What Happens to the Human Heart in Space?

– Parabolic Flights Provide Some Answers

André E. Aubert, Frank Beckers, Bart Verheyden
Laboratory of Experimental Cardiology, Gasthuisberg Hospital, KU Leuven, Belgium

Vladimir Pletser
Microgravity Payloads Division, ESA Directorate of Human Spaceflight, Research and Applications, ESTEC, Noordwijk, The Netherlands

Aircraft parabolic flights provide up to 20 seconds of reduced gravity repeatedly during ballistic flight manoeuvres. They are used to conduct short microgravity investigations in the physical- and life-sciences, to test instrumentation and to train astronauts for forthcoming space flights. As the only Earth-based facility for conducting investigations on humans in real weightlessness, their use is complementary to simulated weightlessness techniques, such as bed rest and water immersion, and therefore a valuable step in preparing for space missions. The real value of parabolic flights lies, however, in the verification tests that can be conducted prior to taking experiments into space, in order to improve their quality and success rate.

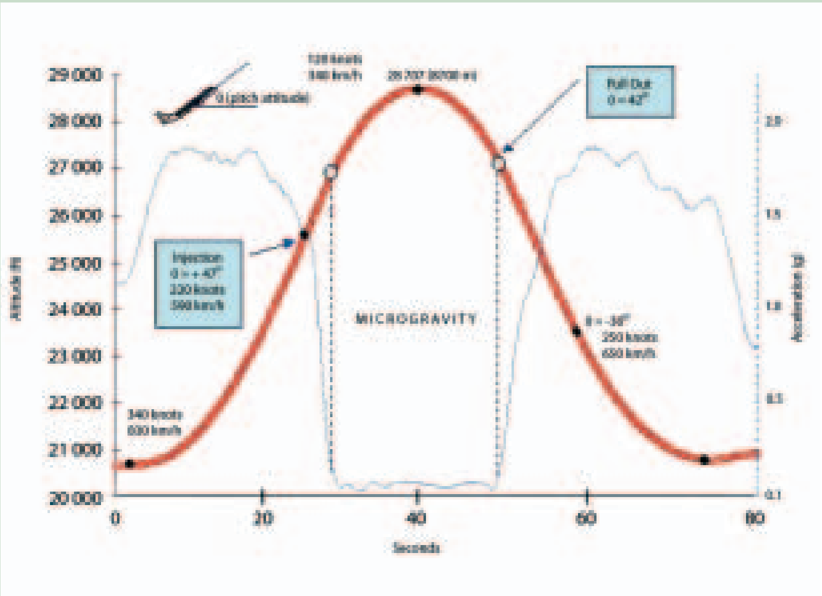
Introduction

ESA has organised thirty-seven aircraft parabolic-flight campaigns for microgravity research experiments since 1984, and seven purely for student-proposed experiments. During these flights, 446 experiments have been performed in the physical- and life-sciences, and technology domains. A total of 3462 parabolas have been flown, providing 19 hours 14 minutes of microgravity in 20 second 'slices', equivalent to making twelve and a half orbits of the Earth.

How Does the Airbus Generate 'Microgravity' ?

The microgravity environment is created by putting the aircraft through a series of carefully orchestrated flight manoeuvres (see figure):

- *From steady horizontal flight at 20 000 ft, the aircraft first climbs to an angle of 47° (pull-up) over a period of about 20 seconds, generating acceleration forces of between 1.8 and 2 g.*
- *At 25 000 ft, the engines are throttled back for about 20 to 25 seconds, generating ballistic free-fall, or 'microgravity' conditions inside the aircraft as it crests the parabola.*
- *The aircraft dives back down to an angle of 42° (pull-out), again generating accelerations of 1.8 to 2 g for approximately 20 seconds, before returning to steady horizontal flight at 20000 ft, and then repeating the whole manoeuvre.*



Flight profile of the Airbus A300 'Zero-G' during a parabola (in red) superposed on acceleration levels along the local vertical axis (Courtesy of Novespace)

The parabolas are flown over the Gulf of Biscay or the Mediterranean Sea. With a typical flight lasting about two and half hours, 30 parabolas are usually flown in sets of five, with two-minute intervals between parabolas and with four to five minutes between sets of parabolas. The intervals between parabolas can be arranged prior to the flight to give investigators sufficient time to change an experiment set-up.

Since 1997, the parabolas have been flown with the Airbus A300 'Zero-G', the largest aircraft being used for this type of research activity anywhere in the World. ESA has already organised 13 microgravity research campaigns on the Airbus, and 15 of the 160 experiments conducted have involved study of the human cardiovascular system.

Why Parabolic Flights?

The microgravity conditions that astronauts experience during space flight can pose severe challenges for the human physiology in general, and our cardiovascular system in particular. Extensive physiology experiments in space are needed to determine the long-term effects, but several practical considerations limit the possibilities, not least:

- the high experiment costs (approximately 20 kEuro per kilogram), including uploading the necessary equipment to the International Space Station (ISS);
- the limited access, especially now when the Space Shuttle fleet is still grounded and all manned travel to and from the ISS depends on just two annual Soyuz flights;
- the small number of available test subjects, with only two permanent crew members currently on the ISS;
- the limited crew time available, as they are also responsible for operational and maintenance tasks;
- no possibility of on-board intervention by the researchers themselves.

These limitations will persist as long as the number of flight opportunities does not increase, and until Europe's Columbus Laboratory, with its European Physiology Module, is launched and attached to the ISS.

There are only three sources of short-duration weightless conditions accessible on Earth: drop towers, providing about 5 seconds of free fall from a height of 110 m; sounding rockets, providing up to 13 minutes of microgravity; and aircraft parabolic flights, providing repetitive periods of 20 - 25 seconds of low-gravity conditions. The first two are not an option for life-science experiments on human subjects, leaving aircraft parabolic flights as the only realistic sub-orbital possibility.

Aircraft parabolic flights also have two major scientific advantages for physiology studies in that they make it possible both to investigate phenomena at different g-levels during successive repetitions of periods of 1, 2 and 0 g, and to study transient phenomena occurring during the changeover from high to low gravity and back again. On the technical side, they allow the early testing of equipment hardware in a microgravity environment, assessment of the safety aspects of an instrument's operation in microgravity, and the training of astronauts in instrument operation and experiment procedures.

Other key advantages of parabolic flights include: short turn-around times,

An early parabolic-flight cardiology experiment onboard NASA's KC-135 aircraft in which a free-floating bed was used to record a ballistocardiogram for the test subject and measure the expulsion of blood from the heart into the bodily circulation under different g-forces (photo NASA)

with typically just a few months between the experiment being proposed and performed; the low costs involved, as ESA provides the flight opportunity free of charge to investigators; the flexibility in experimental approach, as ground-laboratory instrumentation can often be used; the possibility of direct intervention by investigators onboard the aircraft during and between parabolas; and the possibility of modifying the experiment setup between flights.

Today, the Airbus A300 'Zero-G' parabolic flight programme is managed by the French company Novespace (commissioned to do so by CNES), with the technical maintenance and flight operations tasks being handled by the French company Sogerma and the 'Centre d'Essais en Vol' (French Test Flight Centre). Novespace is contracted by ESA to provide the aircraft for its parabolic flights, and to provide some support to the investigator teams and integrate their experiments at Novespace's facilities near Bordeaux-Mérignac airport.

Parabolic Flights and the Human Cardiovascular System

The human cardiovascular system consists of a dual pump: a right part consisting of an atrium and a ventricle whose purpose it is to circulate oxygen-depleted blood (venous blood) through the lungs to re-oxygenate it, and a left part consisting of an atrium and a ventricle to circulate that oxygen-enriched blood (arterial blood) around the body. Both ventricles have an entry valve (between atrium and ventricle) and an exit valve (between ventricle and circulatory blood vessels). From an engineering point of view, the heart can be likened to an electronically driven (by the brain) mechanical pump. It can be viewed as a closed-loop system, with a return loop providing information obtained from pressure sensors – so-called 'baro-receptors' – located at different points in the body, for instance in the carotid arteries that supply blood to the head and neck.

The human circulatory system is unique in that in the standing position the heart is located 130-160 cm above the ground, while the brain, which needs to be constantly 'irrigated' by blood, is 30-40 cm higher! Blood tends to accumulate in the organs that lie below the heart, and needs to be transported back to the heart against the force of gravity. A normal individual has five to six litres of blood, two thirds of which are below the heart. Should fluid leak out of the blood vessels located below the heart, it would accumulate within the tissues of the legs, producing oedema. The body has therefore had to develop oedema-preventing mechanisms, which in effect counteract gravity. Such considerations are of less importance when the human body is in the supine (lying down) position.

These physiological aspects have certain consequences for parabolic flights, during which the brief spell of microgravity is preceded by a period of hypergravity, and the body's orientation with respect to the direction of gravity will influence heart function and circulation. This is not the case during extended periods of microgravity, for instance during stays on the Space Station.

Hydrostatic effects also play a role. In a standing position, the carotid sinuses are 20-30 cm above the heart and therefore they measure a lower pressure than at heart level. At the onset of microgravity, this effect disappears and the baroreceptors will observe a higher pressure. In the absence of gravity, venous blood will rush to the right atrium when it is no longer pulled down by gravity into the compliant vessels of the legs and the abdomen, resulting in increased stroke volume. This in turn may lead to increased pressures in the right side of the heart and a distension of the right atrium (as shown by Norsk and collaborators). The return loop through the baroreceptors will lead to further autonomic nervous influences on the left heart, including the systemic blood pressure and heart rate.

The heart's pumping rate is adapted to prevailing physiological needs mostly through modulation by the body's autonomic nervous system (ANS). Many questions were originally asked about the role of the ANS on cardiovascular regulation during the short periods of microgravity on parabolic flights: Would there be any influence at all because of their short duration? What would be the influence of gravity transitions? Would body position matter? Would gravity transitions influence heart dimensions? Would equilibrium set in during such short time periods? What might be the optimal measuring techniques?

Speculative answers can be given to some of these questions, but others needed to be investigated experimentally. Cardiovascular variability can be expected during parabolic flights as the ANS can control the cardiovascular system within a few heart beats. However, since different phases of the parabolic flight profile last for no longer than 20-25 seconds, it is to be expected that ANS activity will also be influenced by conditions during previous phases, i.e. hypergravity. This activity will elicit changes directly in the cardiovascular system in terms of heart rate and blood pressure, and indirectly in the stroke volume (SV, volume of blood pumped with each heart beat) and cardiac output (CO, total blood volume pumped by the heart in 1 minute). The system can therefore be characterised by two easily measurable parameters: the electrocardiogram (ECG) to determine heart rate (HR), and blood pressure. Sometimes the breathing rate, or more general respiratory function, is also determined. Haemodynamic parameters (SV and CO) can be computed indirectly from the blood pressure, and the cardiac output is the product of the stroke volume

Cardiovascular Experiments Flown on the Airbus A300 'Zero-G' Aircraft

Investigation of cardiovascular haemodynamics during changing gravitational stresses and parabolic flight
J. Watkins, Univ. of Wales, UK; 24th ESA Campaign, October 1997

Arterial pressure in microgravity
B. Pump, DAMEC, Copenhagen, DK; 25th ESA Campaign, October 1998

Effect of Lower Body Negative Pressure (LBNP) on vectocardiography, electrocardiography, and haemodynamic parameters in humans
P. Vaïda, Univ. Bordeaux 2, F; G. Miserocchi, Univ. Milan, I; 26th ESA Campaign, June 1999

Advanced Respiratory Monitoring System (ARMS): does weightlessness induce peripheral vasodilatation?
P. Norsk & R. Videbaek, DAMEC, Copenhagen, DK, CNES Camp., part of 27th ESA Campaign, November 1999

Otolithic control of the cardiovascular system during parabolic flights
P. Denise & H. Normand, Fac. Médecine Caen, F; P. Arbeille, CHU Trousseau, Tours, F; 27th ESA Campaign, October 1999

An assessment of the feasibility and effectiveness of a method of performing cardiopulmonary resuscitation during microgravity
S. Evetts, School Biomedical Sciences, London, UK; T. Russomano, Univ. do Rio Grande do Sul, Porto Alegre, Brazil; 29th ESA Campaign, November 2000

Acute heart rate response to weightlessness conditions during parabolic flight
A. Aubert, F. Beckers & D. Ramaekers, Univ. Leuven, B; 29th ESA Campaign, November 2000

Pulse transit time for the non-invasive determination of arterial wall properties
T. Dominique & P.F. Migeotte, Univ. Bruxelles, B.; 29th ESA Campaign, November 2000

Effect of the Lower Body Negative Pressure (LBNP) on the cardiac electrical activity and the hemodynamical parameters
P. Vaïda , Univ. Bordeaux 2, F; 30th ESA Campaign, May 2001

Does weightlessness induce peripheral vasodilatation?
P. Norsk, DAMEC, Copenhagen, DK; 30th ESA Campaign, May 2001; 31st ESA Campaign, October 2001

Imaging autonomic regulation during parabolic flight
M. Moser & D.M. Voica, Univ. Graz, Austria; A. Noordergraaf, Univ. Pennsylvania, USA; 31st ESA Campaign, October 2001

Acute cardiovascular response to weightlessness conditions during parabolic flights: parallelism with long-term microgravity in space
A. Aubert, B. Verheyden, F. Beckers & D. Ramaekers, Univ. Leuven, B; 32nd ESA Campaign, March 2002 ; 34th ESA Campaign, March 2003

Cardiovascular autonomic responsiveness to hemodynamic changes during parabolic flight: influence of respiration
A.E. Aubert, F. Beckers & B. Verheyden, Univ. Leuven, B; 36th ESA Campaign, March 2004

Dr P. Norsk monitors Dr B. Pump acting as the test subject for the measurement of arterial blood pressure during the 25th ESA Parabolic-Flight Campaign in October 1998

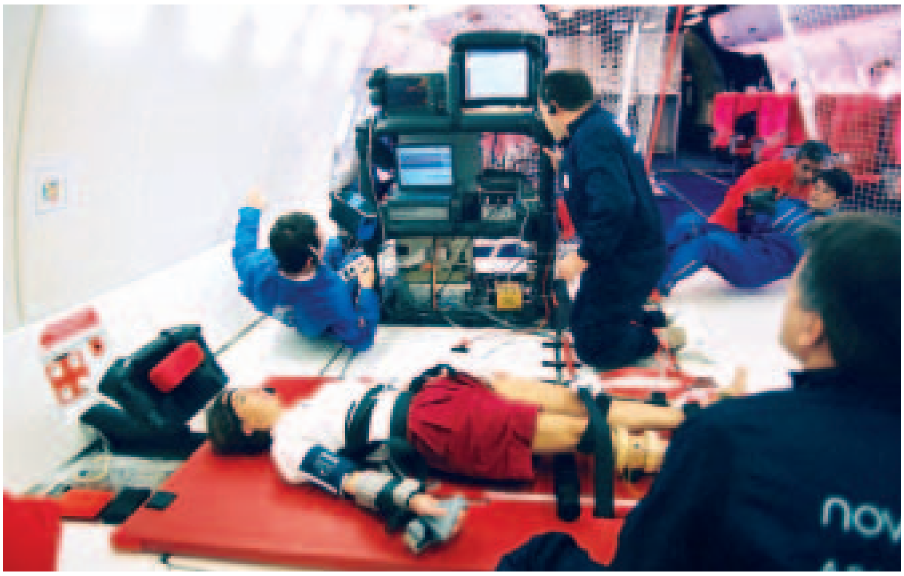
and heart rate. As an alternative to these indirect determinations, Doppler echo-soundings can be used to measure heart dimensions and ventricular and circulatory flow.

The Cardiovascular and Cardiopulmonary Experiments Conducted

Some of the most interesting experiments conducted during the early campaigns on the Airbus A300 'Zero-G' were those using the Advanced Respiratory Monitoring System (ARMS) (see photo). It provides the subject's breathing gas concentration and respiratory flow, blood pressure and an electrocardiogram (ECG). ARMS was flown in space for the first time on the Spacehab/STS-107 mission in January 2003, and was therefore lost in the tragic Columbia accident. Preparatory experiments for this mission had been conducted during several parabolic-flight campaigns in 1999. They provided us with a better understanding of the mechanisms of respiratory gas exchange and the mechanics of human breathing on Earth by measuring specific parameters in weightlessness, as well as providing valuable data on cardiovascular adaptation to microgravity.

One of the ARMS experiments, from Denmark, titled *Does weightlessness produce peripheral vasodilatation?*, tested a hypothesis that dilatation of the heart and the peripheral vascular system could be caused by weightlessness. Several physiological parameters were measured, including arterial pressure by photo-plethysmography, and cardiac output by rebreathing tracer gases (Freon 22 and SF6). The same group also showed that mean arterial pressure decreases during short-term weightlessness to below that when lying down in normal gravity, simultaneously with an increase in left atrial diameter (as measured by echo-cardiography) and an increase in transmural central venous pressure (determined with a catheter with a pressure sensor at the tip). They concluded that distension of the heart and associated central vessels during 0-g might induce the hypotensive effects through peripheral vasodilatation. It was also concluded that the supine position mimics better the effects of weightlessness on mean arterial pressure, heart rate and left atrial diameter.

The Franco-Italian experiment *Respiratory mechanics under 0g* studied pulmonary mechanics. Respiratory volumes and pressures were measured for subjects sitting in a whole-body pressure-



Measurement of various psychological parameters on an instrumented test subject in a supine position for the experiment of P. Denise and P. Arbeille during the 27th ESA Parabolic-Flight Campaign in October 1999

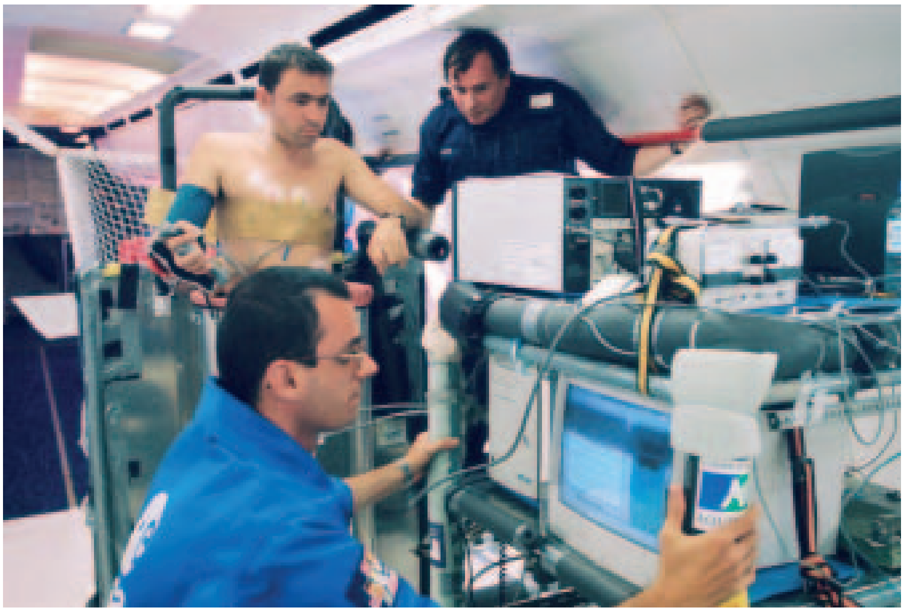
The ARMS equipment was used onboard the Airbus A300 'Zero-G' for several respiratory experiments in 1999. Here Prof. G.K. Prisk (Univ. California, San Diego, USA) is monitoring ESA astronaut Andre Kuipers acting as the test subject

tight caisson and breathing through a mouth-piece connected to external measuring equipment. Oesophageal pressures were also measured using a pressure balloon inserted through the nose into the subject's oesophagus. The data obtained complemented those from previous ground-based (anti-g suit, dry immersion, etc.) and space (ESA and CNES campaigns, and Spacelab D2 and EuroMir-95 missions) studies. It was shown that microgravity causes a decrease in lung and chest-wall recoil pressures as it removes most of the lung parenchyma and thorax distortion induced by gravity transitions and/or posture. Hypergravity does not greatly affect respiratory mechanics, suggesting that mechanical distortion of the organs involved is already close to a maximum in Earth's gravity.

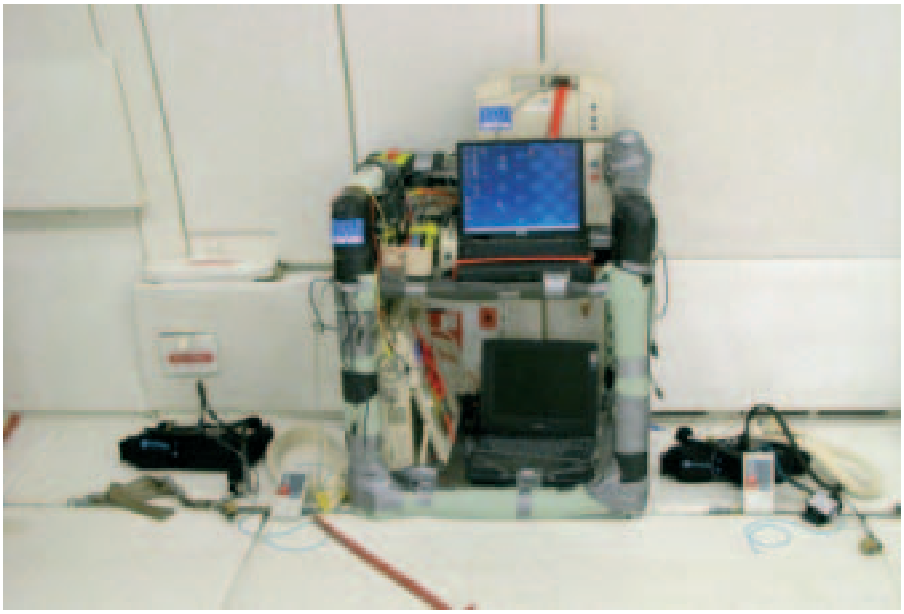
In an initial flight campaign, Aubert et al. studied the influence of position on heart-rate variability, determined from the ECG. They found a higher vagal modulation of the ANS in microgravity compared to 1g and hypergravity, for subjects in a standing position, and no significant differences in supine subjects, between different g-phases. These results were also confirmed by time-frequency analysis, which showed a higher vagal (high-frequency) component in a standing subject compared with a supine one. In later campaigns, they added blood-pressure and breathing measurements and also tested ISS astronauts during parabolic flights to compare results from ultra-short periods of weightlessness with those from a longer duration mission to the ISS. The high-frequency component (corresponding to vagal activity) and the low-frequency component (corresponding mostly to sympathetic activity) during microgravity on parabolic flights are comparable to the values seen during a ten-day mission to the ISS.

In order to stimulate cardiovascular responses, the test subjects often have to perform special exercises. One of the easiest consists of a voluntary elevation of intra-thoracic and intra-abdominal pressures provoked by blowing against pneumatic resistance (i.e. trying to blow with the mouth closed and nose pinched). During the manoeuvre, venous blood return to the heart is impeded, setting off a well-characterised sequence of positive and negative arterial pressure changes heavily influenced by the autonomic nervous system. As the duration of sustained pressure can be as short as 10 s, it is well-suited for use during weightlessness on parabolic flights.

Neck flexion (an anterior flexion of the neck by 70º, maintained by a solid support)



A test subject standing in the LBNP caisson while his heart rate and blood pressure are monitored for the experiment of Prof. P. Vaida during the 30th ESA Parabolic-Flight Campaign in May 2001



A typical instrumented rack for cardiovascular measurements as used by A.E. Aubert et al. during the 36th ESA Parabolic-Flight Campaign in March 2004 (photo A.E. Aubert)

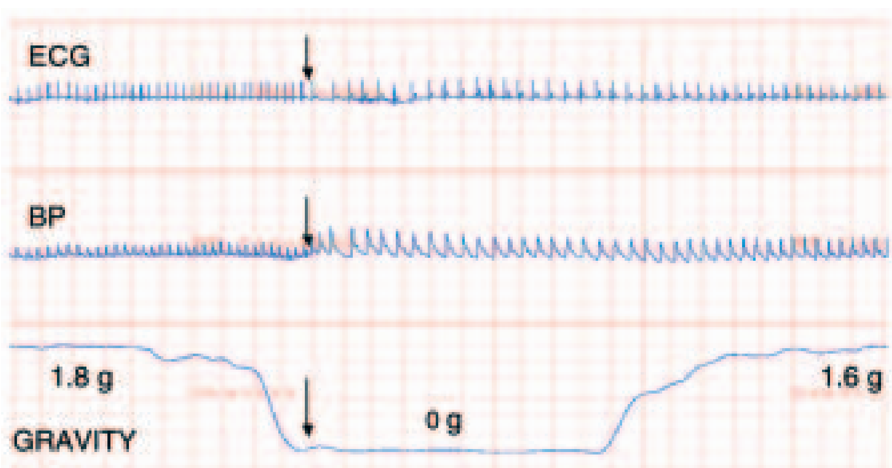
was used in the French experiment *Otolithic control of the cardiovascular system during parabolic flights,* to test the hypothesis that the otolithic receptors (part of the inner-ear balance system) affect the cardiovascular system during parabolic flights. Several physiological parameters - cerebral and femoral blood flow, vascular resistance, mean arterial pressure and heart rate - were measured for several subjects in a supine position and for two head positions (flexion and in line with the trunk). This could lead to a better understanding of the orthostatic intolerance and modifications of the peripheral blood flow and resistance response suffered by astronauts on their return to Earth. The experimenters concluded that in microgravity neck flexion, which stimulates only the neck muscle, induces larger vasoconstriction of the lower limbs and flow changes than in 1 g, where both the neck muscle and the otholiths are stimulated by the flexion. The peripheral vascular response associated with neck flexion could be mediated by the sympathetic nervous system.

Prof. Watkins' experiment used colour-Doppler echocardiography for direct imaging of the heart and major blood vessels in the seated, standing, and supine positions, in order to determine cardiac output and measure lower limb perfusion.

Lower Body Negative Pressure (LBNP) was exploited by Prof. P. Vaïda and his team, using tight-fitting 'trousers' around the lower body to create a negative pressure (compared to the surrounding pressure). In these experiments, LBNP was regulated at a pressure of -50 mmHg during the period of weightlessness. It was found that parasympathetic modulation of the heart by the ANS increased during microgravity, but was reversed while applying LBNP.

A Belgian team (T. Dominique and P.F. Migeotte) measured ECG, continuous finger blood pressure and respiration with an imposed breathing rate. During microgravity they found a slower heart rate, an increase in left ventricular ejection time (time between opening and closing of the aortic valve), a decrease in pre-ejection time (time delay between the contraction of the heart and the opening of the aortic valve), and a similar pulse transit time (time delay between the opening of the aortic valve and arrival of the pulse at the finger tip) compared to 1 g. They concluded that the heart's pre-load volume is increased in microgravity.

The likelihood of cardiopulmonary resuscitation (CPR) being performed successfully in space is seemingly very low, but not non-existent, as one reported incident has shown. During the second month of a four-month tour of duty on the Mir station, a cosmonaut was shown during Holter monitoring to have experienced an episode, lasting 14 beats, of non-sustained ventricular tachycardia. An ergonomic investigation was performed by Evetts et al. on the 29th ESA Parabolic Flight Campaign in November 2000 to study the effectiveness of different



From top to bottom: ECG, blood pressure and gravity level as recorded during a complete parabolic flight manoeuvre: hypergravity at 1.8 g. transition to microgravity and hypergravity at 1.6 g. A decrease in heart rate is apparent almost at the onset of microgravity (lengthening in distance between the successive peaks). This corresponds to increased vagal modulation of the heart rate. In the blood-pressure signal, there is a sudden increase in pulse pressure (difference between maximum and minimum pressure) at the onset of microgravity, indicating an immediate increase in stroke volume

A team from the School of Biomedical Services (London, UK) and the University do Rio Grande do Sul (Porto Alegre, Brazil) assess the best method of performing cardiopulmonary resuscitation (CPR) in weightlessness during the 29th ESA Parabolic-Flight Campaign in November 2000

resuscitation methods in microgravity, and two-rescuer CPR was deemed the most effective.

The Lessons Learned

The ESA parabolic-flight campaigns have provided a wealth of valuable results regarding the human cardiovascular response to space flight, including many that were totally unexpected beforehand. It has been shown, for example, that variations in heart size occur even during short periods of microgravity, and some results concerning heart rate and certain aspects of ANS modulation of the cardiovascular function are comparable to those seen during longer duration space flights.

The accompanying table, which is a compilation of results from several experiments, shows how the human heart behaves when it experiences changes in the gravitational conditions under which it is called upon to function. The results shown are a mean for 36 standing subjects, with an average control heart rate of 83 beats/minute, in five different experiments.

A general finding was that there was an initial increase in the heart rate of a standing subject at the beginning of the parabola, and decrease at the top. The differences were much less pronounced in supine subjects. Gender- and age-related studies have not been performed so far.

Conclusion

The unique and valuable experience acquired by ESA with the Airbus A300 'Zero-G' flights and the many earlier ones on NASA's KC-135, the Russian Ilyushin, and CNES's Caravelle aircraft, is reflected in the large number of physical- and life-sciences experiments successfully conducted in space since their inception, and the many peer-reviewed articles that have been published as result of these studies. ESA will continue to organise parabolic-flight campaigns for the European scientific and technical microgravity communities at a rate of two to three per year, with mixed payloads of physical- and life-sciences and technology experiments. Their frequency has recently been increased to compensate somewhat for the further reduced space-based possibilities since the grounding of the Shuttle.

ESA maintains a permanently open invitation to investigators to submit microgravity experiment proposals for its future parabolic-flight campaigns. In July, within the framework of its Outreach Programme, the Agency conducted its seventh parabolic-flight campaign for experiments proposed by students from European universities and research institutions, to promote awareness among 'tomorrow's scientists' of the attractions and benefits of conducting scientific research in a reduced-gravity environment. In addition, ESA has also decided to fly one to two experiments proposed by students as part of its regular parabolic-flight campaigns.

The flexibility of the experiment programming for the five to six campaigns that are flown with the Airbus A300 'Zero-G' aircraft every year is enhanced by an experiment-exchange agreement between ESA, CNES and DLR. The wide experience of Novespace, the company providing the preparation and logistics support for the Airbus campaigns, is another positive factor in the high success rate in terms of the technical preparation of the experiments proposed and flown. esa

Behaviour of the Human Heart Rate for Different Gravity Transitions

Gravitational transition (g)	Change in heart rate (beats/minute)
1 → 1.8	+13
1.8 → 0	-23
0 → 1.6	+19