HIGHLIGHTED TOPIC | Analogs of Microgravity: Space Research without Leaving the Planet

Parabolic flight as a spaceflight analog

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Shelhamer M. Parabolic flight as a spaceflight analog. *J Appl Physiol* 120: 1442–1448, 2016. First published January 21, 2016; doi:10.1152/japplphysiol.01046.2015.—Ground-based analog facilities have had wide use in mimicking some of the features of spaceflight in a more-controlled and less-expensive manner. One such analog is parabolic flight, in which an aircraft flies repeated parabolic trajectories that provide short-duration periods of free fall (0 g) alternating with high-g pullout or recovery phases. Parabolic flight is unique in being able to provide true 0 g in a ground-based facility. Accordingly, it lends itself well to the investigation of specific areas of human spaceflight that can benefit from this capability, which predominantly includes neurovestibular effects, but also others such as human factors, locomotion, and medical procedures. Applications to research in artificial gravity and to effects likely to occur in upcoming commercial suborbital flights are also possible.

sensorimotor; pulmonary; motion sickness; vestibular; locomotion; spaceflight

PHYSICS OF THE ENVIRONMENT AND GENERAL DESCRIPTION

One of the first of the spaceflight analogs, parabolic flight, is unique in that it can provide true 0 g (weightlessness, or more properly free fall), albeit for only short periods at a time. It can also provide a suitable analog for a wide range of effects seen in orbital and deep-space flight: issues related to physiology, human factors, operational training, and procedures. This short review will concentrate on parabolic flight as an analog for the effects on humans of spaceflight and on its applicability as a training environment. Many studies have used parabolic flight as a general physiological stimulus, for example to induce motion sickness or as a means to investigate other aspects of physiological function. These are not considered here unless they have a clear connection to spaceflight.

Several terms are used to denote the gravitational circumstances of spaceflight: weightlessness, zero g or 0 g, microgravity, free fall, and others. Several other terms for were used in early published articles, such as gravity-free state, null-gravity state, and subgravity (6, 34, 43). (These early publications also show that parabolic flight predates human spaceflight and that the need to study the effects of 0 g was recognized well before even the first artificial satellite was launched in 1957.) It should be recognized that a spacecraft in orbit is not truly in "zero gravity," or it would not be in orbit; it clearly is subject to gravitational force. Likewise, a parabolic-flight aircraft and its occupants are not truly in zero gravity or they would not return to Earth. In each case,

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the proper description is one of free fall, which is continuous in the case of orbital flight and intermittent in the case of parabolic flight. For a spacecraft in deep space and not in orbit, "zero g" or "microgravity" might be a more appropriate descriptor. For the purposes of this review, the term "0 g" is used to denote all of these situations, with the understanding that reference is made to the net gravitoinertial force on the occupants during the periods of time under consideration.

Probably the biggest advantage of parabolic flight as an analog, apart from true free fall, is the ready access for investigators and subjects. Perhaps the greatest disadvantage is the fact that 0 g phases (or other hypo-g phases) are interspersed with hyper-g phases, which can present a substantial confound. Another disadvantage is that the 0 g periods are very brief—on the order of 25 s each. This calls into question the applicability as an analog for the long-duration missions that are now being planned by a number of government space agencies, because significant adaptive and compensatory effects take place over time periods much greater than those available in parabolic flight. Thus the usefulness is not currently as broad as it once was, when human spaceflights were much shorter (days or weeks). Nevertheless, there are still cases in which the short phases of 0 g in parabolic flight have benefit and applicability for long-duration flights and there are also cases of applicability to shorter flights such as those planned by commercial operators.

There are some specific areas in which parabolic flight is particularly useful:

- Where incremental and intermediate g levels are of use;
- Cases in which alternating *g* levels (usually a nuisance) might be put to good use;

- When investigators must fly along with the experiment to operate the experimental apparatus, monitor the results, or oversee the safety and comfort of the human subject. This also enables the ability to, when necessary, make immediate changes to experiment procedures based on results as they are obtained;
- Investigation of phenomena with short time constants or where the effect under study can be built up over multiple repeated 0 g exposures.

Why a parabola? Consider an object in motion under the influence of a uniform gravity field and no other external forces (neglecting air resistance). An example is a ball tossed into the air. From the time the ball leaves the hand until it lands, its trajectory is a parabola. Why is this the case? The simplest answer is that a parabola is the second integral of a mathematical constant. If one desires a constant g level (constant acceleration along the vertical direction), then the second integral of that constant describes the motion of the object along the vertical direction. This second integral is a parabola. There are nuances to this description because of the aerodynamic maneuvers necessary to maintain the flight profile and keep the aircraft in the proper flight regimen (40).

NEUROVESTIBULAR AND SENSORIMOTOR FUNCTION

It is likely that the largest number of parabolic-flight investigations have been in the area of neurovestibular function. This is partly because of experience in the Apollo program of incidences of motion sickness in space (38) and the recognition that this could pose an operational problem during flights of the US space shuttle starting in the 1980s (22). This led to a substantial interest in, and body of work related to, space motion sickness (SMS), more broadly known as space adaptation syndrome (SAS). The majority of studies in this area fall into the overlapping categories of spatial orientation and motion sickness, with several others addressing related issues of sensorimotor adaptation more generally.

Use of parabolic flight to mimic neurovestibular aspects of spaceflight can also be attributed to a simple observation: in both cases the subject is in a state of free fall and in neither case is this perceived, showing the importance of cues other than simply the vestibular otolith organs in generating perceptions of body orientation and motion in an altered-g environment (49). Subjects experiencing their first 0 g parabola also sometimes report a sensation of forward tumbling or pitching, as do some astronauts on first entering orbit, again demonstrating that at least some neurovestibular aspects of spaceflight can be reproduced in parabolic flight.

Space motion sickness—characteristics. In the area of space motion sickness, initial studies reproduced motion sickness in parabolic flight and determined some of its basic characteristics. This included finding that subjects lacking a functioning vestibular system would not develop motion sickness in parabolic flight (56), which confirmed the vestibular origin and connected SMS to terrestrial forms of motion sickness. This was followed by studies that extended this finding, showing that head movements in 0 g are provocative for motion sickness (46), whereas more recent studies have shown that fundamental properties of neurovestibular function such as velocity storage (perseveration of vestibularly driven eye movements after cessation of motion) can be related to susceptibility

(30). This is an example where the parabolic-flight model, developed for investigating spaceflight phenomena, can be of more general use in understanding the underlying physiology.

Space motion sickness—predicting susceptibility. Naturally there has been great interest in using parabolic flight to predict individual susceptibility to space motion sickness, as a tool for astronaut screening or assignment of mission roles (37).

There is little or no correlation between susceptibility to motion sickness in parabolic flight and in orbital flight (58). This is a major problem and calls into question the relevance of parabolic flight as an analog for this aspect of neurovestibular function. There is, however, one aspect of spaceflight that is apparently expressed in the short durations of the 0 g phases of parabolic flight and which might enable prediction of space-based motion sickness. This is the phenomenon of otolith asymmetry, related to tilt-translation interpretation. During the g-level changes of parabolic flight there are changes in torsional eye position (17). These changes can be markedly asymmetric (53, 54) and are on the order of 1 degree. This change in torsional alignment may be due to loss of compensation for otolith asymmetry in unusual g environments; on earth, the nervous system presumably compensates for natural asymmetries (e.g., unequal otoconial mass) in otolith properties (79), but in other than 1 g this compensation is inappropriate and produces torsional misalignment. A similar disconjugate change has been found during spaceflight (28), persisting throughout flights up to 180 days and for many days after flight. Torsional offsets seen in parabolic flight have been proposed as a predictive test for space motion sickness (26, 53). Motion sickness in parabolic flight has likewise been correlated with differences in ocular counterrolling with tilts to the right and left (27, 48); this is intriguing because it implies a link between motion sickness susceptibility in parabolic flight and in spaceflight, whereas other studies have not been able to establish this connection. This line of investigation shows some promise and deserves to be pursued, although as noted it is troubling that there is no correlation of sickness in parabolic flight to actual space sickness, which calls into question its validity as an analog for this use.

Spatial orientation. Closely related to the problem of motion sickness in spaceflight is that of spatial disorientation due to confusing vestibular signals as a result of altered g level. There are clear operational concerns that might arise as a consequence, especially during periods when the g level is changing, which will also be the times when peak human performance would typically be necessary (e.g., piloted planetary landing after a long period of 0 g). This is also an area in which research results can provide information on fundamental mechanisms of sensory signal processing [e.g., the role of the various otolith organs (23)] relevant also to terrestrial physiology and medicine.

Following early studies on motion sickness and orientation were those that investigated the role of tactile and proprioceptive cues in spatial orientation and perception of body position in $0\ g$. Theoretical considerations would suggest that, when static vestibular signals are difficult to interpret because of lack of a constant g vector, other sensory information would take on a more prominent role in providing orientation information. Subsequent studies verified this for somatosensory cues (44,

45) as well as visual cues (see below). There is, for example, a loss of awareness of body orientation in 0 g but recovery of the sense of "down" when touch and pressure cues are applied (49). These cues also influence perceived motion during recumbent rotation in 0 g in parabolic flight (50), showing that they take on increased importance when static vestibular cues are unreliable. Deep knee bends in hyper-g (1.8 g) in parabolic flight, in those adapted to 1 g, provoke a similar percept of the floor moving up to meet them, as do astronauts when doing the same after orbital flight (47).

These and similar results are nicely summarized: "Human spatial orientation and oculomotor control are under multimodal influence. It is not possible in the normal animal to stimulate differentially the vestibular receptors without activating other receptor systems whose activity may have a profound influence on postural control and experienced orientation. Many patterns of behavior and response that have been attributed solely to vestibular function are actually dependent wholly or in part on touch, kinesthetic, and proprioceptive stimulation" (44). Systematic manipulation of *g* level, as in parabolic flight, provides an excellent tool with which to explore these multimodal influences.

Visual orientation cues. Another aspect of multisensory reorganization that occurs in spaceflight is the dominance of more reliable visual cues for orientation, relative to lessreliable static otolith cues. This was found in orbital flights of the ESA Spacelab module in the US Space Shuttle: the visually induced sense of self motion induced by a moving field in the periphery ("vection") is stronger in 0 g than on the ground where the gravity vector provides a conflict to the perception of head-over-heels rotation (83). This perception is reduced by static tactile cues, both in orbital and parabolic flights. The findings have been further confirmed by showing a rapid enhancement of visual cues for orientation in 0 g parabolic flight (18). This is another example where the 0 g phase of parabolic flight can reproduce an effect seen in orbital flight; findings such as this help to define the envelope in which parabolic flight can serve as a spaceflight analog.

Visual orientation illusions. A visual reorientation illusion (VRI) is defined as the phenomenon of a person in an altered g level who feels right side up but has a perception that the surroundings have suddenly changed orientation, so that for example if the feet are toward the ceiling the ceiling is suddenly perceived to be the floor. Astronauts in flight and participants in parabolic flight who experience this phenomenon report that it is "far more compelling than when simply viewing a photograph" that mimics the reorientation (59). Again, a similarity of effect between parabolic and spaceflight establishes the legitimacy of this setting as an analog for vestibular effects.

Neural substrate. The neural substrate for some of the illusions of spatial orientation reported by astronauts in orbital flight (59) has been explored with recordings of rat head-direction cells in parabolic flight (74). In this case, direction-specificity of the cells was absent with the animal on a ceiling or vertical wall in 0 g. There was an occasional firing burst when the rat was on the ceiling, with the head oriented "in directions that were flipped relative to the long axis of symmetry of the chamber compared with the cell's preferred firing direction on the floor." This might provide the neural substrate

for a visual reorientation illusion in 0 g. It is also a good example of a translational study using an animal model in parabolic flight to provide insight into known phenomena experienced by humans in spaceflight.

SENSORIMOTOR ADAPTATION

Context-specific adaptation. One area of work that explicitly makes use of the alternating g levels of parabolic flight is that of contextual adaptation. By this is meant the ability to attain and store two different adapted states, each associated with a context cue, such that the context cue brings into play the associated adapted state. As an example, it has been shown that saccadic eye movements can have two different gains (amplitude of primary saccade in response to a target displacement of a given size), each gain associated with a different g level in parabolic flight. This is true contextual adaptation, because, normally, g level should have no effect on saccade gain (71, 72). This raises the possibility that contextual adaptation might be used to advantage in training procedures or in adapting sensorimotor behaviors that are relevant to spaceflight, where the training or adaptation can take place in a short-duration flight in 0 g and be recalled later on a long-duration flight as needed. An intriguing result in this regard is that one subject in the studies above showed contextual saccade adaptation after a set of parabolic flights, which was retained over an intervening period of 8 mo before a second set of flights was undertaken. Eight months is the approximate time for a journey to the vicinity of Mars under the most likely scenarios, and so this result holds promise for contextual adaptive retention for these missions.

LOCOMOTION IN NONTERRESTRIAL G LEVELS

Locomotion on nonterrestrial surfaces (moon, Mars, etc.) is different from that on Earth. This results from differences in g loading, suit mobility, energy conservation, and surface composition and friction. The effects can be seen in video footage from the Apollo missions, where astronauts adopt a loping "gallop" type of gait. Investigations of the most efficient gait, energy consumption, and suit designs can be fruitfully performed in the different g levels that are available in parabolic flight, using it as a planetary rather than a 0 g analog, and this is another unique benefit of parabolic flight. The biomechanics of exercise countermeasures, both treadmill running and resistive exercise, are also well suited for evaluation during parabolic flight. This work has a long history going back to the Apollo program (52, 69) and continues to the present day (25) and now includes simulations of destinations other than the moon, such as Mars (16). Notably, there are considerable differences between locomotion in parabolic flight and in a horizontal-suspension system used to simulate reduced gravity (24), which speaks to the higher fidelity of parabolic flight for this type of work.

CARDIOVASCULAR FUNCTION AND FLUID SHIFTS

A great many studies on cardiovascular function have been carried out in parabolic flight. Not all of them relate to effects seen in actual spaceflight (1, 2), because some effects have time courses longer than the $0\,g$ phase of parabolic flight, such as a decrease in blood and interstitial fluid volumes. However, a surprising number of phenomena happen rapidly enough to be investigated in parabolic flight (3): vagal predominance and slowing of heart rate, baroreflex alterations (10, 66), and

pressure changes. Fluid shift toward the head and upper body, another well-known consequence of spaceflight, is also seen to some degree during parabolic flight (4, 57). On the other hand, heart volume initially increases in spaceflight [as also seen in parabolic flight (77)] but then decreases, and it is important to recognize this and other limitations of parabolic flight in terms of the different time courses of effects. It is difficult to draw clear conclusions for some of these phenomena, because there may be changes even over the course of the 20-30 s of a single 0 g phase [for example in motor sympathetic nerve activity (39)] related to the dynamics of fluid shifts and likely exacerbated by vestibular contributions.

Parabolic flight has also been useful in interpreting an unexpected finding in orbital spaceflight of an initial rapid drop in central venous pressure (CVP) on entering orbit (10). This was surprising because there is a decrease in CVP and increased heart chamber volumes, whereas cardiac filling and stroke volume remained high. Parabolic flight experiments helped to understand this when it was found (77) in the 0 g phases that CVP decreased and there was a concomitant but larger decrease in intrathoracic pressure so that the pressure across the cardiac wall (transmural pressure) actually increased. Pressure inside the heart increased more than that in the surrounding body space, associated with an increase in atrial diameter, and these mechanical effects are rapid.

An issue of great interest is the change in visual acuity seen in some astronauts after extended stays in space. This is hypothesized to be at least in part a consequence of headward fluid shift. Because it was not apparent until flights of extended duration (months), one might wonder if the short duration of 0 g in parabolic flight would be of any value in understanding its etiology. In parabolic flight, intracranial pressure (ICP) was measured directly in patients with catheters implanted for other diagnostic reasons. In 0 g, ICP is slightly less than when supine in 1 g (51). Because these vision changes are not seen in normal terrestrial life despite being supine for approximately one-third of the time, an elevated ICP per se might not be a precipitating cause of the visual impairments, but rather the prevailing value over time might be the key parameter. This again demonstrates a significant benefit of parabolic flight: the ability to perform research with subjects and procedures (implanted devices) that might pose an unacceptable risk in actual spaceflight.

Orthostatic intolerance is currently well controlled with countermeasures and external assistance upon return to Earth from long-durations missions to ISS. It is, however, a concern for conditions of unassisted egress. There is an increase in orthostatic intolerance after parabolic flight, which is associated with a decrease in total peripheral resistance (67). Orthostatic intolerance could again be an operational issue for commercial suborbital flights, and parabolic flight as an analog of these shorter flights with lesser-trained participants would be helpful in addressing this issue.

These studies demonstrate that, within limits, parabolic flight can be useful to explore findings seen in long space-flights. This may be surprising, because some overt effects are not apparent until spaceflights of several weeks or months. This of course does not mean that underlying mechanisms cannot be profitably investigated in parabolic flight.

OTHER HUMAN PHYSIOLOGY RESULTS RELEVANT TO SPACEFLIGHT

A great many studies have been performed in parabolic flight to investigate other physiological functions in humans, some of which are relevant to spaceflight. These are not included in this review if they do not reach a critical mass of studies that could be considered as having made use of parabolic flight as a spaceflight analog as opposed to using it simply to alter *g* level for basic investigations or to follow up on a specific spaceflight finding with a specific and limited parabolic-flight study. This is a subjective judgment as to whether any given body of work is extensive enough that there is an investigator community and set of established findings that relate parabolic flight and spaceflight findings in the associated field of study.

Pulmonary function. One area that does merit inclusion is that of pulmonary function. Although several studies have been performed in spaceflight using g level to understand basic mechanisms, the use of parabolic flight to understand better the clearance of particulate matter from the lungs is an application that merits special attention. Here, parabolic flight fills a special niche in providing a 0 g or hypo-g environment that can mimic spaceflight or time on a planetary surface while allowing for inhalation of particles that can be tracked to determine clearance rates in a safer and more controlled setting than orbital flight. Thus the ability to provide intermediate g levels and safety monitoring uniquely qualify parabolic flight for this application, which is a spaceflight analog because clearance of particulates may be an issue during planetary exploration, depending on surface composition (21).

Gene expression. Intriguing results have been found for rapid changes in gene expression in a variety of organisms from plants (60) to humans (33). These findings are intriguing, and their implications are not fully understood. In particular, relevance to long-duration flights, where there is time for compensatory mechanisms, might be limited. The interspersed periods of hyper-*g* also lead to problems in interpretation. Nevertheless, findings of *g*-related changes in gene expression might help in understanding longer-term changes in immune function (20) and pathogen virulence (82) that have been found in long missions. The more immediate relevance, however, might be to understanding the effects of acute 0 *g* in suborbital flights and in the investigation of intermediate *g* levels for work on artificial gravity (both of which are discussed subsequently).

HUMAN FACTORS

The use by astronauts of three-dimensional spacecraft volume, body restraints to perform tasks (29, 78), and changes in movement strategies as a result of the lack of gravity can be studied only with high fidelity in a true $0\ g$ setting such as parabolic flight. Nevertheless, many of the anthropometric effects of $0\ g$ on the body are time dependent and express themselves fully only after extended time in space. Thus the use of parabolic flight as an analog for issues such as habitability, suit design, and vehicle configuration is limited.

As one example, in space the body takes on a neutral posture due to the natural muscle positions and lack of the need to fight gravity. This position resembles a partial crouch and is naturally assumed when working at most tasks that do not require a more specific posture to correspond to the work space.

Investigation of effects related to neutral body posture is promising in parabolic flight, because this posture can be seen in that setting. These studies are, however, limited because the posture is more erect in parabolic flight than in space, possibly because of imperfect $0\ g$ and anticipation of the hyper-g phase in parabolic flight (29, 75).

The use of spacecraft volume in three dimensions would seem to be an area for exploration in parabolic flight. At the least, vehicle and habitat designers might find it instructive to experience $0\,g$ in parabolic flight to free their thinking from the constraints of two dimensions (31) and to understand changes in movement kinematics and strategies (19, 75). One study of limb movements suggested that movement variability might be due to difference in cognitive demand in flight and resulting variations in processing capacity available for adaptation. In this case, parabolic flight might provide a better means of controlling this variable (9). Studies of how reaching, for example, might be altered in different g levels (80) and the issue of ergonomics more generally in the design of workstations (81) are also valuable avenues of work that benefit from true $0\,g$.

DEVELOPMENT AND TESTING OF SPACEFLIGHT MEDICAL PROCEDURES

Astronaut crews on future long-distance, long-duration flights may be called upon to perform medical procedures of various kinds. A great many studies on medical procedures and surgery have been performed in parabolic flight (14). Some aspects examined include CPR (5, 63, 64), imaging (predominantly ultrasound) (55, 65), surgery (61), airway management and tracheal intubation (32, 42), endoscopic procedures (12), in-flight apparatus (36), advanced capabilities such as robotically aided procedures (35), and others (65, 73). Animal surgery has also been performed for research investigations with success (13). Although parabolic flight might provide 0 g phases that are too brief to practice or develop the corresponding procedures in full, there are some component tasks and skills that might benefit from such training. A few problems specific to medical and surgical procedures in a weightless environment that have been studied in parabolic flight are worth noting: control of fluids (15), changes in fine motor control (62), and restraint of instruments, patient, and physician (11).

It is conceivable that suborbital spaceflights would be more suitable for this application (see below) given the longer period of near-constant $0\ g$. The repetitions of $0\ g$ available in parabolic flight, however, allow for repetition and refinement of approaches. A combined effort, with initial work in parabolic flight and later verification in suborbital flight, might be the best available strategy.

FUTURE PROSPECTS

Human spaceflight continues to expand. NASA and other government space programs are developing ambitious plans for future expeditions to the vicinity of Mars, to return to the moon, and to establish a permanent presence in low Earth orbit (LEO). Commercial spaceflights will also come into play soon, with flight to ISS to support its mission, suborbital spaceflights for recreation and research, and eventual orbital flights for the

same (nongovernment) participants. In each of these cases, parabolic flights have a role to play as an analog.

Artificial gravity. In the case of extended flights to far-off destinations, artificial gravity might be implemented as a countermeasure to an array of physiological deficits that arise during long stays in a $0\ g$ environment. Here, parabolic flight is uniquely suited in that it can readily provide a variety of g levels intermediate between 0 and $1\ g$. This will be critical in helping to determine the necessary g levels to be implemented in an eventual artificial gravity spacecraft. A range of experimental models will be useful here; in particular it should be noted that plants have demonstrated very rapid changes in gene expression during the short periods of $0\ g$ in parabolic flight (see above).

Suborbital spaceflights. Suborbital flights will soon be available to a very broad range of individuals (70, 76). Given the cost of these flights to the individual and the limited time in which to perform research during the free-fall phase, it would be most unfortunate if participants' first exposure to 0 g and gtransitions was during the suborbital flight itself. Hence, if nothing else, parabolic flight can provide a training ground and stepping stone for those intending to participate in suborbital flights, especially for dealing with g transitions. As an example, there is an increased release of stress hormones in parabolic flight, likely due to a confluence of factors, that might be relevant to suborbital flights (68). Extensive studies with centrifugation have been used to help prepare and screen participants for these flights in terms of tolerance to the hyper-g phases (7, 8), whereas the 0 g phase has received relatively less attention. An intriguing possibility is to use parabolic flight to predict who might have neurovestibular problems (motion sickness and disorientation) in suborbital flight. This would revisit the earlier NASA use of parabolic flights in an attempt to predict susceptibility in orbital flight, as noted previously. However, parabolic flight and suborbital flight have more in common (predominance of g transitions) than do parabolic flight and orbital flight, and this endeavor might be more successful now than previously (41). This would make use of parabolic flight as an analog of suborbital flight.

Summary. In all cases mentioned, it is the author's opinion that the potential of parabolic flight for the development and testing of countermeasures to the debilitating effects of space-flight is significantly underutilized. The possibilities are especially promising for commercial suborbital flight but also for emulation of aspects relevant to long-duration exploration flights in the areas of artificial gravity and procedures training. Because of the short duration of 0 g exposure and the intervening hyper-g phases, a challenge remains in identifying more areas of connection between parabolic flight and spaceflight, where the unique qualities of the former can be used to good advantage to assist the latter.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: M.S. interpreted results of experiments; M.S. drafted manuscript; M.S. edited and revised manuscript; M.S. approved final version of manuscript.

REFERENCES

- Antonutto G, Di Prampero PE. Cardiovascular deconditioning in microgravity: some possible countermeasures. Eur J Appl Physiol 90: 283– 291, 2003.
- Aubert AE, Beckers F, Verheyden B. Cardiovascular function and basics of physiology in microgravity. Acta Cardiol 60: 129–151, 2005.
- Aubert AE, Pletser V, Beckers F, Verheyden B. Cardiovascular responses during gravity changes induced by parabolic flights. ESA Bull 119: 30–38. 2004.
- Bailliart O, Capderou A, Cholley BP, Kays C, Rivière D, Téchoueyres P, Lachaud JL, Vaïda P. Changes in lower limb volume in humans during parabolic flight. J Appl Physiol 85: 2100–2105, 1998.
- Barratt M, Billica R. Delivery of cardiopulmonary resuscitation in the microgravity environment (Conference Paper). Aerospace Medical Association 63rd Annual Scientific Meeting, 1992.
- Beckh H. Subgravity experiments with humans and animals during the dive and parabolic flight. J Aviat Med 25: 335, 1954.
- Blue RS, Pattarini JM, Reyes DP, Mulcahy RA, Garbino A, Mathers CH, Vardiman JL, Castleberry TL, Vanderploeg JM. Tolerance of centrifuge-simulated suborbital spaceflight by medical condition. *Aviat Space Environ Med* 85: 721–729, 2014.
- Blue RS, Riccitello JM, Tizard J, Hamilton RJ, Vanderploeg JM. Commercial spaceflight participant G-force tolerance during centrifugesimulated suborbital flight. Aviat Space Environ Med 83: 929–934, 2012.
- Bock O. Problems of sensorimotor coordination in weightlessness. Brain Res Rev 28: 155–160, 1998.
- Buckey JC, Gaffney FA, Lane LD, Levine BD, Watenpaugh DE, Wright SJ, Yancy CW, Meyer DM, Blomqvist CG. Central venous pressure in space. *J Appl Physiol* 81: 19–25, 1996.
- Campbell MR, Dawson DL, Melton S, Hooker D, Cantu H. Surgical instrument restraint in weightlessness. Aviat Space Environ Med 72: 871–876, 2001.
- Campbell MR, Kirkpatrick AW, Billica RD, Johnston SL, Jennings R, Short D, Hamilton D, Dulchavsky SA. Endoscopic surgery in weightlessness. Surgical Endoscopy 15: 1413–1418, 2001.
- Campbell MR, Williams DR, Buckey JC, Kirkpatrick AW. Animal surgery during spaceflight on the Neurolab Shuttle mission. *Aviat Space Environ Med* 76: 589–593, 2005.
- Campbell MR, Billica RD. A review of microgravity surgical investigations. Aviat Space Environ Med 63: 524–528, 1992.
- Campbell MR, Billica RD, Johnston SL. Surgical bleeding in microgravity. Surg Gynecol Obstet 177: 121–125, 1993.
- Cavagna G, Willems P, Heglund N. Walking on Mars. *Nature* 393: 636–636, 1998.
- Cheung BS, Money KE, Howard IP. Human gaze instability during brief exposure to reduced gravity. J Vestib Res 4: 17–27, 1994.
- Cheung B, Howard I, Money K. Visually-induced tilt during parabolic flights. Exp Brain Res 81: 391–397, 1990.
- Clément G, Reschke MF. Posture, movement and locomotion. In: Neuroscience in Space. New York: Springer, 2008, p. 133–161.
- Crucian BE, Stowe RP, Pierson DL, Sams CF. Immune system dysregulation following short-vs long-duration spaceflight. Aviat Space Environ Med 79: 835–843, 2008.
- Darquenne C, Prisk GK. Deposition of inhaled particles in the human lung is more peripheral in lunar than in normal gravity. *Eur J Appl Physiol* 103: 687–695, 2008.
- Davis JR, Vanderploeg JM, Santy PA, Jennings RT, Stewart D. Space motion sickness during 24 flights of the space shuttle. *Aviat Space Environ Med* 59: 1185–1189, 1988.
- De Graaf B, Bos JE, Groen E. Saccular impact on ocular torsion. Brain Res Bull 40: 321–326, 1996.
- De Witt JK, Perusek GP, Lewandowski BE, Gilkey KM, Savina MC, Samorezov S, Edwards WB. Locomotion in simulated and real microgravity: horizontal suspension vs. parabolic flight. Aviat Space Environ Med 81: 1092–1099, 2010.
- De Witt JK, Edwards WB, Scott-Pandorf MM, Norcross JR, Gernhardt ML. The preferred walk to run transition speed in actual lunar gravity. *J Exp Biol* 217: 3200–3203, 2014.
- Diamond SG, Markham CH. Prediction of space motion sickness susceptibility by disconjugate eye torsion in parabolic flight. *Aviat Space Environ Med* 62: 201–205, 1991.

- Diamond SG, Markham CH. Ocular torsion in upright and tilted positions during hypo- and hypergravity of parabolic flight. *Aviat Space Environ Med* 59: 1158–1162, 1988.
- 28. **Diamond SG, Markham CH.** The effect of space missions on gravity-responsive torsional eye movements. *J Vestib Res* 8 217–231, 1998.
- Didier M. Restraints as an Important Aspect of Habitability (Conference Paper). SAE Technical Paper 911602, 1991.
- DiZio P, Lackner J. Motion sickness susceptibility in parabolic flight and velocity storage activity. Aviat Space Environ Med 62: 300–307, 1991.
- Ferraris S, Musso G, Didier M. Attached Pressurized Module (APM)
 Outfitting Complements to Fit the Crew and Their Needs. SAE Technical
 Paper 941588, 1994.
- 32. Groemer GE, Brimacombe J, Haas T, de Negueruela C, Soucek A, Thomsen M, Keller C. The feasibility of laryngoscope-guided tracheal intubation in microgravity during parabolic flight: a comparison of two techniques. *Anesth Anal* 101: 1533–1535, 2005.
- 33. Grosse J, Wehland M, Pietsch J, Ma X, Ulbrich C, Schulz H, Saar K, Hubner N, Hauslage J, Hemmersbach R, Braun M, van Loon J, Vagt N, Infanger M, Eilles C, Egli M, Richter P, Baltz T, Einspanier R, Sharbati S, Grimm D. Short-term weightlessness produced by parabolic flight maneuvers altered gene expression patterns in human endothelial cells. FASEB J 26: 639–655, 2012.
- Haber F, Heinz H. Possible methods of producing the gravity-free state for medical research. J Aviat Med 21: 395–400, 1950.
- Haidegger T, Sándor J, Benyó Z. Surgery in space: the future of robotic telesurgery. Surg Endosc 25: 681–690, 2011.
- Hayden JA, Pantalos GM, Burgess JE, Antaki JF. A hermetically sealed, fluid-filled surgical enclosure for microgravity. Aviat Space Environ Med 84: 1298–1303, 2013.
- 37. Homick J. Space motion sickness. Acta Astronaut 6: 1259-1272, 1979.
- Homick J, Miller EF. Apollo flight crew vestibular assessment. In: Biomedical Results of Apollo. NASA SP-368, 1975.
- Iwase S, Mano T, Cui J, Kitazawa H, Kamiya A, Miyazaki S, Sugiyama Y, Mukai C, Nagaoka S. Sympathetic outflow to muscle in humans during short periods of microgravity produced by parabolic flight. Am J Physiol Regul Integr Comp Physiol 277: R419–R426, 1999.
- Karmali F, Shelhamer M. The dynamics of parabolic flight: flight characteristics and passenger percepts. Acta Astronaut 63: 594–602, 2008.
- Karmali F, Shelhamer M. Neurovestibular considerations for sub-orbital space flight: a framework for future investigation. *J Vestib Res* 20: 31–43, 2010.
- Keller C, Brimacombe J, Giampalmo M, Kleinsasser A, Loeckinger A, Giampalmo G, Pühringer F. Airway management during spaceflight: a comparison of four airway devices in simulated microgravity. *Anesthesiology* 92: 1237–1241, 2000.
- Knight LA. An approach to the physiologic simulation of the null-gravity state. J Aviat Med 29: 283–286, 1958.
- 44. **Lackner JR.** Some contributions of touch, pressure and kinesthesis to human spatial orientation and oculomotor control. *Acta Astronaut* 8: 825–830, 1981.
- Lackner JR, DiZio P. Vestibular, proprioceptive, and haptic contributions to spatial orientation. *Annu Rev Psychol* 56: 115–147, 2005.
- Lackner JR, Graybiel A. Elicitation of motion sickness by head movements in the microgravity phase of parabolic flight maneuvers. *Aviat Space Environ Med* 55: 513–520, 1984.
- Lackner JR, Graybiel A. Illusions of postural, visual, and aircraft motion elicited by deep knee bends in the increased gravitoinertial force phase of parabolic flight. Exp Brain Res 44: 312–316, 1981.
- Lackner JR, Graybiel A, Johnson WH, Money KE. Asymmetric otolith function and increased susceptibility to motion sickness during exposure to variations in gravitoinertial acceleration level. *Aviat Space Environ Med* 58: 652–657, 1987.
- Lackner JR. Spatial orientation in weightless environments. *Perception* 21: 803–812, 1992.
- Lackner JR, Graybiel A. Parabolic flight: loss of sense of orientation. Science 206: 1105–1108, 1979.
- Lawley J, Williams M, Petersen L, Zhang R, Whitworth T, Levine B. ICP during daily life in healthy adults: what does microgravity add to the mix? FASEB J 29: 990.10, 2015.
- Letko W, Spady A. Walking in simulated lunar gravity. In: Fourth Symposium on the Role of the Vestibular Organs in Space Exploration NASA SP-187, p. 347–351, 1970.
- Markham CH, Diamond SG. A predictive test for space motion sickness. *J Vestib Res* 3: 289–295, 1993.

- Markham CH, Diamond SG, Stoller DF. Parabolic flight reveals independent binocular control of otolith-induced eye torsion. *Arch Ital Biol* 138: 73–86, 2000.
- 55. Martin DS, South DA, Garcia KM, Arbeille P. Ultrasound in space. *Ultrasound Med Biol* 29: 1–12, 2003.
- Miller EF, Graybiel A, Kellogg RS, O'Donnell RD. Motion sickness susceptibility under weightless and hypergravity conditions generated by parabolic flight. Aerosp Med 40: 862–868, 1969.
- Mukai CN, Lathers CM, Charles JB, Bennett BS, Igarashi M, Patel S. Acute hemodynamic responses to weightlessness during parabolic flight. J Clin Pharmacol 31: 993–1000, 1991.
- Oman CM, Lichtenberg B, Money K, McCoy R. MIT/Canadian vestibular experiments on the Spacelab-1 mission: 4. Space motion sickness: symptoms, stimuli, and predictability. *Exp Brain Res* 64: 316–334, 1986.
- Oman C. Spatial orientation and navigation in microgravity. In: Spatial Processing in Navigation, Imagery and Perception. New York: Springer, 2007. p. 209–247.
- Paul A, Manak MS, Mayfield JD, Reyes MF, Gurley WB, Ferl RJ. Parabolic flight induces changes in gene expression patterns in Arabidopsis Thaliana. *Astrobiology* 11: 743–758, 2011.
- Rafiq A, Broderick TJ, Williams DR, Doarn CR, Jones JA, Merrell RC. Assessment of simulated surgical skills in parabolic microgravity. *Aviat Space Environ Med* 76: 385–391, 2005.
- 62. Rafiq A, Hummel R, Lavrentyev V, Derry W, Williams D, Merrell RC. Microgravity effects on fine motor skills: tying surgical knots during parabolic flight. Aviat Space Environ Med 77: 852–856, 2006.
- 63. Rehnberg L, Ashcroft A, Baers JH, Campos F, Cardoso RB, Velho R, Gehrke RD, Dias MKP, Baptista RR, Russomano T. Three methods of manual external chest compressions during microgravity simulation. *Aviat Space Environ Med* 85: 687–693, 2014.
- 64. Russomano T, Baers JH, Velho R, Cardoso RB, Ashcroft A, Rehnberg L, Gehrke RD, Dias MKP, Baptista RR. A comparison between the 2010 and 2005 basic life support guidelines during simulated hypogravity and microgravity. Extrem Physiol Med 2: 11, 2013.
- Sargsyan AE. Medical imaging. In: Principles of Clinical Medicine for Space Flight. New York: Springer, 2008, p. 181–207.
- 66. Schlegel TT, Benavides EW, Barker DC, Brown TE, Harm DL, DeSilva SJ, Low PA. Cardiovascular and Valsalva responses during parabolic flight. *J Appl Physiol* 85: 1957–1965, 1998.
- 67. Schlegel TT, Brown TE, Wood SJ, Benavides EW, Bondar RL, Stein F, Moradshahi P, Harm DL, Fritsch-Yelle JM, Low PA. Orthostatic intolerance and motion sickness after parabolic flight. *J Appl Physiol* 90: 67–82, 2001.
- 68. Schneider S, Brümmer V, Göbel S, Carnahan H, Dubrowski A, Strüder HK. Parabolic flight experience is related to increased release of stress hormones. Eur J Appl Physiol 100: 301–308, 2007.
- Shavelson R.J. Lunar gravity simulation and its effect on human performance. Hum Factors 10: 393

 –401, 1968.

- Shelhamer M. Life-sciences research opportunities in commercial suborbital space flight. Acta Astronaut 104: 432–437, 2014.
- Shelhamer M, Clendaniel RA, Roberts DC. Context-specific adaptation of saccade gain in parabolic flight. J Vestib Res 12: 211–221, 2002.
- Shelhamer M, Zee DS. Context-specific adaptation and its significance for neurovestibular problems of space flight. J Vestib Res 13: 345–362, 2003.
- Taddeo TA, Armstrong CW. Spaceflight medical systems. In: Principles of Clinical Medicine for Space Flight. New York: Springer, 2008, p. 69–100
- Taube JS, Stackman RW, Calton JL, Oman CM. Rat head direction cell responses in zero-gravity parabolic flight. *J Neurophysiol* 92: 2887– 2997, 2004.
- Tengwall R, Jackson J, Kimura T, Komenda S, Okada M, Preuschoft H. Human posture in zero gravity. *Curr Anthropol* 23: 657–666, 1982.
- 76. Vanderploeg J, Campbell M, Antuñano M, Bagian J, Bopp E, Carminati G, Charles J, Clague R, Clark J, Gedmark J, Jennings R, Masten D, McCormick M, McDonald V, McGinnis P, Michaud V, Murray M, Myers KJ, Parazynski S, Richard E, Scheuring R, Searfoss R, Snyder Q, Stepanek J, Stern A, Virre E, Wagner E. Suborbital commercial space flight crewmember medical issues. Aviat Space Environ Med 82: 475–484, 2011.
- Videbaek R, Norsk P. Atrial distension in humans during microgravity induced by parabolic flights. J Appl Physiol 83: 1862–1866, 1997.
- Vogler A. Design Study for an Astronaut's Workstation. SAE Technical Paper 2005-01-3050, 2005.
- von Baumgarten RJ, Thumler R. A model for vestibular function in altered gravitational states. *Life Sci Space Res* 17: 161–170, 1979.
- Whitmore M, Aldridge AM, Morris RB, Pandya AK, Wilmington RP, Jensen DG, Maidaxy JC. Integrating Microgravity Test Data with a Human Computer Reach Model (Conference Paper). In: Proceedings of the Human Factors and Ergonomics Society Annual Meeting 36: 1249– 1253, 1992.
- Whitmore M, Berman AH, Byerly D. Ergonomic evaluations of microgravity workstations. NASA CR-1996-201378, 1996.
- 82. Wilson JW, Ott CM, Honer zu Bentrup K, Ramamurthy R, Quick L, Porwollik S, Cheng P, McClelland M, Tsaprailis G, Radabaugh T, Hunt A, Fernandez D, Richter E, Shah M, Kilcoyne M, Joshi L, Nelman-Gonzalez M, Hing S, Parra M, Dumars P, Norwood K, Bober R, Devich J, Ruggles A, Goulart C, Rupert M, Stodieck L, Stafford P, Catella L, Schurr MJ, Buchanan K, Morici L, McCracken J, Allen P, Baker-Coleman C, Hammond T, Vogel J, Nelson R, Pierson DL, Stefanyshyn-Piper HM, Nickerson CA. Space flight alters bacterial gene expression and virulence and reveals a role for global regulator Hfq. Proc Natl Acad Sci USA 104: 16299–16304, 2007.
- Young L, Shelhamer M, Modestino S. MIT/Canadian vestibular experiments on the Spacelab-1 mission: 2. Visual vestibular tilt interaction in weightlessness. *Exp Brain Res* 64: 299–307, 1986.