

Opinion on a request concerning a study of healthy volunteers during an experiment simulating cardio-vascular and supporting tissues modifications in a weightless environment. Report.

N° 11 - December 6, 1987

Contents

[Opinion](#)

[Report](#)

[Justification for the project](#)

[Technical summary](#)

[Ethical considerations](#)

[Conclusion](#)

Opinion

This space physiology study seeks to gain an understanding of human adaptation processes to the special environment created by micro-gravity and to define physical and pharmacological countermeasures designed to prevent the onset of disorders induced by weightlessness. The object is to provide better conditions as regards comfort and security for future space crews. The experiment is designed to reproduce on earth effects of weightlessness observed on human beings.

The Committee considered that three aspects of the request deserved special attention: risk incurred by subjects and medical care given to them, selection of subjects, and payments made to them.

1) The project as submitted seems very exhaustive as regards the nature of risks incurred, full time medical assistance supplied, and information given to subjects prior to and during the experiment.

2) Since the test includes a great many phases and lasts for some length of time, subjects need to be quite dedicated. The Committee considers that, as a consequence, the selection of subjects should be among future astronauts if at all possible as a first choice, then among researchers in the participating laboratories and students whose work is connected with this kind of problem.

3) Since such personnel would be able to participate actively in the experiment, they would be entitled to expect some payment for their work. In the circumstances, two consequences of this view are:

- firstly, the amount paid to them should not be calculated on a lump sum basis. On the contrary, it should be evaluated according to actual work performed.

- secondly, existing labour legislation should apply, in particular as regards taxes and social security.

As a result, payment granted can in no way be considered as using the human body for commercial purposes.

It would be desirable in such circumstances that a third party, unconnected with any of the participants in the experiment, should decide the amount to be paid.

Report

"Study on healthy volunteers of the effects of depressurising the lower half of the body as a countermeasure to be used in space medicine. This study will be carried out during an experiment simulating cardio-vascular and supporting tissue modifications observed in human beings in a weightless environment".

Preliminary comment

This project, submitted to the National Consultative Ethics Committee by the CNES(1) in Toulouse, represents the French arm of a joint CNES - NASA programme, of which the French portion is due to take place in the summer of 1987, whereas the American portion of the project (various forms of muscular exercises) has already been completed.

Justification for the project

Microgravity (almost total weightlessness) for whatever length of time, induces a number of physiological changes which are the cause of disorders of varying degrees of severity experienced by astronauts, either in flight or after their return.

The disorders with which the CNES project is concerned are of two kinds:

1) A cardio-vascular deconditioning syndrome (40 - 50% of crews), which leads to a decrease in cardiac performance i.e. decreased capacity for effort, and orthostatic intolerance provoking syncope in some cases. On this point, it should be mentioned that microgravity induces a marked redistribution of body fluids (blood, interstitial fluid, lymph, CSF) from the lower half of the body toward thoracic and cephalic areas. In man, volumes of approximately 2 litres are displaced.

2) Changes in supporting tissue: muscle loss (atrophy) and bone loss (decalcification). The aim of space physiology studies on these subjects is to understand human adaptive processes to the special microgravity environment, and to define physical and pharmacological countermeasures to prevent disorders brought about by microgravity, and thereby provide more comfortable and secure conditions for future space crews.

Since freedom from gravity is an impossibility on earth, methodology has been developed to reproduce at ground level some of the cardio-vascular effects and also perhaps some of the effects on bone and muscle which can be observed on human beings in microgravity. These are prolonged bed-rest, either horizontal or even better, anti-orthostatic, with lowered head (from -5 to -15°).

Furthermore, as a physical countermeasure, the lower half of the body can be placed in relative depressurization using a chamber. This method is called LBNP (lower body negative pressure). Apart from the data LBNP contributes as a physical countermeasure for the effects of supination, it is also thought that it might serve to some extent to protect from cardiovascular disorders induced by microgravity.

The LBNP method, which has been used for 20 years in various countries (USA, Soviet Union, FRG) is the centre piece of the CNES project which intends to study its effects on volunteers as regards the cardio-vascular deconditioning syndrome and muscle and bone deterioration.

The French study has two claims to originality:

- it is the first study of specific effects of LBNP (-50 mm Hg) as a prevention of cardio-vascular deconditioning;
- it includes use for the first time of technical innovations such as :

- use of non-invasive technology, e.g. spectrometry and MNR to measure bone and muscle mass and metabolism,
- consideration of the cardiac hormone, ANF, as an important factor in the regulation of hydro-mineral compartments of the body together with the renin-angiotensin-aldosterone system and AVP,
- measuring psychological effects of LBNP (quality of sleep, psychological performance, attention, vigilance).

Technical summary

Subjects

Six healthy subjects will be studied (3 in the control group, and 3 using LBNP). These medical students will be selected, fully informed volunteers. The experiment will last 6 weeks distributed as follows: 1 week baseline measurements, 1 month anti-orthostatic bed rest at -6° , and 5 days recovery.

Measurements

1) The effects of a month of bed rest will be observed and a comparison will be made between values noted during the week of preparation and those during recovery time.

The following parameters will be measured:

- cardiovascular and hormonal tolerance to orthostatism (tilting tables);
- capacity for effort (exercise bicycle)
- muscle mass (MNR imagery and electromyography);
- muscle metabolism (MNR spectrograph);
- bone density (photonic absorptiometer)
- bone metabolism (metabolites, and urinary and blood hormones, before and after 5 minutes of exercise);
- cardiac output (Fick CO₂);
- intracranial circulation output (Doppler);
- volume of lower limbs (plethysmography);
- neuro-humoral regulation of hydro-mineral volumes (urine and blood biochemistry);
- psychological performance, sleep, mood, (battery of tests and EEG).

2) Throughout anti-orthostatic -6° bed rest phase:

- daily, 3 to 6 20 minute LBNP sessions (-50 mm Hg); before and after the sessions: plethysmography of lower limbs (to measure volume and as a preventive check for phlebitis), urinary biochemistry; psychological tests;
- once a week, muscle mass test, 1 cardiac output test and blood biochemistry, 2 EEGs;
- every two weeks: 1 bone metabolism test.

Location

The entire study will take place in the Toulouse regional hospital Centre which will be providing for this purpose a team of nurses and paramedics (4 registered nurses, 4 hospital attendants, 1 dietician, 1 physiotherapist).

Medical Support Team

- Each experimental protocol will be under the responsibility of two scientists (specialist professors of the Schools of Medicine of Toulouse, Lyons, and Tours).
- Also on the medical team, two physicians from CNES, one from COMEX, four specialists, one aerospace medical specialist, one resuscitation specialist.
- During the bed rest phase, subjects will be seen twice a day by doctors.
- A medical emergency standby system will be operating.

Ethical considerations

Aim of human experimentation

Although cognitive factors (physiology of human adaptation to critical life conditions) are not entirely eliminated from the study, its aim is essentially to discover physiopathological causes for disorders of varying degrees of severity connected to being in a microgravity environment which astronauts have suffered since space flight began, and to find means of preventing them. This is a predominantly medical study, following other less sophisticated studies performed in the last twenty years (inter alia in the USA and Soviet Union). Animals were the subject of even earlier studies.

Human subjects of the study

Rather than selecting researchers from participating laboratories for these studies, those in charge decided on a group of volunteer medical students. The advantages of this decision are the following:

- the group is homogenous and composed of young men with no particular medical history,
- a severe preselection was carried out by the COMEX physicians, on the basis of medical criteria from "Air Force Class 3" (flight crews in the Air Force),
- informed consent based on easily understood data,
- active cooperation with the medical staff involved in the study.

Risks incurred

1) The first point to be emphasised is that, with the exception of blood biochemistry measurements which require the use of a temporary venous catheter, all the measuring methodology is non invasive.

2) Risks are therefore basically those of any study where human beings are exposed to critical conditions and considerable external constraint. In fact, the protocol includes taking out an insurance policy for each subject.

However, the conditions of this experiment seem optimal for the following reasons:

- severe selection of human study subjects,
- hospital environment and excellent medical and paramedical staffing for the study,
- long standing experience of aerospace biomedical research of those in charge of the study.

The technical report mentions that neither accident nor incident have been reported by countries where similar studies took place previously.

Payment

The protocol provides for a lump sum allowance of 15 000 French Francs net, per subject.

Since the experiment will require active and informed cooperation from subjects during six weeks around the clock, and cannot become a regular source of income, the principle of lump sum remuneration does not seem unethical nor does the amount seem abnormal (it represents about 10% of sums allocated to subjects of hyperbaric COMEX experiments).

Conclusion

Following in the steps of several other countries, CNES is undertaking a joint study project with NASA to investigate the biological disorders brought about by time spent in microgravity during space flight, and to prevent such disorders. The study is planned at a time when France is taking a more active part in inhabited space flight programmes, in association with other existing space powers.

The project submitted to the National Consultative Ethics Committee - and this is probably a rare example of such a project being submitted to a Committee of Ethics world wide - is a full description. It is therefore possible to assess the quality of technical arrangements, and of medical and social welfare provided for participants.

The Rapporteur has no scientific or ethical objection to make to this study as regards its justification, conditions of implementation, or feasibility.

Notes

1. Centre National d'Etude Spatiale (French National Space Study Center)

N.B. : The particular expertise of specialists from teaching hospitals in Toulouse, Lyons, and Tours as regards space physiology and all other medical disciplines involved in the project, must be emphasised.

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