both the short-term and long-term responses of cardio baroreflex during space flight. The dynamic adaptation in short term was investigated by the STS 107 Columbia Space Shuttle mission, whereas the long-term study was carried out by the 9-month mission on Mir.

Before continuing our discussion, it is worthy mentioning the STS 107 space mission carried out by the Space Shuttle Columbia. The mission was launched on January 16th, 2003 and lasted 16 days, before it tragically ended when the shuttle was disintegrated during its reentry into the earth’s atmosphere. Despite the accident, data were instantaneously transmitted back to the earth during the flight, so that scientists were able to finish this study.

3 Method

3.1 Factors Considered

The baroreflex sensitivity was evaluated by the so-called “sequence method”, which is based on fluctuations in systolic blood pressure (SBP), diastolic blood pressure (DBP) and the R-R interval (RRI). The RRI was derived from ECG signals as the interval between the peaks of two consecutive
R waves. The variations of blood pressures and RRI comprises two major components: a low-frequency component and a high-frequency component. The low-frequency component of blood pressure, referred to as Mayer’s wave, is mediated by the sympathetic nervous system, whereas the high-frequency component is unaffected by the autonomic activity. The high-frequency component of RRI is mediated by the respiratory activity and reflects parasympathetic function, while the low-frequency component of RRI is associated with the sympathetic nervous system as well as neurohormonal and endogenous vascular factors. Recent studies have shown that changes in RRI are regulated by baroreceptor reflex in response to Mayer’s wave of blood pressure.\textsuperscript{7} Therefore, blood pressures and RRI provide a practical means to assess baroreflex sensitivity. This method is called “the sequence method”.

Specifically, beat-by-beat SBP and RRI series were scanned in search for sequences of three or more consecutive heartbeats during which 1) SBP progressively increased and, after a lag of zero, one or two beats, RRI progressively lengthened or 2) SBP progressively decreased and, after the same lag, RRI progressively shortened. The slope of the regression line between SBP and RRI values from each sequence was taken as a measure of the baroreflex sensitivity on the heart rate control (BRS). Calculation was also made of the ratio between the number of progressive SBP increases or decreases that were followed by RRI changes (i.e., the number of spontaneous baroreflex sequences) and the total number of progressive SBP increases or decreases identified over the whole recording period, regardless of whether or not they were followed by RRI changes. This ratio was reported to provide information on how often the baroreflex takes control of the sinus node in response to spontaneous BP changes [baroreflex effectiveness index (BEI)],\textsuperscript{8} providing another measure of baroreflex function in addition to BRS.

3.2 Experimental Protocol

Both the short-period and long-period mission adopted similar experimental protocols. In the 16-day Columbia Shuttle mission, measurements were conducted on four astronauts. For each subject, baseline data were collected four times within a period between 279 and 59 days before the launch. During the flight data were recorded 4 times: (1)between hour 8 and 13 (early test), (2)between hour 14 and 29, (3)between day 6 and 8 (mid mission) and (4)between day 12 and 14 (end mission). The air pressure on board was 1atm and the orbital altitude of the shuttle was 307km. Noninvasive and continuous systolic pressure, diastolic pressure and ECG were recorded, and respiratory movements were monitored by an inductance plethysmograph. Left ventricular ejection time (LVET) was estimated as the time interval between the start of upstroke and the dicrotic notch in each blood pressure wave.

Data were recorded both at rest and during moderate exercise on a cycle ergometer (75W), according to the following schedule. First, the subjects were sitting at rest on a cycle ergometer
and data were recorded for 15 minutes. Then the recordings were suspended for 40 minutes when the astronauts were engaged in other scientific activities. The subjects then rested for 3 minutes to ensure the baseline condition was restored. Finally data were recorded in a second round when the subjects were pedaling at 75-W workload.

Similar experiment was taken in the 9-month Mir mission. In addition to blood pressure and ECG measurements, respiratory airflow was recorded, too. The recordings were performed periodically before, during and after the flight. The recording procedure was similar to that in the Columbia Shuttle mission, except that controlled-frequency breathing was used in replace of the pedaling exercise as a method to perturb autonomic functions.

4 Results

Blood pressures and R-R interval (RRI) recorded during the 16-day flight are shown in Figure 2. When subjects were at rest, the mean values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) increased shortly after the launch whereas their corresponding standard deviation decreased, as compared with preflight conditions. After one week in flight, both blood pressures returned toward preflight values. RRI also increased during early exposure to zero-gravity, but it tended to stay above the preflight level throughout the flight. During exercise, no significant difference was observed in SBP, DBP and RRI (Fig 2, C and D).

Figure 3 shows the baroreflex sensitivity (BRS) values obtained by the sequence method as described in the previous section. BRS at rest increased remarkably in the early phase of the flight among all subjects. The increased BRS was sharply reduced near the preflight level after approximately 7 days. BRS during exercise was markedly lower than that at rest, and it did not change much in the flight compared to preflight values. These findings about BRS were confirmed by statistical analysis shown in Figure 4, which also shows the baroreflex effectiveness index (BEI), the ratio indicating how often the baroreflex regulates sinus node in response to spontaneous blood pressure changes. BEI was smaller during exercise than at rest, but did not change much between preflight and inflight conditions.

For comparative purposes an ancillary experiment was performed on the ground with the same astronauts. The systolic and diastolic blood pressures and ECG signals were recorded when the subjects were resting with supine postures. The BRS was derived from these data by the sequence method. Results indicate that the BRS (at rest) adaptation during rapid exposure to space weightlessness was similar to BRS measured in supine posture on earth.

As shown in Figure 5, the respiratory frequency at rest decreased notably shortly after the entry into weightless space, and recovered nearly to the preflight level in the late flight. The respiratory frequency was greater during exercise than at rest. Figure 5 also shows the left ventricular ejection
Figure 2: Systolic blood pressure (SBP), diastolic blood pressure (DBP), and R-R interval (RRI) recorded preflight and during the flight. Data are presented in the form of mean value (A and C), standard deviation (B and D), at rest (A and B) and at exercise (C and D). EARLY 0G: early exposure to zero-gravity. LATE 0G: 1-2 weeks after launch. *P* is the statistical significance.

Figure 3: Baroreflex sensitivity (BRS) under zero-gravity plotted against time since the launch. The solid circles represent results at rest whereas the hollow circle means results during exercise. BRS values before the flight (PRE) are also shown.
time (LVET), which increased significantly in the early exposure to zero-gravity and lowered subsequently, but still maintaining in a higher level than the preflight condition. The LVET was shorter during exercise and did not show much differences over time.

In the 9-month space flight, all cosmonauts reported decreased RRI fluctuation and decreased RRI spectral power at low-end respiratory frequencies. Reduced RRI fluctuations were accompanied by augmented systolic arterial pressure fluctuations before and after microgravity exposure. The transfer function between RRI and the systolic pressure was reduced in flight and was reduced further after landing.

5 Discussion

In the first study investigating the dynamic adaption of cardiac baroreflex regulation to microgravity, scientists discovered that the baroreflex sensitivity (BRS) was not impaired in weightlessness, but rather increased in the early period of the space flight. The similarity between the flight data and data collected in ground tests suggests that the BRS increasing during in the early phase in space is primarily caused by the rising pressure at the carotid sinuses due to centralization of body fluids and loss of blood volumes.

In light of the observed BRS increase in early exposure to microgravity, along with the BRS increase due to blood centralization in the head-down tilt test performed on the ground, it is likely that the blood redistribution under microgravity may take effect by stimulating baroreceptors and then the vagal-cardiac activities. The arterial baroreceptors is known to be a strong determinant of vagal-cardiac efferent flows.

The effect on vagal-cardiac nerves was also confirmed by the observations of R-R wave intervals (RRI). The RRI is assumed to be primarily mediated by the vagal nerve activity according to the following understanding. Large dose of atropine nearly eliminates all RRI fluctuations, but it does not affect the rate of denervated human sinoatrial nodes. It can be inferred that atropine takes effects by suppressing ongoing vagal-cardiac nerve activities, and that these activities determines RRI fluctuations. The 16-day sts-107 space mission observed increased RRI both in the mean value and in the standard deviation (Figure 2), indicating that the vagal-cardiac activities were not attenuated under microgravity.
The initial increase of RRI and blood pressure (both systolic and diastolic) seems to contradict to conventional understanding that microgravity reduces cardiac output and stroke volumes. In fact, the fluid centralization early in microgravity increases the ventricle filling and the end-diastolic volume. Meanwhile the diastolic myocardial compliance becomes greater without gravitational stresses. These effects combine to increase the cardiac filling and blood pressure. However, this process is transient. As the brain progressively decreases the blood volume by excretion, the cardiac filling and blood pressure gradually decreases below the preflight level.

When the subjects were practicing exercise, the BRS value did not differ much before and during the flight. This observation is not in favor of the general hypothesis that exposure to microgravity leads to baroreflex deconditioning. Conversely, it implies that the response of baroreflex to mild physical workload is not subject to microgravity within a period of 2 weeks or so. In the situation of strenuous activities, other physiological mechanisms are likely to be triggered to influence the cardiovascular system and consequently intervene the effectiveness of baroreflex. For instance, another experiment performed during the STS-107 mission found that heavy physical exercises in space enhanced the metaboreflex mechanism, which may interfered with the baroreflex vagally mediated.

The effect of long-term exposure to microgravity, as revealed by the 9-month study on Mir, differs from the dynamic responses in short periods and is more in favor of hypotheses that are extrapolated from the current physiological knowledge. Reduced RRI fluctuation and the lowered transfer function between RRI and systolic pressures provide indirect evidence that both the vagal-cardiac nerve activity and the baroreflex sensitivity were reduced by prolonged exposure to micogravity.

The studies on cardiovascular adaptations during space flight are far from being conclusive yet. A few limitations still exists in the current knowledge and methodology. First, the small number of subjects under investigation do not well support any statistically significant observations. Second, the short term and long term responses of cardiovascular system to microgravity do not exhibit fully compatible results. Although 16-day inflight data and post flight data after 9 months’ flight have been available, there is still a gap for the period in between. This deficiency of data is cur-
rently compensated by experiments simulating microgravity on the ground, such as the prolonged bed rest or water immersion. But real space data are the ultimate means for scientists to judge incompatibilities.

6 Conclusions

This paper discusses the effects of microgravity on human bodies during space flights, with emphasis on the adaptation of the cardiovascular system. We discussed the short-term and long-term responses of cardiac baroreflex regulation under microgravity. A 16-day inflight study reported that the baroreflex activity was not impaired during the flight, but rather slightly enhanced in the early exposure to microgravity. This enhancement was attributed to the initial blood fluid centralization, which increased the volume filling and the cardiac output. Studies after a 9-month mission in space indicated that prolonged exposure to weightlessness reduced most cardiac variables and vagal-cardiac baroreflex activities probably due to loss of blood volume and changes of the autonomic nerve system. More studies are still needed to understand the effects of microgravity on the cardiovascular system of the human bodies.

References


