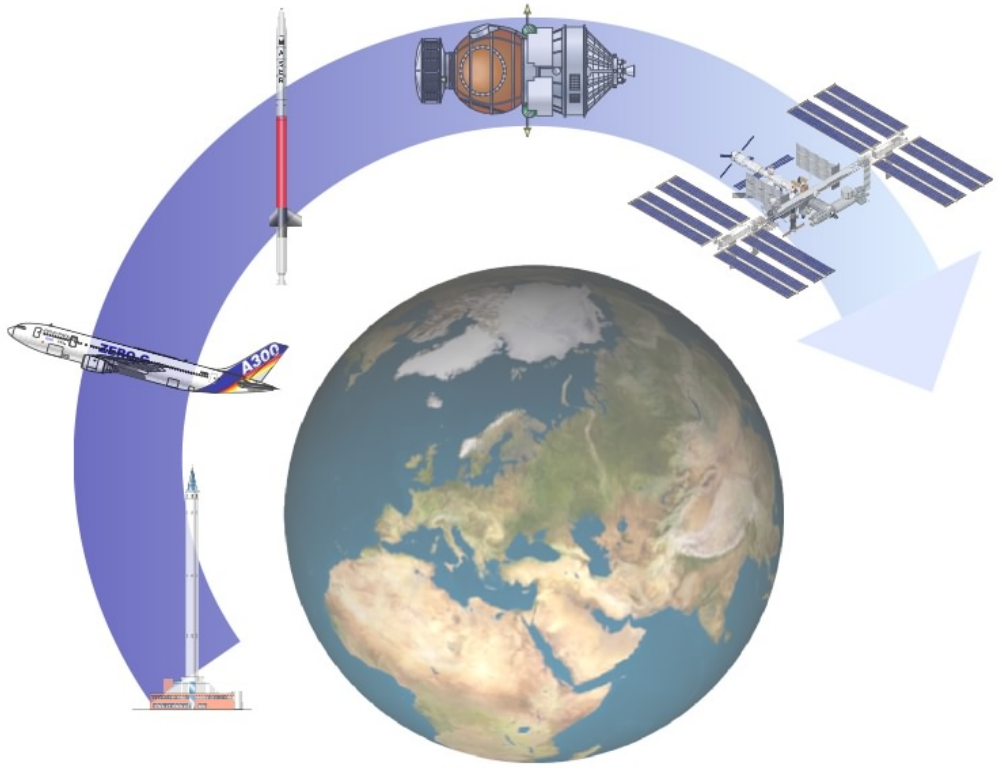
Summary Review of the European Space Agency's Low Gravity Experiments

Volume 5: ISS Increment 11



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PURPOSE OF DOCUMENT

The Summary Review of the European Space Agency's Low Gravity Experiments is intended to provide a concise, but clear, overview of the objectives and scientific results obtained from ESA sponsored low gravity research, executed on/in the five low gravity platforms and other ground based facilities supported by ESA.

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1 INTRODUCTION

1.1 Background to ESA Low Gravity Research

European involvement in low gravity research began approximately 30 years ago, with nationally funded programmes (in particular those of France and Germany) and US collaborations. Later, in January 1982, a European Space Agency (ESA) funded programme was initiated by the ESA Member States, who agreed to a small programme to which governments could contribute according to their interests and budgets. The first phase of this new ESA programme (Microgravity Programme: Phase-1) was established for the period 1982-1985. This allowed ESA to participate in the German Texus Sounding Rocket programme (later extended to include Swedish Maser Sounding Rockets) to perform short duration microgravity experiments. The Phase-1 programme also covered the development of a first set of multi-user experiment facilities to be flown on the Space Shuttle Spacelab and SpaceHab missions.

Since then, ESA has sponsored more than 2000 experiments, payloads and facilities, which have been integrated and operated on various types of low gravity platforms, including:

- Drop Towers;
- Parabolic Flights;
- Sounding Rockets;
- Retrievable Capsules;
- Space Shuttle;
- MIR Space Station;
- International Space Station.

1.2 The Five Major Low Gravity Platforms

This document mainly covers the research executed on/in the 5 major low gravity platforms currently supported by ESA, which are:

- the ZARM (Zentrum für Angewandte Raumfahrt Microgravitation) Drop Tower, located in Bremen, Germany, which was officially declared an ESA External Facility on 2 October 2003;
- the Novespace Airbus A-300 "Zero-g" aircraft based at the Bordeaux-Mérignac airport, which has been used by ESA since 1997;
- the four ESA supported sounding rockets (miniTexus, Texus, Maser and Maxus), which are launched from the Esrange base near Kiruna, Sweden;
- the Russian Foton retrievable capsule, an unmanned Earth-orbiting spacecraft offering microgravity and space exposure, that ESA has used since the early 1990's;
- the most complex platform currently accessible through ESA, the International Space Station (ISS).

Besides the five major low-gravity platforms presented above, ESA also supports access to specific facilities and environments on Earth that simulate low gravity and the confinement of long duration space missions. Extensive and timely use of the research capabilities offered by these facilities, will not only improve the preparation of spaceflight experiments, but will also increase the level of scientific knowledge of the influence of gravity and/or extraterrestrial environments on life, physical and interdisciplinary processes.

Specific ground facilities that simulate space and planetary conditions like climate, physical and psychological isolation, low gravity, extreme environments, high velocity impacts, etc., are available in a wide range of scientific disciplines. Recent examples of these are Long Term Bed Rest Studies (refer to the following web site http://www.spaceflight.esa.int/users/file.cfm?filename=miss-gbfac) and Antarctic Isolation Studies (see http://www.esa.int/esaCP/SEMOS4T1VED_index_0.html). Both types of studies are aimed at investigating the physiological and psychological problems that may arise in conditions of isolation and confinement, such as those that will be experienced during a long duration space mission.

More detailed information regarding the above-mentioned platforms/facilities and how to access them can be found in the ESA publication "European Users Guide to Low Gravity Platforms", which can be viewed at the following web site http://www.spaceflight.esa.int/guide. A hard copy of the Users Guide can also be requested from:

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1.3 Release and Structure of Summary Review Document

This Summary Review document will be released in separate volumes, where each individual volume will cover the research carried out during one or more campaigns (Drop Tower, Parabolic Flight, Sounding Rocket, Ground-based), missions (Foton) or increments (International Space Station). The document will be comprised of two main parts:

- Section 1 will provide general information and a background to ESA's low gravity research, including a summary of the Research Cornerstones.
- Section 2 and beyond will introduce the platform or facility being covered, before providing an experiment-per-experiment summary, broken down per research cornerstone, for each specific campaign, mission or increment.

1.4 Research Cornerstones

In 2000, ESA prepared a comprehensive Research Plan defining the scientific priorities in the life and physical sciences for a 5-year period, with a horizon of 10 years. The compilation of this Research Plan was initiated by a bottom-up analysis of all the research proposals received at that time by ESA. As a next step, ESA asked the European Science Foundation (ESF) to assess the research priorities in a dedicated user consultation meeting, which took place in Bischenberg, France in November 2000. At this meeting and in the subsequent ESF recommendations, the concept of Research Cornerstones was defined.

The Research Cornerstones describe areas of research where concerted efforts at the European level have already produced, or are promising to lead to, eminence if not a leading position on a global level. They provide therefore, an excellent basis for ensuring that new proposals will address issues that have been recognised as constituting a particular strength in Europe. A particular advantage of this will be that the research objectives of the ESA programme will be better harmonised with those of other research funding agencies or entities in Europe, leading to a more efficient and complete coverage of the research efforts involved. It will also further promote the teaming of research groups at European level, thus combining strengths and increasing European knowledge and competitiveness. Finally, it will allow ESA to streamline and optimise the available and future research infrastructure to sustain those objectives.

Already at Bischenberg it was identified that the Research Plan is by definition a living document. Research priorities may shift, new promising research fields may emerge, or new results taken into account. For that reason, it was envisaged that the process of user consultation should be repeated at regular intervals.

Following this, a second user consultation on Life and Physical Sciences in Space was organised again by ESF at Obernai, France in May 2004. On this occasion a larger number of scientists participated and more time was available to discuss the individual disciplines during two workshops. After this consultation ESF recommended

updated Research Cornerstones, which ESA and its advisory committees analysed. After a full investigation, ESA produced an updated Research Plan, in which also the new Research Cornerstones were defined.

It should be stressed, however, that the Research Cornerstones are **not** used as a selection criterion in the evaluation of research proposals. In other words, the final selection of projects is based on scientific quality, regardless of the research topic addressed. This, in the view of ESA, is the only way to ensure that promising new research is identified and pursued. The Research Cornerstones should therefore be seen as a guideline to potential users who wish to carry out research in the life and physical sciences on the ISS.

1.4.1 Life and Physical Sciences Research Cornerstones

The following tables summarise the updated Life and Physical Sciences Research Cornerstones defined in 2004 for the period 2005-2009.

Table 1-1: Fluid Physics Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Fluid and Interface Physics	Study of multiphase systems (their phase transitions and related dynamics), critical and supercritical fluids, granular materials, liquid-solid interface phenomena and complex fluid phases. Geophysical fluid flows.	Quantify heat transfer, mass exchange and chemical processes in multiphase systems and supercritical fluids; Measure diffusive processes in mixtures; Study the stability of foams and emulsions; Describe dynamic coupling in granular materials under vibration.	Develop reactors for supercritical oxidation of industrial contaminants; Develop high-efficiency heat exchangers; Improve reactor design in industrial plants; Design improved oil recovery techniques.
Combustion	Study combustion phenomena that are dominated on the ground by buoyancy convection.	Quantify fuel droplet and spray evaporation, autoignition and combustion processes; Detail the process of soot formation in flames and the conditions for flammability of solid fuels.	Improve efficiency of electrical power plants; Reduce emissions of engines; Fuel-efficient and safe spacecraft for human exploration; Improved flammability test procedures.

Table 1-2: Fundamental Physics Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Physics of Plasmas and Solid/Liquid Dust Particles	Understand the three dimensional behaviour of particles in complex plasmas and aggregation processes that require weightlessness.	Enhance theoretical description of complex plasmas, including self-ordering and phase transition phenomena; Improve modelling of the interaction of protoplanetesimals, their optical properties and of the behaviour of pollutants in the atmosphere.	Develop novel plasma coating techniques; Nucleation and growth of novel substances for solar cells and plasma screens; Improved modelling of Earth climate and environment.
Cold Atom Clocks, Matter Wave Interferometers and Bose-Einstein Condensates	Study properties and applications of cold atoms, including Bose-Einstein condensates.	Develop and operate a cold atom clock in space; Check limits of validity of theories of relativity and quantum electrodynamics.	Improved accuracy of absolute time measurements; Increased accuracy for navigation and geodesy systems.

Table 1-3: Material Sciences Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Thermophysical Properties of Fluids for Advanced Processes	Utilise the extended possibilities of containerless processing in space to measure critical properties of fluids for processes that are required as input parameters for adequately describing balances in volume phases and at interfaces.	High accuracy measurements of the properties of stable and metastable (undercooled) liquid metals.	Increase the reliability of numerical simulation and control of casting facilities in the metallurgical industry.
New Materials, Products and Processes	Understand the physics of solidification and crystal growth of metals, organic and inorganic materials and biological macromolecules.	Quantify the influence of the growth conditions on the homogeneity and the defects in crystals, including protein crystals; Enhance numerical models of the microstructure formation in metals and alloys.	Improve and validate models for predicting grain structures in industrial castings; Develop processes towards new metallurgical products; Improve efficiency of production of industrial crystals.

Table 1-4: Biology Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Molecular and Cell Biology	Study the impact of gravity at the cellular and molecular levels.	Study gene expression in an altered gravitational environment in relation to cellular phenomena; Improve understanding of the impact of gravity on signal transduction and the specific properties of cellular entities such as the membrane; Clarification of the role of mechanical forces including those derived from gravity in triggering proliferation, differentiation, apoptotic processes and tissue formation.	Provides the basis for other disciplines, including developmental biology, physiology, health science and biotechnology; Develop artificial functional tissues and targets for drugs screening; Depression of the immune system; Identify pharmacological substances for tissue regeneration; Develop bio-regenerative life support systems for human exploration missions; Develop novel microencapsulated drugs and cells.
Plant Biology	Understanding the impact of gravity on plant systems; Study mechanosensory elements involved in mechanisms of graviorientation and gravishaping.	Identify molecular and cellular elements of mechanosensory mechanisms and gravity-related signalling pathways; Study how gravity shapes plant morphology; Identify gene interactions important in the gravistimulus response chain.	Improvement of plant growth and mechanical properties of plants; Develop and improve biological life support systems; Provide the basis for biotechnological applications utilised on future long-term human spaceflight; Develop techniques for plant survival and growth in space.
Developmental Biology	Study the effect of gravity on whole-body developmental and reproductive processes.	Study altered gene expression in an altered gravitational environment; Study the impact of the cytoskeleton architecture on signal transduction e.g. functional genomics; Identify gravity-sensitive phases in multicellular organisms; Understand the effect of gravity on the development of the vestibular and sensori-motor systems in vertebrates.	Design pharmacological relevant substances for animal and human applications relevant to human development; Evaluation of the possible outcome of extraterrestrial colonisation attempts; Develop techniques and pharmacological substances for tissue regeneration.

Table 1-5: Physiology Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Integrative Gravitational Physiology	Explore, in an interdisciplinary way, systems that are sensitive to gravity, e.g. cardiovascular system, pulmonary system, nervous system, fluid-electrolyte homeostasis, skeletal system, immune system, etc.	Study cardiovascular control and regulation; Study the mechanisms for fluid regulation by the kidneys; Investigate the interaction of the vestibular system with other inputs relevant to locomotion and posture (e.g. vision, proprioception); Study effects of changes in load on muscle atrophy and plasticity; Understand and quantify bone mass turnover as a function of e.g. local blood perfusion and mechanical stress; Study the mechanisms of osteoporosis.	Improve techniques and devices for medical applications e.g. sports medicine; Improve rehabilitation after long-term incapacitation, particularly involving bed rest; Improve treatment of patients with decreased lung-function; Develop improved approaches for the treatment of neurological diseases; Improve means for diagnostics, prevention and treatment of osteoporosis, and reduce bone loss in astronauts for future long duration missions; Improve treatment of diseases like hypertension.
Non-Gravitational Physiology of Spaceflight	Explore the effects of the non-gravitational extreme environment of space, e.g. radiation, isolation, nutrition, confinement, noise, disruption of circadian rhythms, hypobaric conditions (e.g. EVA), etc.	Study effects of isolation, group dynamics, cultural differences, etc.; Study effects of radiation on DNA damage; Study close coupling between nutrition and health, e.g. testing new space foods; Investigate effects of dust inhalation on airway inflammation; Investigate possibilities of decompression sickness in connection with EVA.	Improve crew selection techniques for future long duration missions; Develop new nutritional methods for the improvement of health; Develop new protection measures for people exposed to radiation; Improve prevention and treatment for patients suffering from decompression sickness.
Countermeasures	Develop physiological, pharmacological, psychological, and mechanical countermeasures.	Understand the mechanisms leading to various problems such as: spatial disorientation (nausea, imbalance), orthostatic intolerance, bone loss and microarchitectural deterioration, muscle atrophy and weakness, cardiac atrophy, etc.	Develop improved approaches, treatment and countermeasures for a variety of Earth and space based disorders and maladies.

Table 1-6: Exobiology Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Origin, Evolution and Distribution of Life	Study the survivability of organisms under extreme conditions on Earth (extremophiles) and in space.	Investigate the contribution of space conditions, including radiation, to the formation of prebiotic molecules; Identify the conditions for survivability of micro-organisms from and in space, including planetary surfaces; Identify markers and tools to search for extinct and extant life.	Identify novel enzymes and bacteria from extreme physical and chemical environments with industrial application e.g. biocatalysis.

Table 1-7: Exploration Research Cornerstones

RESEARCH CORNERSTONES	DESCRIPTION	SCIENCE TARGETS	POTENTIAL APPLICATIONS
Human Planetary Exploration	Study novel aspect of human planetary expeditions.	Quantify radiation risk for human beings and understand the specific biological action of space radiation; Study effects of isolation in high-stress environments; Quantify needs for consumables during missions; Perform simulation tests on in-situ resource utilisation potential.	Develop advanced radiation sensors and countermeasure devices; Develop technology for telemedicine/telesurgery in remote areas; Develop protocols for handling stress effects; Develop methods for in-situ resource utilisation; Develop life-support systems for use in space and other isolated environments; Develop the technologies for identification and utilisation of in-situ resources.

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1.5 Erasmus Experiment Archive (EEA)

An important resource for low gravity research scientists and users is the Erasmus Experiment Archive (EEA), maintained by the Erasmus Centre (HME-UC). The EEA is a database of ESA funded or co-funded experiments covering a wide range of scientific areas, which were performed during missions and campaigns on/in various space platforms and microgravity ground-based facilities over the past 30 years. The archive is continuously being updated and as of July 2007, contained more than 2000 experiment records. The major items of information covered in the EEA include:

- Research cornerstone;
- Date of experiment;
- Mission name;
- Team members and institutes;
- List of publications/references;
- Experiment objectives;
- Experiment procedures;
- Experiment results;
- Attachments (figures, graphs, videos, etc.).

The EEA depends highly on the support provided by users; therefore users are encouraged to send inputs to the contact coordinates below, once they have executed an experiment. In fact, users who perform ESA funded experiments have the obligation to provide an abstract to the EEA. Failure to meet this obligation will be taken into account when deciding on new experiment opportunities/proposals from the user team in question.
Users are invited to visit the database, from which they can, among other things, obtain further information regarding experiments in their field of research already carried out in the past. The EEA web address is the following: http://www.spaceflight.esa.int/eea. For further details regarding the EEA, please contact the following by phone, fax, mail or e-mail:

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2 THE INTERNATIONAL SPACE STATION (ISS)

2.1 ESA Utilisation Rights and Additional Flight Opportunities

The National Aeronautics and Space Administration (NASA) provides the overall leadership of the ISS programme development and implementation, and together with Russia provides the major building blocks of the ISS. The European Space Agency (ESA), together with the Japan Aerospace Exploration Agency (JAXA) and the Canadian Space Agency (CSA) are providing additional elements, which significantly enhance the Space Station. The overall ISS utilisation rights are divided among the Partners, according to the elements and infrastructure they provide (e.g. Columbus Laboratory for ESA). The main principle is that each International Partner may utilise equipment and facilities in or on each other Partner's elements in accordance with their respective "utilisation rights". Those rights are defined in the Intergovernmental Agreement (Article 9) and the different Memoranda of Understanding signed by all of the Partners.

In return for its contribution to the ISS, ESA has a resource allocation of 51 % of the internal and external user accommodation of the Columbus Laboratory. Other allocation rights to ESA comprise 8.3 % of the total ISS utilisation resources and 8.3 % of the total crew time. Note that this excludes all of the Russian accommodations and resources, as this is retained by Russia for its own use.

In May 2001, ESA and the then Russian Aviation and Space Agency (Rosaviakosmos), now Roscosmos, signed a Framework Agreement for the provision of Russian ISS flight opportunities. The Agreement documents the principles, terms and conditions for the cooperation between ESA and Roscosmos concerning ISS operations and utilisation, through the provision by the latter of fare-paying ISS flight opportunities in the period 2001-2006, for members of the European Astronaut Corps. The actual commitment for a specific flight opportunity is entered by ESA upon signature of an ISS Flight Order Contract (IFOC) for a specific flight.
The Framework Agreement, establishes a solid and stable basis for the strategic planning of the European Astronaut Corps, and it represents an important step towards the further development of operational expertise of the ESA astronauts prior to the full European utilisation of the ISS with the launch of Columbus.

Two types of flight opportunities are considered under the Agreement as ISS flight opportunities:

- ISS "taxi flights" (this term is reported in the original agreement, but is no longer used), which are defined as short duration Soyuz flights to the ISS for the purpose of exchanging the ISS docked Soyuz, including a short duration stay (approximately 7-8 days) on-board the ISS;
- ISS increment flights, which are defined as ISS crew exchange flights, including a 3-6 months (one increment) stay on-board the ISS.

The assignment of back-up astronauts/cosmonauts for ISS flight opportunities, involving ESA astronauts, is agreed upon between ESA and Roscosmos for each flight.
On-board activities are not restricted to the mandatory system operations and maintenance activities, but also allow for the conduct of activities or experimental programmes in the interest of ESA and national organisations of the ESA Member States. The terms and conditions of such activities are agreed upon in each specific IFOC. The IFOC defines the terms and conditions specific to the implementation of an agreed ISS flight opportunity. Such terms and conditions take precedence over the terms and conditions defined in the Framework Agreement.

The following table (Table 2-1) summarises the Russian ISS flight opportunities that have thus far included an ESA astronaut on-board, following the signature of the Framework Agreement in May 2001.

Table 2-1: ESA Russian flight opportunities deriving from ESA/Roscosmos Framework Agreement (May 2001)

ISS MISSION	ESA MISSION NAME	VEHICLE ID	LAUNCH DATE	LANDING DATE	ESA ASTRONAUT	ASTRONAUT NATIONALITY
ISS 3S	Andromede	Soyuz TM-33	21/10/2001	31/10/2001	Claudie Haigneré	French
ISS 4S	Marco Polo	Soyuz TM-34	25/04/2002	05/05/2002	Roberto Vittori	Italian
ISS 5S	Odissea	Soyuz TMA-1	30/10/2002	10/11/2002	Frank De Winne	Belgian
ISS 7S	Cervantes	Soyuz TMA-3	18/10/2003	28/10/2003	Pedro Duque	Spanish
ISS 8S	DELTA	Soyuz TMA-4	19/04/2004	30/04/2004	Andre Kuipers	Dutch
ISS 10S	Eneide	Soyuz TMA-6	15/04/2005	25/04/2005	Roberto Vittori	Italian
ISS ULF1.1	Astrolab	Shuttle STS-121	04/07/2006	22/12/2006	Thomas Reiter	German

2.2 Increment Timeline

The summary review of experiments carried out on board the ISS will be presented per Increment, i.e. the period of time between the launch of a vehicle carrying an exchange crew to the ISS, and the undocking of a vehicle for return of that crew. The length of an increment ranges anywhere from 3 months to about 6 months.
The Summary Reviews of European ISS experiments will be covered as from the Belgian Soyuz Mission ("Odissea"), i.e. as from the end of Increment 5.
The following schematic (Figure 2-1) presents a basic timeline of launch events and Increments of the ISS programme, and serves as a quick reference for users of this document.

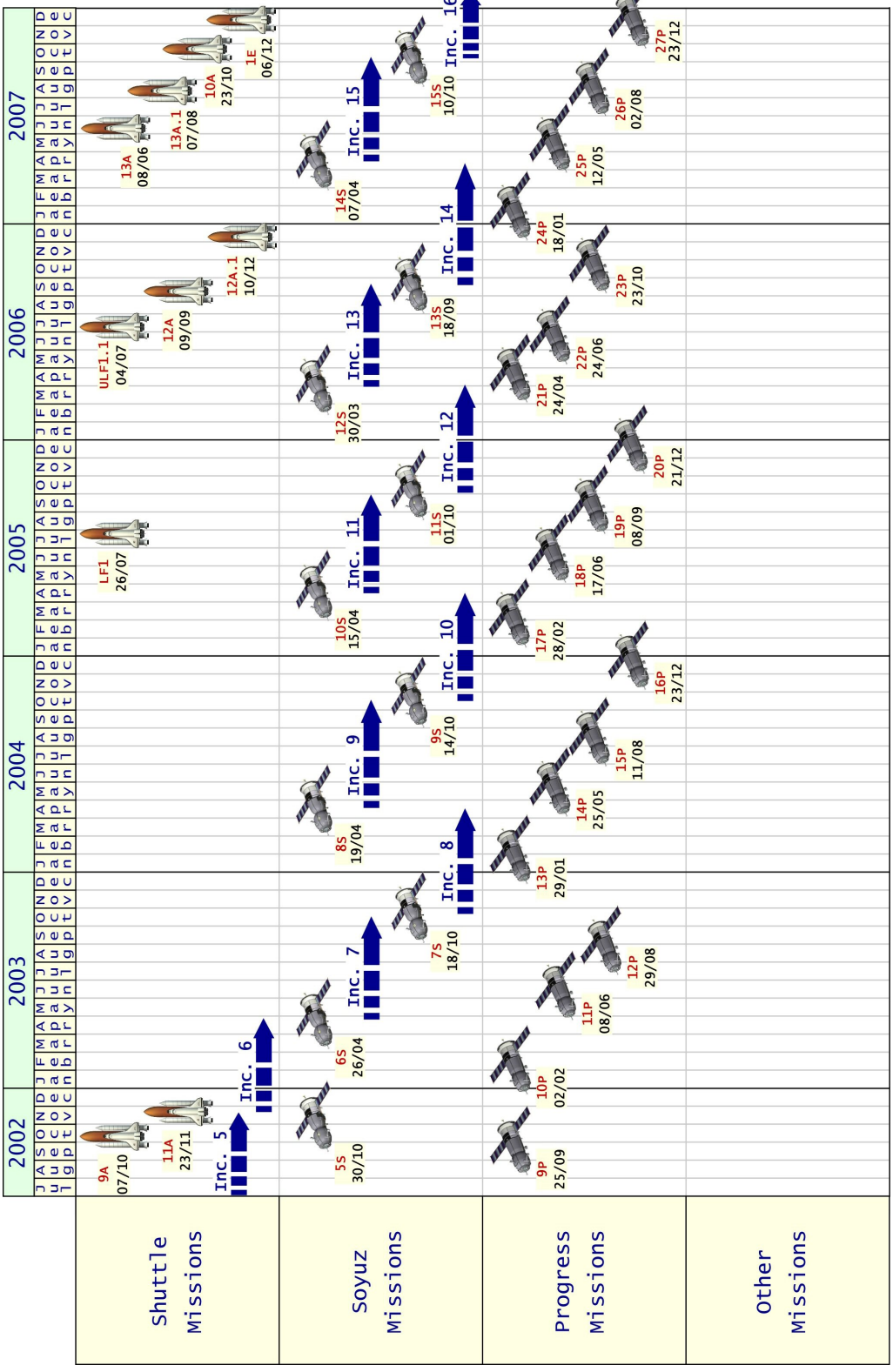

Figure 2-1: ISS Programme Launch Events and Increments (July 2002 - December 2007)

2.3 Increment 11: ESA experiments

The following table (Table 2-2) lists the 6 ESA experiments that will be covered by this report. Four of these experiments formed part of a larger scientific programme (24 experiments) that was developed for the Italian Soyuz Mission, "Eneide", launched on April 15th, 2005, carrying the Italian ESA astronaut Roberto Vittori on his second mission to the ISS.

Table 2-2: List of Life Sciences ESA experiments for Increment 11

NAME OF EXPERIMENT	RESEARCH CORNERSTONE
Study of the linear energy transfer, energy and charge distribution in a human phantom in space **(MATROSHKA-1)**	Biology: Molecular and cell biology
Study of the influence of period of neuronal proliferation on the development of gravity sensory systems in Crickets **(CRISP-2)**	Biology: Developmental biology
The influence of prolonged microgravity on the orientation of Listing's plane and eye-to-head coordination **(ETD)**	Physiology: Integrative gravitational physiology
Vestibular adaptation to G-transitions: Motion perception **(MOP)**	Physiology: Integrative gravitational physiology
Directed attention brain potentials in virtual 3-D space in weightlessness **(NeuroCOG)**	Physiology: Integrative gravitational physiology
Sympathoadrenal activity in humans during spaceflight and bed rest **(SYMPATHO-1)**	Physiology: Integrative gravitational physiology

2.3.1 Life Sciences

2.3.1.1 Biology: Molecular and cell biology

2.3.1.1.1 Study of the linear energy transfer, energy and charge distribution in a human phantom in space (MATROSHKA-1)

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2.3.1.1.1.1 Background, Objectives and Procedures

The scientific objective of the experiment was to investigate the dynamics of the radiation dose accumulated in various parts of an astronaut simulator and tissue-equivalent anthropomorphous phantom. The purpose is to improve space dosimetry methods, and evaluate the radiation hazard of astronaut exposure to radiation. The MATROSHKA facility was launched by the Russian Progress Cargo Vehicle and installed during an EVA on the outside of the Russian Service Module "Zvezda" of the ISS.

The MATROSHKA facility basically consists of a human phantom upper torso equipped with several active and passive radiation dosimeters, a base structure and a container. The container as well as the phantom torso is mounted to the base structure, which serves as a footprint for the human phantom. The container is a carbon fibre structure and forms, with the base structure, a closed volume that contains a dry oxygen atmosphere at ambient pressure.

The MATROSHKA facility is intended to provide a science platform for the determination of the depth and the organ dose in a simulated human upper torso. For radiation risk assessment the knowledge of organ (or tissue equivalent) doses in critical radiosensitive organs is an important prerequisite. The main objective of the

experiment was therefore to use the MATROSHKA facility in order to determine the empirical relations between measurable absorbed doses and the required tissue absorbed doses in a realistic human phantom. Therefore, several passive and active sensors are exposed at the surface and at different locations inside the phantom.
MATROSHKA was used for the first time for measurements of the radiation distribution inside a human phantom under EVA conditions. These measurements shall be continued and expanded using the facility for at least a second external exposure (MATROSHKA 2 – Phase C) to investigate the depth dose distribution for different times inside the solar cycle. In addition, MATROSHKA will also be used for measurements inside the station (MATROSHKA 2 Phase A/B).

Sets of passive detectors, such as thermoluminescence dosimeter (TLD) and nuclear track detector (NTD) foils with and without converter foils were provided for mission integrated measurements of absorbed dose, neutron dose and flux of heavy ions and their spectral composition with respect to charge, energy and linear energy transfer (LET). The installed active detectors developed by the investigators, the silicon detector telescope DOSTEL, the scintillator/silicon detectors (SSDs) and the tissue equivalent proportional counter are used to measure the flux of neutrons and of charged particles and the corresponding dose rate and LET spectra separately for galactic cosmic particles and trapped particles as a function of time. All detector systems are calibrated using different on ground irradiation sources. For the passive devices an on-ground reference program was performed. The different systems allow for in-flight cross-calibrations.

The results of MATROSHKA shall provide a baseline for further testing of the current established radiation transport codes, and shall, in the future, lead to a better risk assessment for long duration space flight.

The figure below (Figure 2-2) shows the uploaded MATROSHKA hardware: (from left to right) the phantom torso, the torso equipped with poncho and hood, the torso with carbon fibre glass container simulating the EVA suit, and the torso with multilayer insulation (MLI) two days prior to launch.

Figure 2-2: MATROSHKA facility uploaded hardware

The Poncho and the Hood are equipped with polyethylene stripes with sewn-in TLDs (around the whole torso) to measure the skin dose. Further, the Poncho is equipped with six NTDP (Nuclear Track Detector Packages) in similar dimensions as in the organs (two in front, two in the back and one on each side of the torso). To account for neutrons, 20 neutron detector packages are mounted on the Poncho. At the top of the phantom head, a NTDP as well as the Silicon Telescope DOSTEL are located. Inside the torso, in the organ dose slices, a plastic scintillator covered with silicon diodes with anticoincidence to measure the neutron dose, is positioned.

The 33 slices of the phantom are equipped with 356 channels where the TLDs from the participating groups are located at a total of 1634 positions arranged in a one-inch grid at each of the slices. Figure 2-3 below provides an example of Slice #4 (Phantom Head) with the dosimeter distribution and 26 dosimeter positions for depth dose determination.

Figure 2-3: Dosimeter distribution in Phantom Head slice #4

After storage of the facility inside the ISS, MATROSHKA was mounted outside the Russian Service Module by the Expedition 8 crew, Alexander Kaleri and Michael Foale, in February 2004. The MATROSHKA facility was activated during Increment 9 and remained outside the ISS for 539 days during Increments 9, 10 and 11. Within this timeframe the "housekeeping data" and the "scientific data" of the active radiation detectors were transmitted to the onboard computer inside the ISS, and later stored on PCMCIA cards, as well as down linked via the US Voice Link.

On August 18th, 2005 a 2nd EVA was performed by the Expedition 11 crew, Sergei Krikalev and John Phillips. The MATROSHKA facility was brought back into the ISS and on September 14th, 2005 the passive detectors were removed from the facility and downloaded with a Soyuz capsule in October 2005. After returning to ground, the passive detectors were distributed to the science team members for data evaluation (November 2005 to January 2006).

Data coverage does not exist for the whole exposure period. This is due to some difficulties with the Russian onboard computer (PLSU), and the communication between the MATROSHKA facility and the PLSU. Therefore the active radiation detectors could not deliver data for the whole exposure period, resulting in only part time radiation measurement coverage for the whole exposure time. The same applies to the "housekeeping data". The facility was equipped with six temperature and two pressure sensors. The figures below show the data from these sensors for the total time period of the experiment.

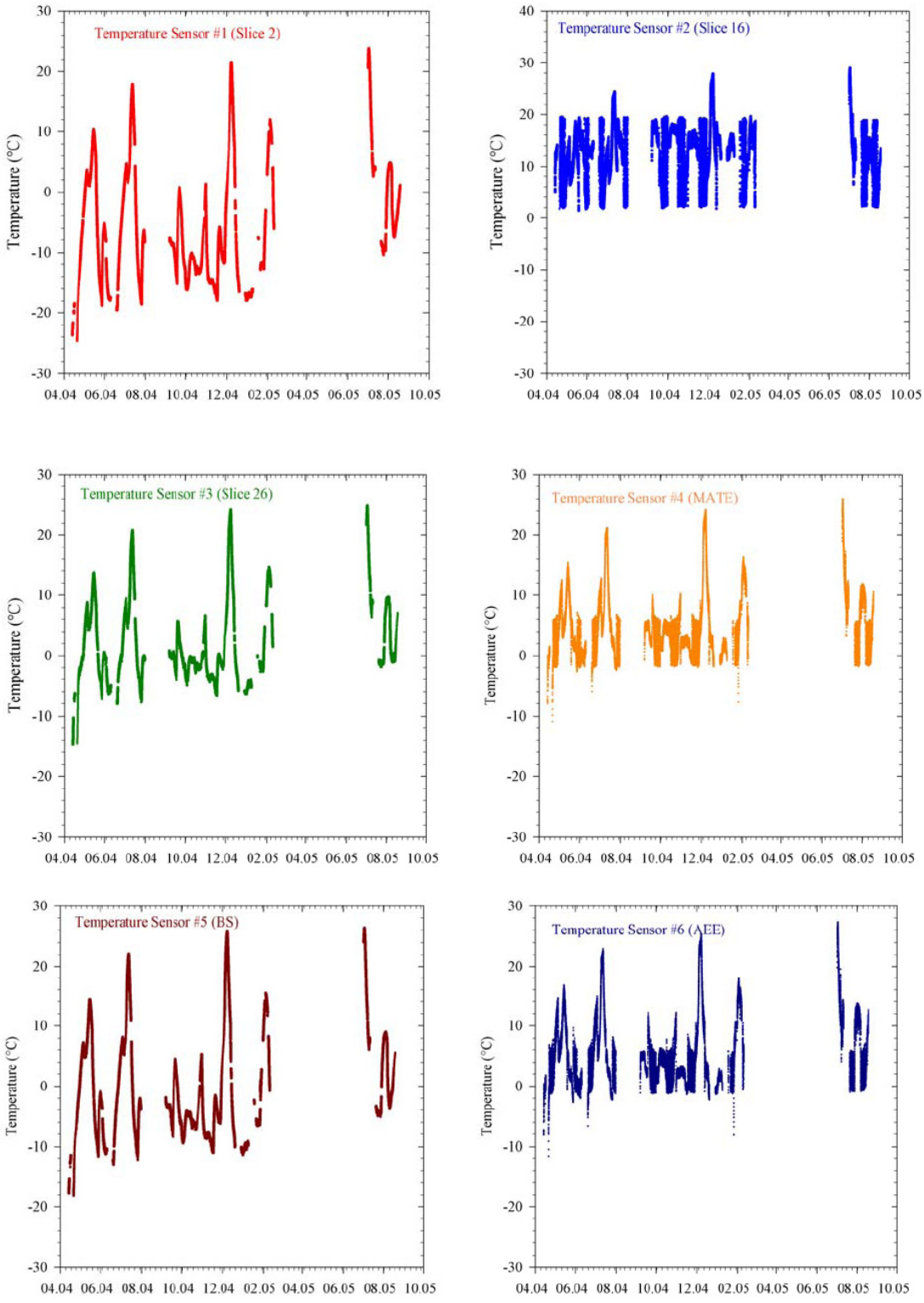

Figure 2-4: Temperature sensor data - Sensors 1 – 6

As can be seen from the six temperature sensors the temperatures in the facility ranged mostly in the temperature regions between 0 and 25°C. So no impact on the science data from the temperature inside the facility is expected.

Prior to launch the facility was filled with dry air at ambient pressure. The air is important for the measurement with the plastic nuclear track etch detectors, since these detectors need oxygen for the formation of the heavy charged particle tracks. The pressure inside the facility was very stable for the complete exposure period, resulting in no loss of science data for the passive nuclear track detector packages.

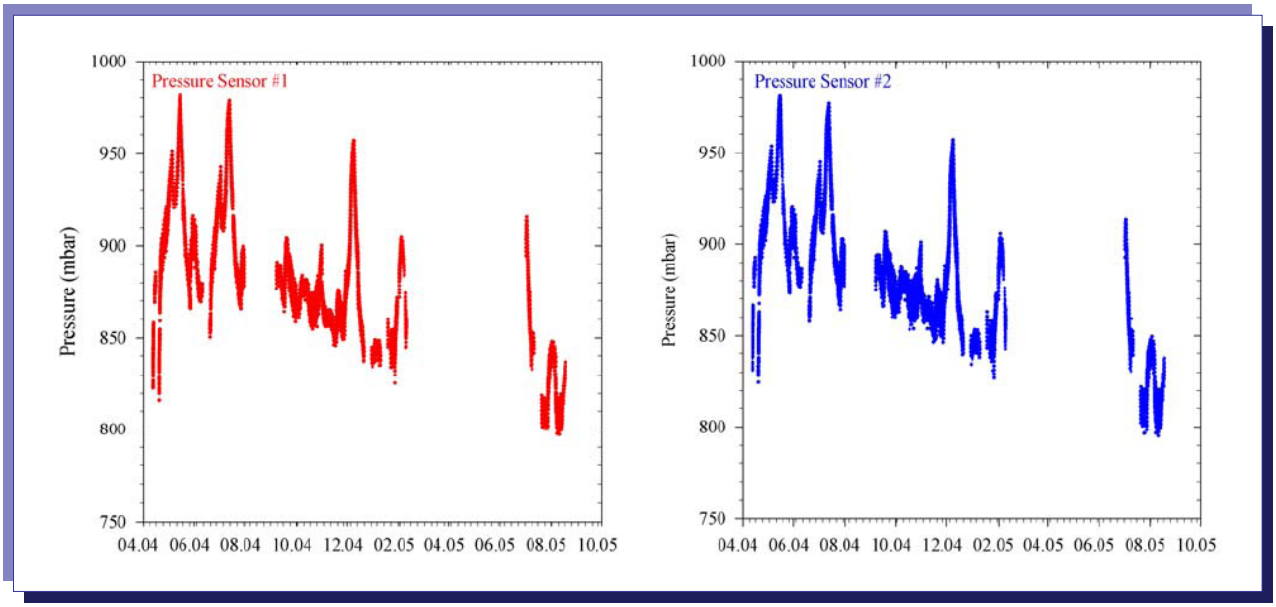

Figure 2-5: Pressure sensor data

2.3.1.1.1.2 Results

Passive Radiation Detectors
The only observed anomaly was for the exposed detectors that were directly mounted on the MLI of the facility. These passive detector packages were exposed to high levels of UV irradiations from the sun, as well as to high temperature gradients. This feature only applied to the detectors on the "front" side of the MLI. The front side packages, sewn into white Nomex, changed colour during the exposure time, due to the UV irradiations from the sun (ML1 package 1 and 2 are shown in the pictures above). For comparison, the MLI packages 4 and 5, from the back side of the MATROSHKA facility showed no change in colours. The read out of the Thermoluminescence detectors (TLDs) and Optical luminescence detectors (OSL) has been completed by all participating groups. Due to the vast amount of data, the analysis of the data is still ongoing.

Active Radiation Detectors
The data evaluation for the active radiation detectors from the University of Kiel (providing the DOSTEL and the SSD detectors) is partly finished. The University of Kiel is working on a database for the DOSTEL results, including the absorbed dose and dose equivalent values on a daily-based timeline. The data evaluation for the SSD detectors is in progress, including some reference irradiations with the ground-based equipment at neutron reference facilities, e.g. CERN, Switzerland. The data evaluation for the Tissue Equivalent Proportional Counter (TEPC) provided by NASA is currently on hold due to some difficulties with the detector system itself.

As an example a dose rate profile of the active instrument DOSTEL (located on top of the head of the MATROSHKA facility) is shown in the figure below. The profile shows the contribution from heavy ions to the dose rate (low oscillation due to passing of the north and south poles) and the contribution from protons – high peaks – due to the passing of the South Atlantic Anomaly (SAA). For this special period – in 2004 – the daily average dose accounts to around 1.3 mSv – indicating an increase of a factor of 3 in dose rate compared to the exposure inside the ISS for this time period.

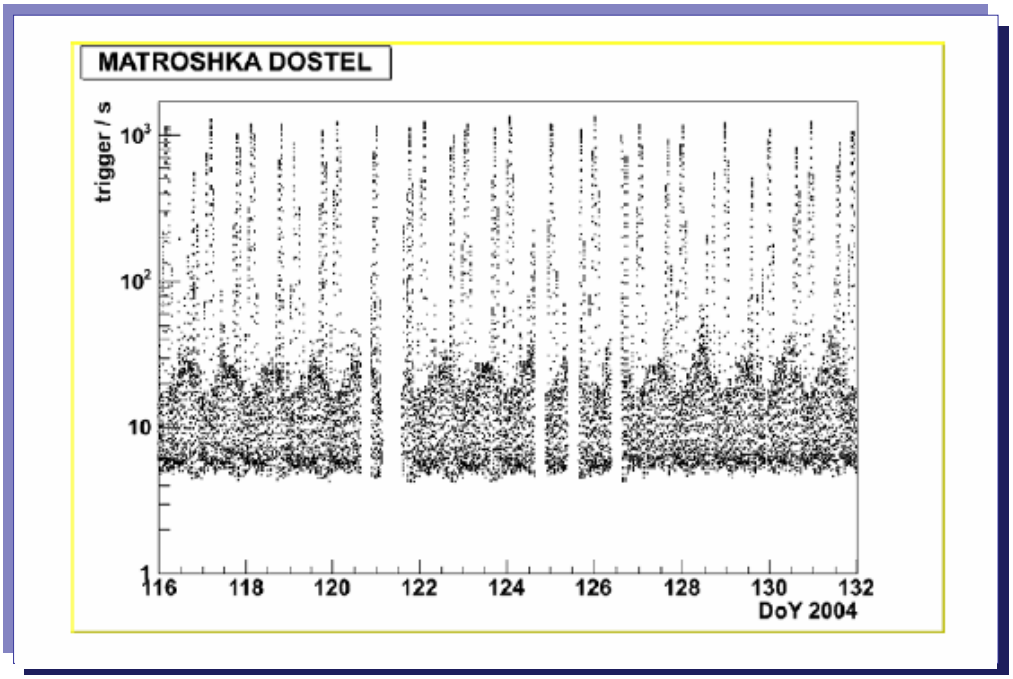

Figure 2-6: Dose rate profile of the active instrument DOSTEL

2.3.1.1.1.3 Conclusions and Recommendations

The MATROSHKA experiment, followed up by MATROSHKA 2A and MATROSHKA 2B, offers for the first time, if all the data from the phases are evaluated, the comparison of a three-dimensional dose distribution measured in a human phantom from inside and outside the space station. This is the baseline for the further development and refinement of radiation transport codes as well as radiation models, resulting in an enhanced and better risk assessment for future long duration space missions.

2.3.1.1.1.4 Publications

1. J. Dettmann, G. Reitz, G. Gianfiglio (2007), "MATROSHKA-The first ESA external payload on the International Space Station", *Acta Astronautica 60:1*, pp. 17-23.
2. G. Reitz, T. Berger, (2006), "The MATROSHKA facility: dose determination during an EVA", *Radiation Protection Dosimetry, Vol. 120, No. 1-4*, pp. 442-445.

2.3.1.2 Biology: Developmental Biology

2.3.1.2.1 Study of the influence of period of neuronal proliferation on the development of gravity sensory systems in Crickets (CRISP-2)

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2.3.1.2.1.1 Background, Objectives and Procedures

Experimental models from both the cellular and the integrative levels are necessary to study basic mechanisms of how modified gravitational conditions affect embryonic and postembryonic development of sensory, neuronal and motor systems. Internationally, studies have been conducted on mammals, birds, amphibians, fish and invertebrates. The comparative approach is useful to find out basic mechanisms of how animals and probably man adapt to the microgravity environment.
With respect to developmental biology, special interest has been given to early embryonic development. In particular, the fertilization aspect has particular importance, because each experiment which will allow complete development in microgravity has to make clear that the basic step, fertilization, is possible in orbit.
We proposed crickets as a suitable animal to test the influence of in-flight fertilization on the development of the neuronal system for three reasons:

1. The behaviour of female crickets allowed the construction of a suitable fertilization hardware that is easy to handle and offers the possibility to produce embryos of defined ages;
2. Due to the clearly defined topographical arrangements of inter- and motoneurons, and due to a prominent gravity-related behaviour such as geotaxis acute and residual effects can be studied morphologically and physiologically in larvae hatched from eggs fertilized in space;
3. As in most insects, the period of neuronal proliferation is completed before hatching, and the full set of neurons exist in the animal at the time of hatching.

In crickets, neuronal proliferation is completed after approx. 50% of embryonic development. Cricket larvae *(Acheta domesticus)* which flew on the Neurolab mission (STS-90) revealed specific effects of gravity deprivation on the physiology of the PSI-Interneuron that transmits postural information from the cercal gravity receptors to the motor system, and is therefore linked in the gravity related behaviour.

For the Crisp-2 experiment, the topography of neurons immunoreactive to allatostatin (AST), perisulfakinin (PSK), or crustacean cardiac-active protein (CCAP), and geotactic behaviour during walking on an inclined surface were used as experimental parameters.

It was essential to achieve fertilization during microgravity exposure. Due to their behaviour, crickets are useful model animals. They can be inseminated and sperm can be stored for a long time; fertilization takes place during the deposition of the eggs. It is only necessary to offer females a suitable substrate for a defined period of time that they can use for egg deposition. Thus, early embryogenesis can be induced without any complicated technical requirements for the flight hardware, and after flight the age of the embryos is well known. These facts were taken into consideration for the construction of a new transport container.

It was mandatory to allow deposition of eggs and fertilization as early as possible after launch to obtain a long time of neuronal development under microgravity condition. In addition it was planned to get a second set of embryos that spent only some days in microgravity and could not complete neuronal proliferation. Therefore, two 20-hour periods of egg deposition were defined, one from flight day 3 (FD3) to FD4, the other from FD6 to FD7. Movement of the females were videotaped during these periods. Similar procedures were planned after landing.
All experimental procedures with embryos and 1st larvae including fixation for neuroanatomical studies and behavioural observations were performed after landing of the Soyuz. Experimental tests included immunocytological staining techniques to identify 3 types of peptidergic neurons, allatostatin-(AST)-ir-, CCAP-ir-, and perisulfakinin-(PSK)-ir-neurons. These neuropeptides are involved in developmental and neuronal processes. AST inhibits the synthesis of juvenile hormone. AST neurons are usually equipped with short axons; rarely do they extend to more than 4 segments. CCAP has myotrope function with strong effect on heart activity; it probably contributes to the regulation of moulting. PSK is a myotrope neuropeptid but also effects on the central nervous system were described. Due to its wide projections, P-PC1 neurons probably exert a modulating effect on neuronal activity.

2.3.1.2.1.2 Results

The original timeline required in-flight egg deposition shortly after arrival on ISS and 3 days before undocking from ISS. Due to the death of females in the mid-period of the "Eneide" mission, embryos were obtained only from the first collection period. This means that the technique for in-flight fertilization was successful but that an improvement of the ambient conditions within the cricket containers is mandatory for future experiments in this field.

A sufficient number of embryos obtained from the first egg deposition period was fixed; the quality of the subsequent immunohistological staining for the neuroanatomical studies were of high quality so that the main answers about proliferation susceptibility to µg could be answered. The post-hatching behavioural investigation could be performed with 33 1st stage larvae for the flight sample. This number is high enough to get a statistically reliable result.

A total number of 112 embryos and 1st larvae from in-flight fertilization were available for the studies. The number of ground controls was 103. The 1g-ground control experiment included a group in which similar to the flight experiment 2 levels of containments were used, and a second group in which the outer bioFolie25 bag was not used, so that only 1 level of containment was used. Interestingly, the µg-exposed larvae hatched earlier than larvae from the 1g ground controls.

A first fixation of embryos was done 6 hours after landing in Kazakhstan; a second fixation at about 40 hours after landing in Moscow, and a third fixation after hatching and recording of the geotactic behaviour of the larvae.

Neuroanatomical studies: The results coming from the Eneide flight revealed that after microgravity fertilization, the AST-ir-, PSK-ir- and CCAP-ir-neurones developed similarly to the on-ground fertilization. This holds not only for neurons with only short neurites located either only within the cerebrum (Figure 2-7), the thoracic or the abdominal ganglia chain (Figure 2-8), but also for those neurons such as PSK-ir neurons that project throughout the whole nervous system, with cell somata lying in the protocerebrum and dendritic arborizations within the cerebral, thoracic and abdominal ganglia (Figure 2-9).

Lack of significant differences between 1g- and post-flight larvae does not exclude a post-flight sensitivity during early development. Compensatory mechanisms might be activated during on-going flight conditions to overcome transient deviations from normal neuronal development. The earlier hatching of the 1st instar larvae after in-flight fertilization as demonstrated for the space flight experiment CRISP-2 makes this hypothesis very likely.

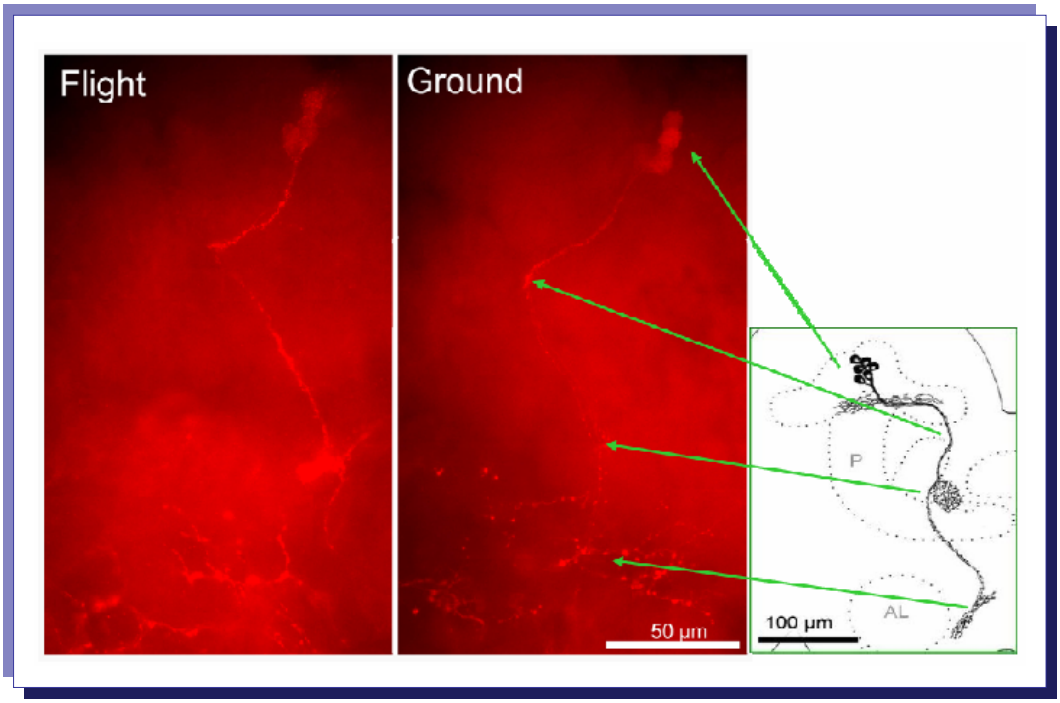

Figure 2-7: Allatostatin-ir APC2 neurons and their primary neurits within the right hemisphere: flight and ground embryo.

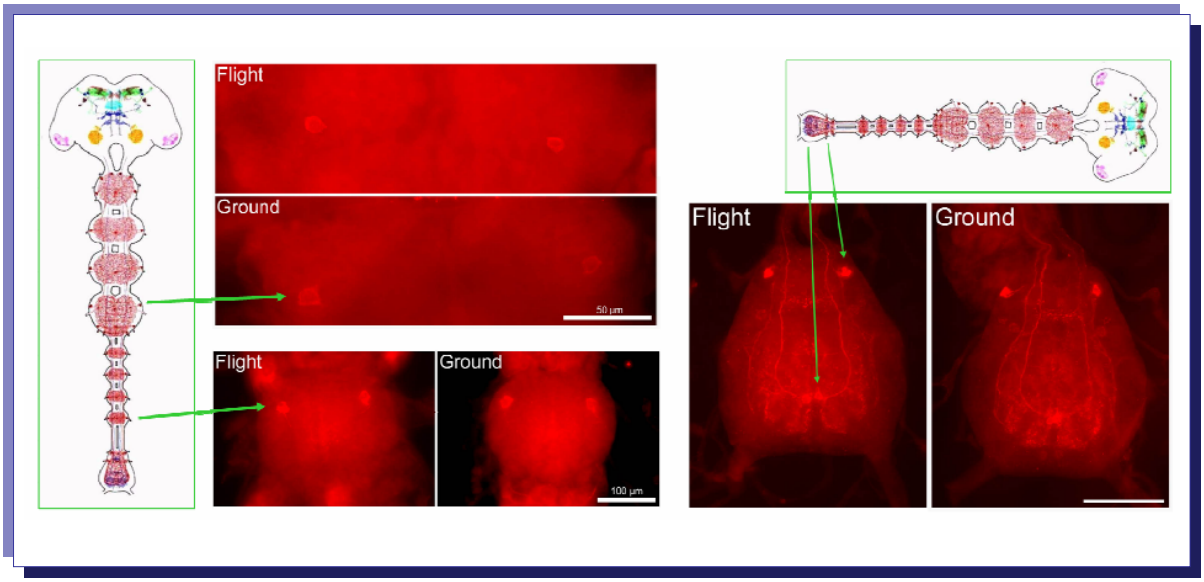

Figure 2-8: CCAP-ir-Neurons in the nervous system of cricket embryos and 1st instar larvae.

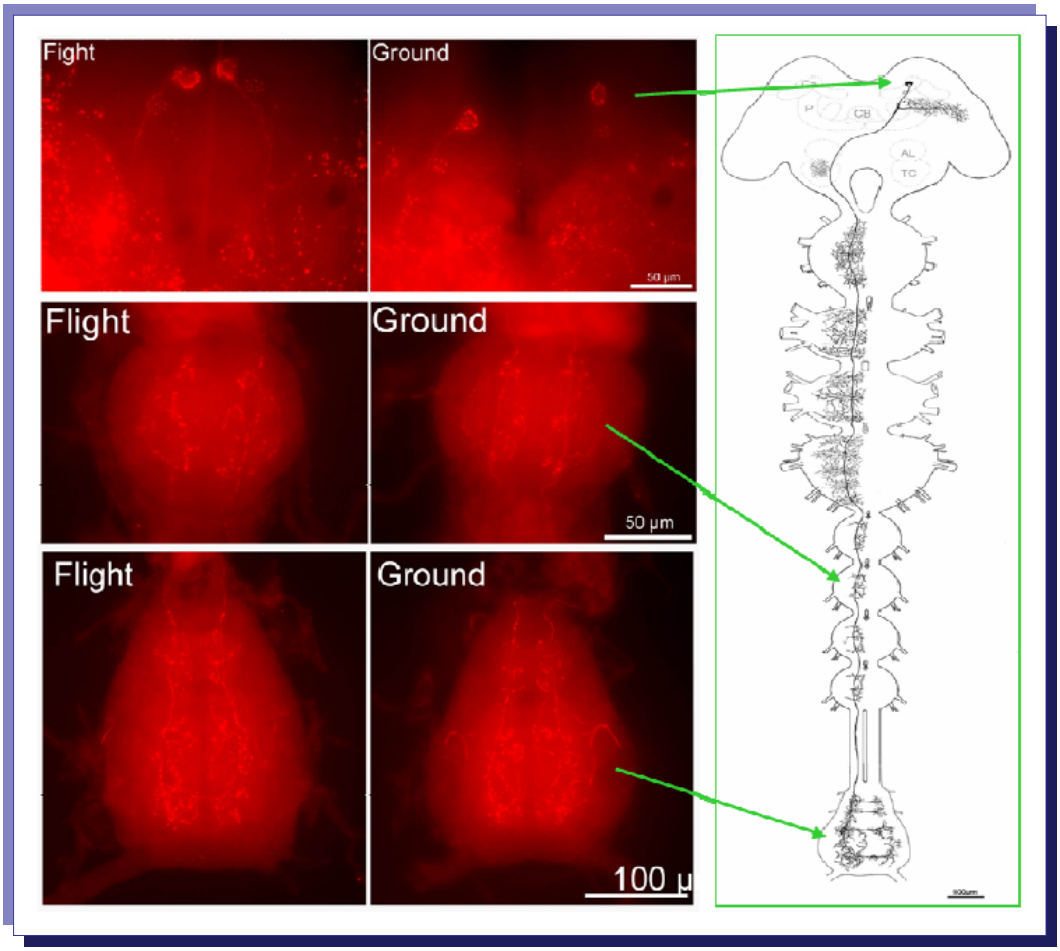

Figure 2-9: Perisulfakinin neurons PC 1,2 from 65% embryos – flight and ground group

2.3.1.2.1.3 Conclusions and Recommendations

Despite failure of the second egg collection and the problems of adult survival, the experiment CRISP-2 can be considered as partially successful. The following main goals were achieved:

1. Successful in-flight fertilization was obtained;
2. High-quality neuroanatomical stainings from embryonal nervous systems were obtained;
3. After landing, embryos could be reared until hatching to test consequences of in-flight fertilization even on the behavioural level.

One important component of the experiment performance was that experimenters received the permission to take care of the samples at the landing site and, therefore, start with sample fixation close to termination of microgravity conditions.

Studies like this should be part of future programs to explore the impact of the microgravity environment on the general development of animals. CRISP-2 is only a step in the analysis of the structural and functional consequences of in-flight (in-orbit) fertilization. Crickets can be considered as excellent model animals because of the easy way to get embryos after in-flight fertilization and because of the well-defined structural organisation of the nervous system with its identified neurons.

2.3.1.2.1.4 Publications

1. U. Kirschnick, H.J. Agricola, E. Horn, (2006), "Effects of altered gravity on identified peptidergic neurons of the cricket *Acheta domesticus*", *Gravit. Space Biology Vol. 19*, pp. 135-136
2. E. Horn, C. Dournon, J.P. Frippiat, R. Marco, S. Böser, U. Kirschnick, (2007), "Development of neuronal and sensorimotor systems in the absence of gravity: Neurobiological research on four Soyuz taxi flights to the International Space Station", *Microgravity Science and Technology* (in press).

2.3.1.3 Physiology: Integrative gravitational physiology

2.3.1.3.1 The influence of prolonged microgravity on the orientation of Listing's plane and eye-to-head coordination (ETD)

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2.3.1.3.1.1 Background, Objectives and Procedures

Orientation and the perception of movement in three-dimensional space involves transduction of three degrees of freedom for angular rotation and three degrees of freedom for linear translation. In the vestibular system, this is provided for by the semicircular canals and the otolith organs, respectively. Via the vestibulo-ocular pathways in the brainstem, the afferents from the vestibular end organs are utilized synergistically for the purpose of gaze stabilization and are reflected by compensatory eye movements in the three orthogonal planes governed by the extraocular muscle pairs. Thus, any physiological stimulation to the vestibular receptors, either by rotatory, gravitational or translatory acceleration, or a combination thereof, will potentially elicit a systematic, compensatory eye movement consisting of horizontal, vertical and/or torsional components, i.e. the three-dimensional vestibulo-ocular reflex.
For a full understanding of the vestibulo-oculomotor system, it is necessary to examine the three-dimensional processing of the afferent information from the semicircular canals and otolith organs and to determine their respective contributions to the elicitation of the compensatory reflex eye movements. Adequate measurement of the vestibulo-oculomotor response is an important inroad in the case of human experimentation.

Since the late 19th century it has been known that under normal visual conditions the torsional orientation of the eye is independent of the path that the eye takes to reach any secondary or tertiary eye position. This restriction implies a reduction from three to two degrees of freedom for the eyeball, and is known as Listing's law; thus, all axes about which the eye rotates from the so-called primary position lie in one plane, called Listing's plane. Listing's plane can be visualised by plotting 3D eye positions as quaternions or rotation vectors. Recent investigations have verified the validity of Listing's law during fixations, saccades and smooth pursuit, and it has been argued recently that Listing's plane is primarily under visuomotor control.

Spatial aspects of the vestibulo-oculomotor system can be evaluated by measuring the orientation vectors associated with slow phase eye velocity generated by the vestibulo-oculomotor response (VOR). In the present study, attention will be directed towards the three-dimensional gain matrix and vector representations of head and eye movement. Examination of the collinearity between the Listing and VOR co-ordinate systems is of key importance for the hypothesised existence of a uniform representation of three-dimensional space across of those central nervous system (CNS) areas related to spatial orientation.

Examination of the orientation of Listing's plane during the course of a prolonged microgravity mission is of particular interest, given the evidence that under 1g conditions it appears to be dependent on head position to gravity, i.e. dependent on otolithic input. A related question is to what extent the orientation of Listing's plane is altered by the vestibular adaptation to microgravity.

A corollary aspect is to what extent Listing's Plane is dissociated from the internal co-ordinate frame of reference of the vestibulo-oculomotor response (VOR) during prolonged microgravity. Under one-g condition the two have been shown to be collinear (Crawford et al, 1991), but preliminary findings in microgravity indicate that the VOR frame of reference is modified by the absence of otolithic loading, whereas Listing's Plane remains stable.
A further question is whether compensatory mechanisms substitute for the missing sensory input from the otolith organs during long-term spaceflight. Possible sensory information which could serve as compensatory input are neck afferents and vision. Accordingly, it is proposed to record Listing's plane with different static head postures without visual input and with different static whole body orientations within the spacecraft with visual input.
Supporting experiments are being carried out during parabolic flight, where the influence of short-term hypergravic and hypogravic conditions can be examined.

The working hypothesis is that in microgravity the orientation of Listing's Plane is altered, probably to a small and individually variable degree. Further, with the loss of the otolith-mediated gravitational reference, it is expected that changes in the orientation of the coordinate framework of the vestibular system occur, and thus a divergence between Listing's plane and the vestibular coordinate frame should be observed.
While earlier ground-based experiments indicate that Listing's Plane itself is to a small degree dependent on the pitch orientation to gravity, there is more compelling evidence of an alteration of the orientation of the VOR in microgravity. The proposed experiment is intended to resolve these questions.
With regard to eye-head co-ordination, sensory control of movements under normal 1g conditions is ensured by mutual cooperation of different sensory-motor systems. Withdrawal of any of the contributing afferent signals will introduce a decline in motor performance. In microgravity the loss of the gravity reference (i.e. mediated by the otolith apparatus and the proprioceptive system) will seriously compromise spatial orientation and trigger adaptive modification of motor control strategies.
This phenomenon manifests itself particularly clearly in the sensory-motor coordination of eye and head movements.

The objectives of this experiment are threefold:

- To determine the influence of prolonged microgravity and the accompanying vestibular adaptation on the orientation of Listing's Plane.
- To determine whether Listing's Plane as a measure of the coordinate frame of the visual system dissociates with that of the vestibular system.
- To determine the influence of prolonged microgravity on the velocity and accuracy of eye and head movements during visual fixation tasks.

2.3.1.3.1.2 Results

The data collected during Increments 9, 10, 11 and 13, and during the DELTA and ENEIDE short missions are currently being processed. Further recordings will be made over the course of Increments 16 and 17 to complete the database. To date, the results demonstrate that Listing's Plane reorientates in microgravity. In all tested subjects a backward tilt of LP was observed throughout the period of microgravity. During the first two weeks after landing a re-adaptation, i.e. return to pre-flight one-g values, was also observed.

2.3.1.3.1.3 Conclusions and Recommendations

Besides the scientific objectives, an important aspect of the experiment has been the development of the Eye Tracking Device as a universal measurement instrument for neurovestibular, neurophysiologic and orientation experiments. A commercialised version of the equipment is now manufactured by Chronos Vision GmbH. Over 30 systems are used worldwide in terrestrial research laboratories. Numerous publications have been made, establishing the technology as a state-of-the-art research instrument. In addition the eye tracking technology is integrated into refractive surgery systems for corneal shaping.
The experiment is designed for a one-man operator/subject scenario. Given the heavy workload of the astronauts, the lack of control by a second observer/operator has led to the loss of some in-flight data, i.e. due to fatigue the image recordings of the eyes has proven very difficult to analyse. In future, if possible, a second crew member should be recruited to monitor the quality of image recordings while the main operator/subject is performing the experiment procedure.

2.3.1.3.1.4 Publications

A.H. Clarke, T. Halswanter, (2007), "The influence of microgravity on the orientation of Listing's Plane", *Vision Research (in print)*.

2.3.1.3.2 Vestibular adaptation to G-transitions: Motion perception (MOP)

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2.3.1.3.2.1 Background, Objectives and Procedures

During the first days in space 50-80 % of astronauts and cosmonauts suffer from Space Adaptation Syndrome (SAS). The symptoms of SAS, like nausea and dizziness, are especially provoked by head movements, and hamper the astronaut's functioning to a large extent. Although it is generally agreed that the vestibular system is involved in the underlying mechanism causing SAS, no distinct clue has been found to the etiology of SAS or the individual susceptibility and predictability. Preliminary results from the European astronauts of the D1 Spacelab Mission suggest that we can simulate SAS on earth by means of a long duration (i.e. ≥ 1h) 3g run in a human centrifuge. For several hours after such a centrifuge run head movements may provoke symptoms that are equivalent to those of SAS. This suggests a transition from 3 to 1g may trigger the same mechanism as a transition from 1 to 0g. Thus, that it is the G-transition rather than the microgravity environment per se that causes the symptoms. An experiment during the EUROMIR Mission of 1994 was performed to investigate whether susceptibility to SAS correlates with susceptibility to this Sickness Induced by Centrifugation (SIC). The Dutch Soyuz Mission, "DELTA", provided the opportunity to further elaborate the hypothesis concerning the correlation between SIC and SAS. The SIC – SAS relationship is of interest since a correlation implicates a general vestibular adaptation mechanism to changing G-levels.
The current experiment aims at validating the hypothesis that SIC and SAS share the same underlying mechanism. To this end, the astronaut's susceptibility to SAS during space flight with his susceptibility to SIC after a ground based centrifuge run, is compared. Second, during the ground based study various vestibular tests before and after centrifugation were performed, that hopefully will provide insight into the adaptation process.
In SIC, head movements that change the orientation of the head relative to gravity strongly affect motion and attitude perception (e.g. in an erect position roll and pitch are more provocative than yaw). Therefore it is suggested that in the absence of gravity, head movements would have mutually equal effects on motion and attitude perception, regardless the axis of rotation.

The specific aims of this experiment are:

- To obtain insight into the process of vestibular adaptation to G-transitions. Two important parameters are the (change of) perception of body motion and attitude during the adaptation process. This will be assessed in a ground based centrifuge study (transition from 3 to 1g) and during the space flight (transition from 1 to 0g).
- To correlate the astronauts' susceptibility to SAS with the susceptibility to SIC.

In the ground based experiment the astronaut is exposed to a sustained hypergravity load of 3gx for 60 minutes in a human centrifuge. A number of vestibular tests are performed both before and after the centrifuge run:

Motion Perception: In the first test the astronaut completes the Motion Perception Questionnaire. This questionnaire addresses motion perception (illusions) and experienced discomfort as a consequence of active head and body movements. The astronaut is asked to perform a total of 10 head movements about all three principal axes and report on visual or motion illusions and discomfort. This questionnaire is used to rate the astronauts' susceptibility to SIC.
Eye movements: The second test focuses on vestibular driven eye movements. The so called Listing's Plane (LP) in different body positions is recorded. Head tilt in pitch is known to affect the orientation of LP, illustrating the dependence of LP on vestibular function. Since long duration centrifugation is expected to affect the vestibular system, it is anticipated that there will be a change in the orientation of LP after the centrifuge run. The LP is determined from a series of voluntary eye movements recorded using Video OculoGraphy.
Subjective Vertical: In the first part of the test, the astronaut is tilted into various body positions in a tilt chair and is asked to give a tactile indication of the subjective vertical and the longitudinal body axis. In the second part, the chair is perturbed in the pitch direction and the astronaut is asked to align it with the vertical. For the experiment during this increment, the postural stability in a moving room was also tested. This test was not included in subsequent missions.

During the in-flight experiment the astronaut completes the same Motion Perception Questionnaire, involving active head movements in yaw, pitch and roll. The questionnaire is completed from L-2 to R+14.

2.3.1.3.2.2 Results

Together with the 8 astronauts that have been participating in a similar ground based centrifuge study, SIC and SAS susceptibility in 12 astronauts has been determined. A positive correlation between SIC- and SAS-susceptibility has been found. Subjects that were suffering from SAS during their flight were also the ones that were experiencing symptoms of SIC after centrifugation.
Concerning the vestibular test results, it is still too early to draw conclusions. Differences between SIC-susceptible astronauts and non-susceptible astronauts have been observed, but also within both groups there is a substantial variation.

2.3.1.3.2.3 Conclusions and Recommendations

Not available.

2.3.1.3.2.4 Publications

Not available.

2.3.1.3.3 Directed attention brain potentials in virtual 3-D space in weightlessness (NeuroCOG)

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2.3.1.3.3.1 Background, Objectives and Procedures

The NeuroCOG experiment was designed to further investigate modifications in the perception of whole-body motion in space found during the French Soyuz Mission, "Andromede", in October 2001. The NeuroCOG experiment went a step further in understanding the neural mechanisms underlying the perceptual processes by combining the psychophysical experiments with measurements of visually-evoked EEG potentials.

The human being in his natural environment moves, because of the constraints of gravity, over a relatively flat two-dimensional surface. During Earth-bound navigation, only yaw rotations are typically used when moving from one place to another. Even when moving through three-dimensional structures, human beings tend to remain upright with respect to gravity. In weightlessness, astronauts can translate and rotate in any direction, thus their trajectory is no longer ascribed to two-dimensional surfaces. In contrast with Earth-bound navigation, astronauts can freely use pitch and roll rotations when moving through three-dimensional space. The semi-circular canals measure relative rotations around all three axes (roll, pitch and yaw). This provides relative information about the amplitude of a rotation, but does not provide absolute information about orientation. The otoliths and other graviceptor cues (tactile sensors, proprioception, etc.) can potentially indicate the absolute orientation of the head and body with respect to the vertical axis. Neural processes that allow us to perceive, interact and navigate within this world may thus be specialised for the internal representation of spatial relationships with respect to gravity.
The novel conditions of microgravity might therefore place an increased load on the cognitive capacity of the human brain because sensory signals must be processed and interpreted in a new context. By placing electrodes on the scalp of a human subject one can get a glimpse at the electrical activity underlying perceptual processes in the brain. Through the analysis of the variations in electrical potential between different locations on the scalp, one can make inferences about various neural processes such as the sensitivity to sensory information, the attention state of the system and the decision making process.
This project studies how the brain functions with respect to gravity through the use of electroencephalography (ECG) or EEG. In this experiment the role of gravity in the perception of self-motion is evaluated. In a series of psychophysical tests, a comparison is made on how human subjects interpret visual-flow information both on the ground and in the weightless conditions of orbital flight. Also, evoked potentials through surface electrodes applied to the scalp are measured in order to determine the spatial and temporal components of information processing in the brain in the absence of gravity. Through these experiments observations were made on how the CNS (Central Nervous System) adapts from its habitual environment in which gravity plays an ever-present and

dominant role, to a novel environment in which the movements of our bodies no longer adhere to the constraints imposed by gravity.

The hypothesis is that gravity should influence the perception of pitch but not yaw turns. Performing perception tasks in microgravity should evoke different cognitive responses and should activate different cortical circuits, depending on whether the information to be interpreted by the subject involved turns around a pitch or yaw axis.

Subjects performed a set of 2 psychophysical tasks with simultaneous recording of EEG activity. For each subject, the performance of these tasks was compared to a set of pre-flight, in-flight and post-flight procedures to test for an effect of weightlessness on the visual perception of orientation and movement and on the ability to navigate in three dimensions. Backup crewmembers were asked to perform all pre-flight training and baseline data collection (BDC) tests and were asked to work in parallel with the orbital crew-members during and after the flight to provide a matched control group for comparison.
Subjects take up the position and postural support depending on the gravitational conditions (ground or in-flight) and on the instructions for a particular protocol:

1. *Ground Seated*: The subject sits upright in a chair, with the elbows resting on adjustable-height elbow supports of the ground support stand. The ground support stand is adjusted to position the mask/tunnel/laptop at the level of the eyes for viewing. The height of the elbow pads is adjusted to allow the subject to comfortably grasp the grips on the laptop support.
2. *In-flight Restrained*: The subject sits in front of the laptop, which is attached to a mechanical support. Waist and foot straps are used to hold the subject securely in a seated posture.
3. *In-flight Free floating*: The subject adopts a free-floating posture and has no rigid contact with the Station structure during the performance of the experiment in this mode. A second cosmonaut assists the subject to stabilise his/her posture at the beginning of this phase of the experiment.

In all cases, the subject places his/her face into the facemask and attaches an elastic band behind the head to hold the head in place. By manipulating the buttons and trackball, the subject starts the experiment program on the laptop, identifying him/herself to the program and performs a set of experimental trials consisting of the following:

- Virtual Turns – The subject is situated in a visually-presented 3-D virtual tunnel. On the press of a button, the subject will virtually either move through a tunnel at constant speed, passing through a single bend between two linear segments or undergo a rotation in place (no apparent translation). At the end of the trial, the subject indicates the extent of the turn (i.e. how many degrees) in one of two ways:
    1. The subject observes a bird's eye view of a planar workspace with two cylindrical tunnels connected by a variable angle. By manipulating the trackball, the subject adjusts the magnitude of the turn to reconstruct a planar representation of the virtual tunnel just experienced.
    2. The subject sees a pictogram indicating his/her starting orientation in the plane. By manipulating the trackball, the subject changes the orientation of the pictogram to indicate the amount of rotation that is perceived.
- EEG Recordings – EEG signals from 14 locations on the scalp are recorded during the above trials. The subject performs a total of 48 trials for either stimulus type, for a total of 96 trials per session. Trials are broken into blocks of 12 trials each, with pauses imposed between blocks. At a nominal rate of 4-5 trials per minute (including pauses), complete execution of this protocol (turning in-place or passage through the tunnels) is performed within 20-25 minutes. EEG is also recorded under four control conditions:
    1. The subject relaxes and does nothing, first with his/her eyes closed, then while looking at a neutral screen.
    2. An alternating checkerboard is presented to the subject on the screen, with the colours switching between black and white every 3 seconds.
    3. The subject follows the movement of a luminous spot as it makes a sinusoidal movement across the screen.
    4. Subjects blink their eyes in synchrony with an audible metronome. Control recordings last no more than 5 minutes.

2.3.1.3.3.2 Results

After subjects emerged from the end of the tunnel, they were asked to report the perceived turn angle by adjusting a visual indicator with a trackball. Figure 2-10 shows the difference between left and right turns (left–right) and between upward and downward turns (downward–upward) as a measure of this asymmetry. On Earth, yaw turns led to equal, symmetrical errors in the estimation of the perceived angle change, but the estimation of pitch turns was greater for forward (nose-down) versus backward (nose-up) turns. The interest of this experiment lies in this asymmetry. One can observe a clear reduction in the asymmetry of vertical turns in microgravity. In summary, it appears that the microgravity conditions of orbit reduce the asymmetry of vertical turn estimation, but only in the free-floating condition. The NeuroCOG experiment revealed interesting EEG correlations of these effects observed via psychophysical measurements. Alpha rhythms were analysed in response to a standard alternating checkerboard pattern (visual evoked potential, VEP) and in response to the initial presentation of the virtual 3D tunnel (event related potentials, ERP). It was demonstrated for the first time that the VEP responses and phase locking of alpha rhythms are preserved in the microgravity. In contrast, the ERP evoked by the presentation of the tunnel was considerably perturbed in the ISS. Unspecific factors such as a noisy environment in the ISS, anxiety, stress, muscular artefacts and basic physiological factors (brain and body blood circulation differences) seem to be unlikely culprits because the classical VEP in response to the reversing checkerboard pattern is maintained. This latter phenomenon occurs through the conservation of the phase locking mechanism of the VEP in the alpha band frequency, as seen on the ground. These results (see Figure 2-11) can be interpreted in light of the specific informational content of the different visual stimuli (checkerboard vs. tunnel) that the associated task demands. The major difference between the classical checkerboard testing and the virtual tunnel task is that in the former situation the subject was mainly passive (only looking at the computer screen) while in the latter situation the subject was involved in a 3D spatial perception task. This task directly contained directional information related to the gravitational frame of reference, which may play the role of a top-down control. In the presence of gravity, this neural context implicitly contributed to the evoked response. Thus a change of perceptual context or a basic interference in the dynamics of the neural networks could be expected, resulting in the different patterns in EEG measurements between the 2 tasks.

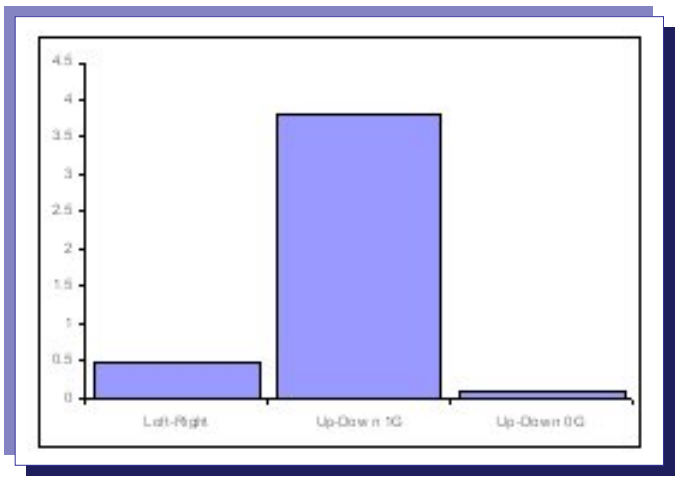

Figure 2-10: Asymmetry in the estimation of turn angles for virtual rotations around horizontal and vertical axes

In the NeuroCOG experiment before the navigation task, the arrest reaction of the alpha rhythm was used (Berger, 1929) because it is a highly stable reaction, which occurs over a large part of the brain and provides two distinct physiological states induced by opening or closing the eyes. The head figurines of Figure 2-12 illustrate the difference in the power gain of 10 Hz activity between the recordings performed in the ISS and on Earth (with data recorded before and after flight pooled together) for cosmonauts (A) and for control subjects (B). Statistical analysis revealed that the gain values recorded in parieto-occipital (O1, O2, Pz, P3, P4) and central (C3, C4, Cz) loci were significantly increased in weightlessness. The three latter electrodes are situated over the sensorimotor cortex, which is the site of the mu rhythm. In contrast, the 10 Hz gain value of the frontal recordings (Fz, F3, F4, F7, F8) remained unchanged in the absence of gravity. The same analysis performed in the control subjects showed a great stability of the gain value throughout the same period of time in all recorded channels. The

findings demonstrate that the power of the spontaneous EEG alpha rhythm recorded in the parieto-occipital regions and in the sensorimotor areas (mu rhythm) are increased and that the spectral perturbations of these rhythmic activities produced by eye-opening/closure state transition, increase in the absence of gravity. This demonstrates the influence of the absence of cues related to gravity on alpha oscillation, which is likely to be linked to the gating of sensory input. Alpha and mu rhythms may also participate in memory and cognitive processing. In this context, the finding of enhanced alpha and mu rhythm in weightlessness supports their physiological implication in the gain-field mechanism allowing the adaptation of the neural representation of space.

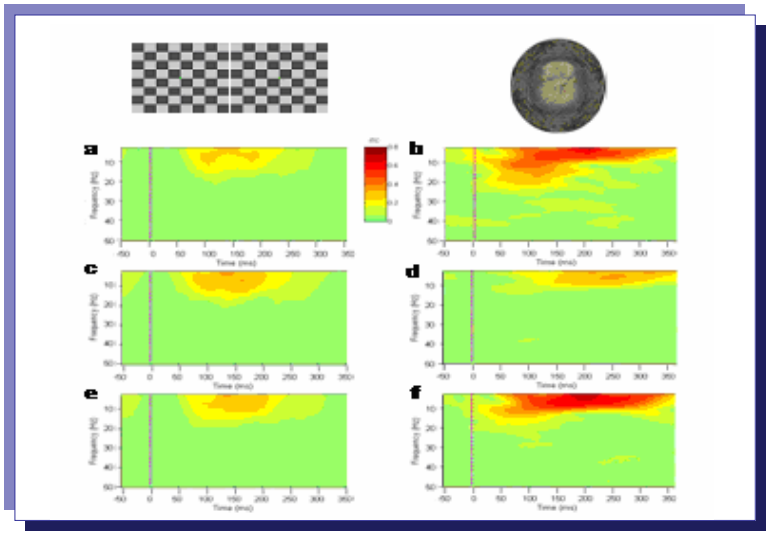

Figure 2-11: Inter-trials coherence of theta and alpha rhythms in response to a standard checkerboard pattern (a, c, e) and to the presentation of a curved tunnel (b, d ,f) on the ground before flight (a, b) in flight (c,d) and on the ground after flight (e, f)

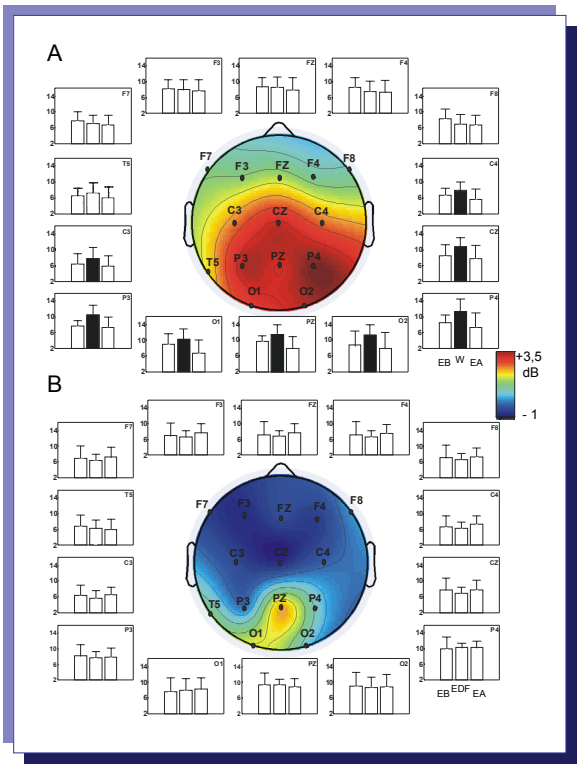

Figure 2-12: Difference in the power gain of 10 Hz activity between the recordings performed in the ISS and on Earth

Motion-onset related visual evoked potentials (M-VEPs) were recorded at a latency of ~200 ms (N200) when the first in depth motion appeared during the virtual navigation. The N200 was supported by a very significant phase locking in the theta range oscillation. It was shown for the first time that this N200 and the related phase locking in theta oscillation are suppressed during the first days in weightlessness and that this effect is reinforced in free-floating condition. Interestingly, this M-VEP reappeared with the time passed in weightlessness and will be carefully followed in the long-term ISS missions.

2.3.1.3.3.3 Conclusions and Recommendations

Three main conclusions can be made from the results obtained:

1. Weightlessness specifically affects event related potential related to the presentation of a virtual 3-D navigation tunnel.
2. Weightlessness increases alpha rhythm gain during transition between eyes-closed and eyes-open states.
3. Moving in virtual navigation induced midfrontal N200 event related potentials supported by a transient theta ringing altered in weightlessness.

In any given EEG recording session a complete loss of signal (flat line) was sometimes observed on one or more of the 14 EEG channels. This loss of signal is often accompanied by a zero impedance level during the impedance check prior to the start of recording. This may be due to changing characteristics of the conductive cream with time, differences in environmental conditions between ground and flight (humidity, temperature, etc.) or due to the application of a greater quantity of cream during in-flight sessions than on the ground. Post-flight debriefing with the cosmonaut suggested that the latter may have been the case.
Future experiments using EEG should provide real-time or quasi-real-time monitoring of EEG signals on the ground. Downlink should be timely enough to allow for the correction of problems during the course of a data collection session, or at least soon enough to allow for the repetition of a session in the case of data loss.
The assurance of adequate training time should be a critical factor in the planning of future experiments.

2.3.1.3.3.4 Publications

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4. G. Cheron, A. Leroy, C. De Saedeleer, A. Bengoetxea, M. Lipshits, A. Cebolla, A. Berthoz, J. McIntyre, (2005), "Alteration of the visual evoked potentials related to the presentation of a virtual 3D tunnel in weightlessness", *Life in Space for life on Earth (Cologne2005),* pp. 213-214
5. J. McIntyre, G. Cheron, C. De Saedeleer, A. Bengoetxea, M. Lipshits, A. Cebolla, A. Berthoz, M. Vidal, D. Chaput, E. Lorigny, (2005), "Effects of gravity on perceiving the angle of turns during virtual movement", *Life in Space for life on Earth (Cologne2005),* pp. 236
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7. A. Bengoetxea, A. Cebolla, C. De Saedeleer, A. Leroy, A. Berthoz, J. McIntyre, G. Cheron, (2006), "Weightlessness effects on visual evoked potential related to virtual in-depth motion", *Proceedings of the Science on European Soyuz Missions to the International Space Station (Toledo, Spain),* pp. 63
8. A. Cebolla, C. De Saedeleer, A. Bengoetxea, A. Leroy, A. Berthoz, J. McIntyre, G. Cheron, (2006), "Microgravity specifically affects visual evoked potential related to a virtual 3D navigation tunnel", *Proceedings of the Science on European Soyuz Missions to the International Space Station (Toledo, Spain),* pp. 64
9. M. Vidal, M.A. Amorim, J. McIntyre, A. Berthoz, (2006), "The perception of visually presented yaw and pitch turns: assessing the contribution of motion, static, and cognitive cues", *Percept Psychophys., Vol. 68, No. 8*, pp. 1338-1350

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2.3.1.3.4 Sympathoadrenal activity in humans during spaceflight (SYMPATHO-1)

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2.3.1.3.4.1 Background, Objectives and Procedures

It was previously shown that sympathoadrenal activity contrary to expectation was increased during spaceflight as compared to ground-based observations in the supine position. Plasma norepinephrine (NE) concentrations were increased in four astronauts studied on the 5th and 6th day of the D2-mission (J Appl Physiol 1995; 78: 2253-2259). Furthermore, urinary excretion rates of both NE and epinephrine (E) obtained from two astronauts during a MIR-mission were above supine levels obtained in ground-based experiments. No correlation was obtained between urinary excretion rate of NE and E and the length of the mission between day 5 and 164 (Lancet 2000; 356: 1577-1578).
Therefore the following hypothesis was proposed: Sympathoadrenal activity is low during the first 24 hours as suggested by simulation studies of microgravity, but the activity increases subsequently due to a pronounced decrease in intravascular volume.
The sympathetic system is that part of the nervous system that accelerates the heart rate, constricts blood vessels, and raises blood pressure. To test this hypothesis, measurements of mean 24-hours plasma NE and E concentrations as evaluated by quantification of thrombocyte NE and E concentrations were proposed. These measurements are not dependent on renal function and included NE derived from the gastrointestinal tract. The ratio between plasma NE and thrombocyte NE and between plasma E and thrombocyte E is constant and independent of the actual plasma level. The half-time of thrombocyte NE is approximately 2 days. Blood samples were therefore obtained before the mission and early post flight. In addition thrombocyte NE and E in blood samples obtained in ground based experiments were measured before and during head-down bed rest. Plasma and thrombocyte NE and E were analysed by a sensitive and precise radioenzymatic assay.

From the research it was expected to find increased thrombocyte NE and E concentrations early post flight indicating increased sympathoadrenal activity during spaceflight. Furthermore, it was also expected to find a low 24-hours sympathoadrenal activity in the head-down bed rest study.
Previous studies and the proposed study are of importance to the space programme, because the present findings indicate that the head-down tilted procedure cannot be applied to simulate microgravity as observed in space. It is therefore important to develop another more reliable model for simulation of microgravity. Furthermore, the elevated plasma NE and E concentrations observed in space may have an important secondary effect on cellular function in the immune system and in the endocrine system.
All study protocols were reviewed and approved by Ethics Committees at the ESA Medical Board and were in compliance with the declaration of Helsinki II.

SYMPATHO-1 was first conducted as part of the experimental package of the ESA supported Soyuz missions during increment 8, 9, 10 and 11.

The Head Down Bed Rest (HDBR) study.
Nine normal subjects participated in all 4 study phases (see Table 2-3).

Table 2-3: Study design and phases

ADAPTATION PERIOD (9 DAYS)	INTERVENTION PERIOD (14 DAYS)
Normocaloric diet, ambulatory	Phase 1: Normocaloric diet, ambulatory
	Phase 2: Normocaloric diet, 6° head-down tilt
	Phase 3: Hypocaloric diet, ambulatory
	Phase 4: Hypocaloric diet, 6° head-down tilt

One subject participated only in phase 1 and another subject participated in the following three study periods. The mean age was 23.8 years (range 21 to 29 years). The mean body mass index was 23.0 kg/m^2 (range 19.2 to 27.8 kg/m^2). All subjects were healthy and had a normal heart rate and blood pressure.
Study phase 1 and 2 started with an adaptation period of 9 days (-9 to -1) where the subjects were ambulatory. This was followed by an intervention period of 14 days (+1 to +14), where the subjects at random were either ambulatory or subjected to -6° HDBR and vice versa. Study phase 3 and 4 was performed in the same way except that all subjects were on a hypocaloric diet during the intervention period. Phase 2 and 4 were the HDBR study and phase 1 and 3 the ambulatory study.
The daily normocaloric diet consisted of protein (1 g per kg body weight per day), fat (30% of the energy, the fatty acid composition was saturated and polyunsaturated fatty acids) and carbohydrate (remaining calories). In addition the subjects received 50 ml of water per kg body weight, 2.5 mmol sodium/kg, 1000 mg Calcium and 400 IU vitamin D per day. The hypocaloric diet had an energy intake of 75% of the respective normocaloric ambulatory diet.
All subjects received the same amounts of water, protein, sodium, calcium and vitamin D. Intake of alcohol and caffeine was not allowed. All other nutrients without experiment-specific requirement matched dietary recommended intake levels of the German Nutrition Society. In the adaptation period in the 4 phases all subjects received the normocaloric diet of identical nutrient composition. Total energy expenditure was calculated as basal metabolic rate multiplied by the physical workload plus the calculated thermic effect of feeding.
The test subjects stayed in the laboratory at all times also during the ambulatory study phases. Subjects were not allowed to do any exercise on a voluntary basis. However, in phase 1 and 3 subjects followed an exercise protocol, which was two times 15 minutes of bicycle ergometry (about 125W).
Blood samples for plasma and platelet catecholamines were collected from an antecubital vein. The samples were always collected in the morning at 7 a.m. with subjects in the supine position. The blood samples were immediately brought to the laboratory and prepared for analysis. Blood samples were obtained on day -4 and day -2 in the adaptation period and again on day +5, +9 and +14 during the intervention period. No samples for catecholamine analysis were obtained in the recovery period.
For practical reasons, the preparation of blood samples differed in the HDBR study compared to the microgravity study. For this reason no comparison was made of absolute values between the two groups. Relative changes observed in relation to the corresponding basal values in the adaptation period and pre-flight were compared.

Spaceflight study

Blood samples for platelet measurements were collected from an antecubital vein in 5 male cosmonauts. The mean age was 41 years (range 37 to 45 years). The cosmonauts participated in 3 Soyuz missions to the International Space Station. Samples were collected approximately 14 days before launch, after 11 to 12 days in flight, within 12 hours upon landing and finally at least 14 days thereafter.

Samples for platelet norepinephrine and epinephrine measurements should preferably have been obtained in-flight, but this was not possible because no centrifuge with an adjustable speed was available on the International Space Station. Due to the long half life of platelet norepinephrine and epinephrine (see below) a sample taken after 11 to 12 days in flight and within 12 hour after landing would still reflect the microgravity state. The half life of platelet norepinephrine was tested in 5 normal subjects during the first 4 days of another HDBR study.

The mean half life for platelet norepinephrine was 54 ± 12.5 hours. There was a tendency for an inverse relationship between the half life and the basal platelet norepinephrine values.

The platelets could not be counted at the sampling site and therefore the preparation of the platelets had to be modified. After the initial centrifugation at 350 G, samples of 0.5 ml were added to eppendorf tubes and centrifuged, decanted and frozen at -20°C. In addition at least two times 0.3 ml plasma samples were obtained and added to eppendorf tubes. These samples were not centrifuged but frozen and later applied for counting the number of platelets. A preliminary study indicated that the number of platelets remained the same before and after freezing. The mean platelet level in the cosmonauts pre-flight and within 12 hours after landing averaged 243 ± 20 and 261 ± 56 x 10^9/l. These values were not significantly different and well within normal range (140-340 x 10^9 platelets/l). Plasma and platelet norepinephrine and epinephrine concentrations were quantified by a sensitive and precise radioenzymatic assay.

2.3.1.3.4.2 Results

Platelet norepinephrine decreased significantly during HDBR. The tendency for platelet norepinephrine to decrease during the normocaloric ambulatory study was not significant. The hypocaloric diet had no effect on platelet norepinephrine levels, which decreased during the HDBR but remained unchanged during the ambulatory study period. The mean platelet norepinephrine level in the four experiments in the adaptation period before the intervention averaged 42.9 ± 9.8 (mean ± Standard Error (SE); *phase 1*), 41.2 ± 7.4 (*phase 2*), 34.4 ± 8.3 (*phase 3*), and 32.9 ± 8.3 (*phase 4*) pg/10^8 platelets. The values obtained in the adaptation period in phases 1 and 2 tended to be higher than in phases 3 and 4 .

Platelet norepinephrine levels varied between individual subjects, but values in the same subject in the two samples obtained in the four adaptation periods were correlated. There was also a strong positive correlation between platelet norepinephrine values in the adaptation period and during the intervention, indicating that the relative decrease in platelet norepinephrine was approximately the same in all subjects. The corresponding values for platelet epinephrine in the adaptation period were 2.7 ± 0.7 (*phase 1*), 2.9 ± 0.9, 2.3 ± 0.8, and 2.6 ± 0.5 pg/10^8 platelets (not significant). Platelet epinephrine did not change significantly during HDBR and was not influenced by the hypocaloric diet.

Table 2-4: Plasma norepinephrine in 10 normal subjects during the adaptation and intervention periods

PHASE	DAY -4	DAY -2	DAY 5	DAY 9	DAY 14	P-VALUE
1	0.18 ± 0.04	0.11 ± 0.02	0.12 ± 0.04	0.11 ± 0.03	0.15 ± 0.04	Not significant
2	0.24 ± 0.06	0.15 ± 0.04	0.09 ± 0.01	0.09 ± 0.01	0.11 ± 0.01	0.01
3	0.16 ± 0.03	0.09 ± 0.01	0.07 ± 0.01	0.11 ± 0.03	0.22 ± 0.05	0.002
4	0.21 ± 0.04	0.09 ± 0.01	0.07 ± 0.01	0.06 ± 0.01	0.11 ± 0.02	0.001

Table 2-4 shows plasma norepinephrine during the four phases. In the HDBR with normocaloric diet plasma norepinephrine decreased significantly, but the decrease occurred already between the first and second sample in the adaptation period. A similar response was seen in the adaptation period of phase 4. During phase 3 (hypocaloric and ambulatory), plasma norepinephrine increased significantly at the end of the intervention period. Thus there was no change in plasma norepinephrine that could be related to HDBR. Plasma epinephrine values were low, with mean values ranging from 0.00 to 0.02 ng/ml. No significant differences were observed.

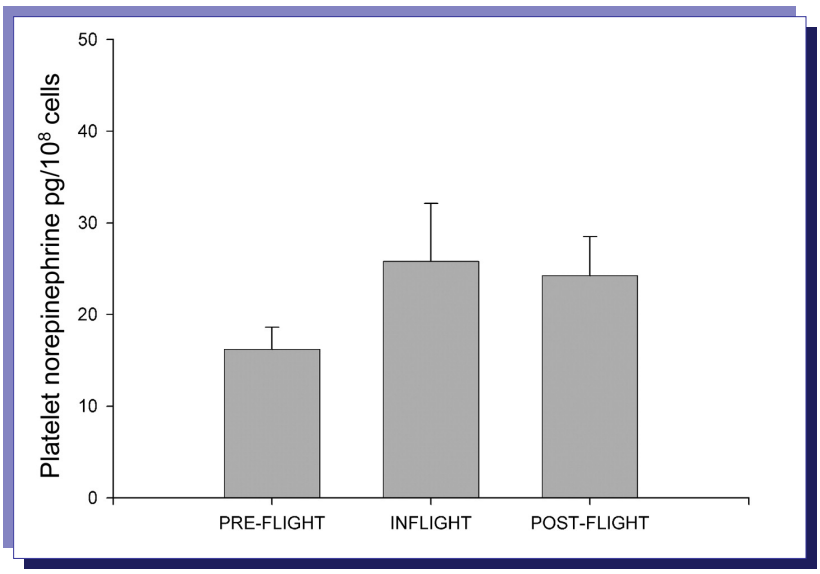

Figure 2-13: Mean platelet norepinephrine values (+/- SE) in 5 cosmonauts (one value was missing post flight)

Figure 2-13 shows platelet norepinephrine values in the cosmonauts. Pre-flight values were within normal range but in the lower end. Epinephrine values averaged pre-flight 1.5 ± 0.3, in-flight 3.8 ± 1.1, and post flight 2.1 ± 0.2 pg/10^8 platelets. Platelets from subjects participating in the HDBR study and from the cosmonauts were processed and stored in different ways, and a comparison of the absolute values may not be relevant. The relative changes may, however, be compared. Platelet norepinephrine during microgravity and during HDBR expressed in percentage of basal values (pre-flight or pre-HDBR values, respectively) were significantly different (152.6 ± 28 vs. 59.8 ± 5.7%) for a difference between in-flight and HDBR (Figure 2-14).

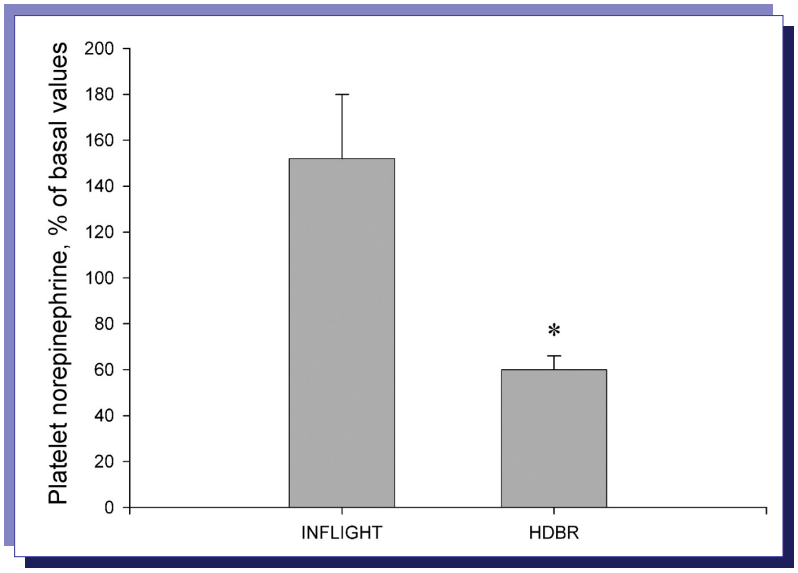

Figure 2-14: Platelet norepinephrine during microgravity and during HDBR expressed in percentage of basal values

Comparison of in-flight values with values from the phase 4 study was also significant (152.6 ± 28 vs. 57 ± 6.6%). Comparing platelet epinephrine in the same way as norepinephrine indicated that platelet epinephrine was significantly different during microgravity compared with the HDBR experiment [293 ± 85 vs. 90 ± 12% (*phase 2*) and 89 ± 18% (*phase 4*)]. Thus there was a marked and highly significant difference in platelet norepinephrine and epinephrine responses during microgravity compared with HDBR. The lack of a decrease in platelet norepinephrine in cosmonauts compared with participants in the HDBR study cannot be explained by the relatively lower pre-flight values. In the phase 4 study, four subjects had mean values in the adaptation period below 20 pg/10^8 platelets (range from 5 to 17.5), and all values decreased during HDBR.

2.3.1.3.4.3 Conclusions and Recommendations

Several studies have now demonstrated, contrary to expectations, that sympathetic nervous activity is not decreased during microgravity, and it is most likely increased compared with ground-based values. In 1995 it was reported that plasma norepinephrine values were elevated in-flight and above values observed in the seated position in ground-based experiments. Ertl et al. concluded that baseline sympathetic neural outflow was increased moderately in-flight. Furthermore, in the same study it was demonstrated that the norepinephrine spillover rate was significantly increased in space. In this study, the steady-state concentration of the norepinephrine tracer was measured in venous blood and not in arterial blood, and the calculated clearance values are therefore too high and to some extent dependent on variations in the local uptake of the tracer in the forearm tissue. Results of the present study are in accordance with previous study in which it was shown that plasma norepinephrine concentrations were increased during microgravity. Thus results from all three studies, which applied different techniques to study sympathetic nervous activity, support the concept that sympathetic activity is moderately increased during microgravity. The platelet measurements showed high epinephrine values during microgravity that were not observed in the previous study. The reason may be that in the first study samples were obtained from a forearm vein and epinephrine in arterial blood is extracted by forearm tissues. Platelets circulate through all parts of the body and take up catecholamines from plasma. Platelet epinephrine may therefore be a more reliable index of epinephrine release in the body than epinephrine in forearm venous blood. The exact interrelationship during microgravity between the initial increase and gradual decrease thereafter in cardiac output and plasma volume and the increment in sympathetic nervous activity during spaceflight remains to be elucidated. Furthermore, the difference in the norepinephrine response to HDBR and microgravity should also be explained. Very early during microgravity cardiac output is markedly increased and there may well be universal cardiovascular dilatation. With the decrease in plasma volume cardiac output decreases and sympathetic activity must be increased to maintain arterial blood pressure at a nearly normal level. Thus cardiovascular variables in flight are maintained at a level between supine and sitting in ground based observations (Norsk et al. Hypertension 2006; 47: 69-73). The sympathetic nervous system has relatively little influence on the cardiovascular system above the heart and sympathetic vasoconstriction is therefore mainly observed in the lower part of the body (Watenpaugh et al. J Appl Physiol 2001; 90, 1552-1558). Thus in flight there is vasoconstriction in the lower part of the body and dilatation above the heart.

The reduction in plasma volume during HDBR has little influence on basal sympathetic nervous activity as long as the subjects are supine. After prolonged bed rest the subjects have a tendency to develop orthostatic hypotension, which largely can be corrected for by fluid intake.

The possibility that the increase in sympathetic activity during microgravity is due a decrease in the sensitivity to catecholamines is not likely. It has clearly been shown that there is vasoconstriction in flight both as measured by total vascular resistance and by measuring calf blood flow.

In conclusion, a relative high sympathoadrenal activity compared with pre-flight values seems to be an integrated part of the regulatory response to microgravity. Furthermore, HDBR cannot be applied to simulate changes in sympathoadrenal activity in humans during microgravity.

2.3.1.3.4.4 Publications

N. J. Christensen, M. Heer, K. Ivanova, P. Norsk, (2005), "Sympathetic nervous activity decreases during head-down bed rest but not during microgravity", *J Appl Physiol, 99*, pp. 1552-1557

3 ACRONYMS

ARGES	Atomic densities measured Radially in metal halide lamps under microGravity conditions with Emission and absorption Spectroscopy
ATCC	American Type Culture Collection
BDC	Baseline data collection
BPV	Blood pressure variability
BRS	Baroflex sensitivity
CARDIOCOG	Cardiovascular adaptation to weightlessness
CHROMOSOME	Chromosomal aberrations in blood lymphocytes of astronauts
CNS	Central nervous system
CSA	Canadian Space Agency
DGGE	Density Gradient Gel Electrophoresis
DNA	Deoxyribonucleic acid
E	Epinephrine
ECG	Electrocardiogram
EEA	Erasmus Experiment Archive
EEG	Electroencephalogram
EGF	Epidermal growth factor
ERP	Event related potential
ESA	European Space Agency
ESF	European Science Foundation
ETD	Eye tracking device
EVA	Extra Vehicular Activity
EVP	Event related potential
FISH	Fluorescence in-situ hybridisation
FO	Flight operations; Functional objective
HDBR	Head down bed rest
HDT	Head down tilt
HF	High-frequency
HID	High-intensity discharge
HMI	Human machine interface
HP	Heat pipes
HR	Heart rate
HRV	Heart rate variability
HUT	Head-up tilt
IBI	Interbeat interval
IFOC	ISS Flight Order Contract
ISS	International Space Station
IU	International units
JAXA	Japan Aerospace Exploration Agency
LBP	Low back pain
LED	Light-emitting diode
LET	Linear energy transfer
LF	Low frequency
LP	Listing's plane
MASER	MAterial Science Experiment Rocket
MESSAGE	Microbial experiment on Space Station about gene expression
MLI	Multilayer insulation
MSG	Microgravity Science Glovebox
M-VEP	Motion-onset related visual evoked potential
NASA	National Aeronautics and Space Administration
NE	Norepinephrine
NeuroCOG	Directed attention brain potentials in virtual 3-D space in weightlessness
NO	Nitric oxide

NRS	Numeric rating scale
NSR	Nose, skin and rectum
NTD	Nuclear track detector
NTDP	Nuclear track detector packages
OI	Orthostatic intolerance
OLP	Ordered liquid phases
OSL	Optical luminescence detectors
PBU	Plunger box unit
PCB	Printed circuit board
PromISS	Counterdiffusion protein crystallisation in microgravity and its observation with the Protein Microscope for the ISS
Q-PCR	Quantitative polymerase chain reaction
ROI	Region of interest
Roscosmos	Russian Space Agency
SAA	South Atlantic Anomaly
SAS	Space adaptation syndrome
SBP	Systolic blood pressure
SE	Standard error
SIC	Sickness induced by centrifugation
SSD	Scintillator/silicon detectors
SV	Stroke volume
SYMPATHO	Sympathoadrenal activity in humans during spaceflight
TEPC	Tissue equivalent proportional counter
TEXUS	Technologische EXperimente Unter Schwerelosigkeit
TIM	Thermotoga marirtima triose phosphate isomerase
TLD	Thermoluminescence dosimeter
US	United States
VEP	Visual evoked potential
VOR	Vestibulo-oculomotor response
ZARM	Zentrum für Angewandte Raumfahrt Microgravitation