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ALTEA: ANOMALOUS LONG TERM EFFECTS IN ASTRONAUTS. A PROBE ON THE INFLUENCE OF COSMIC RADIATION AND MICROGRAVITY ON THE CENTRAL NERVOUS SYSTEM DURING LONG FLIGHTS.

L. Narici[1], V. Bidoli[1], M. Casolino[1], M. P. De Pascale[1], G. Furano[1], A. Morselli[1], P. Picozza[1], E. Reali[1], R. Sparvoli[1], S. Licoccia[2], P. Romagnoli[2], E. Traversa[2], W.G. Sannita[3], A. Loizzo[4], A. Galper[5], A. Khodarovich[5], M.G. Korotkov[5], A. Popov[5], N. Vavilov[5], S. Avdeev[6], V.P. Salnitskii[7], O.I. Shevchenko[7], V.P.Petrov[7], K.A. Trukhanov[7], M. Boezio[8], W. Bonvicini[8], A. Vacchi[8], N. Zampa[8], R. Battiston[9], G. Mazzenga[10], M. Ricci[10], P. Spillantini[11], G. Castellini[12], P. Carlson[13], C. Fuglesang[13]

[1] *Dept. of Physics, Univ. of Rome "Tor Vergata" and INFN Sez. Rome2, Italy*
[2] *Dept. of Sciences and Chemical Technologies, Univ. of Rome "Tor Vergata'*
[3] *DISM-Univ. of Genova, Genova, Italy and Dept. of Psychiatry, SUNY, Stoony Brook, NY, US*
[4] *Istituto Superiore di Sanità - Roma, Italy*
[5] *Moscow State Engineering Physics Institute, Moscow, Russia*
[6] *Russian Space Corporation "Energia" by name Korolev, Korolev, Moscow region, Russia*
[7] *Institute for BioMedical Problems, Moscow, Russia.*
[8] *Dept. of Physics of Univ. and Sez. INFN of Trieste, Italy*
[9] *Dept. of Physics of Univ. and Sez. INFN of Perugia, Italy*
[10] *L.N.F. - INFN, Frascati (Rome), Italy*
[11] *Dept. of Physics of Univ. and Sez. INFN of Florence, Italy*
[12] *IROE of CNR, Florence, Italy*
[13] *Royal Institute of Technology, Stockholm, Sweden.*

ABSTRACT

The ALTEA project partecipates to the quest for increasing the safety of manned space flights. It addresses the problems related to possible functional damage to neural cells and circuits due to particle radiation in space environment. Spcifically it aims at studying the functionality of the astronauts' Central Nervous Systems (CNS) during long space flights and relating it to the peculiar environments in space, with a particular focus on the particle flux impinging in the head. The project is a large international and multi-disciplinary collaboration. Competences in particle physics, neurophysiology, psychophysiology, electronics, space environment, data analyses will work together to construct the fully integrated vision electrophysiology and particle analyser system which is the core device of the project: an helmet-shaped multy-sensor device that will measure concurrently the dynamics of the functional status of the visual system and passage of each particle through the brain within a pre-determined energy window. ALTEA is scheduled to fly in the International Space Station in late 2002. One part of the multy-sensor device, one of the advanced silicon telescopes, will be launched in the ISS in early 2002 and serve as test for the final device and as discriminating dosimeter for the particle fluences within the ISS.

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INTRODUCTION

The reports from astronauts, since Apollo missions, of Anomalous Phosphenes Perception (APP) during orbital flights (Pinsky et al. 1974, 1975), is a demonstration that space environment can affect CNS functions. Several experiments performed both on ground laboratories in the 70s (Charman et al 1971, Tobias et al. 1971, Charman and Rowlands 1971, McAulay 1971, McNulty 1971, McNulty et al. 1972, Budinger et al. 1972, McNulty and Pease 1978) and in space (Osborne et al. 1975, Bidoli et al. 2000), appear to link such APP phoenomenon to the passage of heavy nuclei through the astronauts' head, most probably through their retina. Beside the open question about the specific mechanism governing this interaction, its site is still unclear (retina? visual cortex? optic nerve? all of them?). Furthermore APP may be caused *just* by particle passages, or may be a consequence of several instances, among which particles passages play the *final triggering* role. In other words the same particle that causes the APP, could, in principle, be totally unobserved by the same astronaut on earth.

Prolonged stay in space may, in fact, modify the functional status of visual system (and in general of the CNS) so to enable it to respond to (particle related) visual inputs otherwise ineffective. Indications of modification of visual system due to permanence in space can be found in studies during previous space missions (see, for example, Clement and Reschke 1996). However functional changes of the visual system may go undetected by the astronauts if not resulting in subjective percepts, but would be recognized if using electrophysiological testing procedures. An electrophysiological study appears mandatory when planning year-long space permanencies in orbit (International Space Station) or even travelling outside the protective earth magnetic shield (Mars missions).

RATIONALE

Early studies on the effects of particles focused on the retina. However phosphenes may be perceived in several pathological or experimental conditions (migraine, partial epilepsy, direct electrical stimulation of the cortex, etc). Particle-related phosphenes have been perceived in accelerator experiments in the 70s, as well as during ion cancer therapy, and, as mentioned, during orbital and moon flights up to our most recent experiments in the MIR station.

It should be mentioned that the variety of APP reports from the many astronauts involved in orbital and moon flights is quite wide. Shapes of many kinds have been reported, as well as apparent movement or color. Finally, a broad range of frequency of these events has been observed: from astronauts who never reported APP, to those who had problems in sleeping due to their too high number. Unfortunately it appears quite difficult, if not impossible, to retrieve all these information in a form suitable for statistical analysis as most details derive from astronauts' informal reports. A suggestion clearly rise from this panorama: the causes for APP may be several. Furthermore reports of olfactory sensations during ground experiments in accelerators suggest that these interactions are not specific of one single sensory pathway.

The astronauts' frequent reports of visual abnormalities (APP) nevertheless proposes the visual system as a privileged probe for studying sensory pathways interaction with particles and, more in general, with space environment.

It should also be mentioned that the sensory systems are just the most immediate targets of our investigation. Higher, cognitive functions may as well be affected. This interaction may in fact produce undetected anormalities, for example in latency and discriminative power. The importance of assessing this hazard in a space mission, where all abilities and competences of the crew may be in any instant vital for the whole mission, would be large. Studies of interactions between brain functions and particles/space-environment is mandatory when planning long manned orbital flights for the International Space Station (ISS) and, more so, for the manned journey to Mars.

In order to give a complete answer to these problems the ALTEA project has been designed. It has been financed by the Italian Space Agency (ASI) and by the National Institute for Nuclear Physics (INFN), rated "Highly recomended" by the European Space Agency (ESA). It has a flight opportunity on the ISS for late 2002. A particle telescope from the larger ALTEA device plus an EEG is due to be launched on the ISS (Russian segment) in the early 2002.

To fulfill its goals, ALTEA must concurrently monitor particle radiation (type and trajectory of particles, energy released in the eye and brain), and the time and frequency dynamics of the electrophysiological signals of the retina and brain. In order to quantitatively measure the *functional state* of the visual system and the dynamics of sensory processing, ALTEA features a dedicated visual stimulator and procedures for visual function testing. To be able to study APP phenomena the astronaut will sign the phosphene perception with the pushing of a joystick. All this information will be acquired and analysed off line, partly on ISS, partly on ground.

Normative studies are being conducted beforehand on ground on voluntaries and a complete baseline database will be created working on the flying crew, before launch.

The design and construction of the integrated device (*Fully Integrated Vision Electrophysiology and Particle Analyser System*: FIVEPAS), the electrophysiological measurement procedure and the off line data analyses are the three major steps in the project preparation.

Several parallel investigations will be carried on to supplement the ALTEA findings and provide comparable data under laboratory controlled experimental conditions. The project includes developing and testing an animal model to be studied in accelerators. This will allow to obtain information helping in the prediction of the electrophysiological changes induced by particles for designing the FIVEPAS, the experimental procedure and the most suitable data analysis. The laboratory investigations mentioned above, performed in the 70s, were conducted by experimenters serving as subjects in accelerator experiments receiving particles in their eyes to define the particle parameters (type of particles, energies, etc) and the conditions under which the phosphenes could be experienced. No concurrent electrophysiological measurements were carried on and ethical reasons do not allow to repeat those measurements in humans. We are therefore working on a project using mice to build such a model. Normal and transgenic mice with progressive degeneration of retina receptors will be used in order to infer the location of the particle-cells interactions.

Another side issue is the design and construction of dermal electrodes that will permit a fast montage of the the system for electrophysiological recordings in space environment (we plan to use 32 channels). Prototype electrodes have been built out of non-toxical components, with composite materials made from polymeric gel, doped with alcaline and mineral salts, after a gelification process in organic solvents. The conductivity (a few parts x 10^{-4} Scm^{-1}) and the quite good stability are very promising. First EEG tests also indicate the validity of the chosen technique. Results of this work will be presented elsewhere.

Needless to say ALTEA can produce results that go well beyond its original goals. In addition to the planned baseline experiments, ALTEA is designed to qualify as a ISS *facility* to perform, for instance, real time particle identification and dosimetry inside the ISS, or sensory and cognitive electrophysiological experiments during microgravity and under high particle fluences. Proposals for these investigations are being triggered within the proper communities; suggestions for the use of this apparatus are still coming and always welcome.

A GENERAL DESCRIPTION OF THE ALTEA MULTIFUNCTION SENSORS

The *core* of ALTEA is an helmet shaped device, which will be worn by the astronauts during the data acquisition (Figure 1).

This helmet accomodates twelve active particle telescopes, the visual stimulator and the EEG.

This multifunction device, FIVEPAS, will be most probably mounted on the ISS wall. The ergonomy of the FIVEPAS is being carefully studied in order to insure maximum comfort and easyness of installation.

The different components of the FIVEPAS are designed together in order to allow for an easy and reliable integration, but they are being constructed and tested separately .

Two requirements have to be fulfilled in the FIVEPAS. The device must be easy to use and require the minimum amount of astronaut time to set up the measurements. At the same time it must feature a high degree of flexibility, in order to permit different experiments to be conducted, even experiments that at launch time may not be formalized yet. This is achieved with the use of hardware and software implemented algorhithms/procedures. Re-programming will be possibly executed from ground. The main idea is that the astronaut will wear the FIVEPAS, turn on the device, and press the 'start' button. Everything else will be pre-programmed.

We will now briefly describe the components of the FIVEPAS.

The large solid angle particle detector system features 12 Advanced Silicon Telescopes (AST), mounted in pairs in six boxes, so to have maximal covering of the head (see Figure 1).

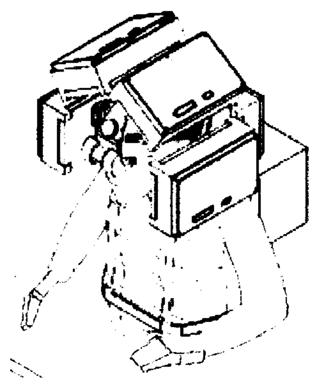

Fig. 1. A schematic view of the astronaut with the ALTEA system (frontal AST not shown)

a) The AST

The ASTs are active silicon based particle telescopes allowing for detection and discrimination of particles, particle energies, trajectories. Each AST will feature three silicon planes, each with double detector chips (view X e Y) and an area of 8 x 8 cm^2. The pitch is 2.2 mm, thickness 380 μm. Therefore 32 strips will be used for each view. The threshold will be about 1 MIP and saturation will occur at 2600 MIP. The distance between planes is 2 cm. With this number we expect an angular resolution af about 2°. The technologies are developped in SilEye, NINA and PAMELA projects, in which the ALTEA investigating team is active.

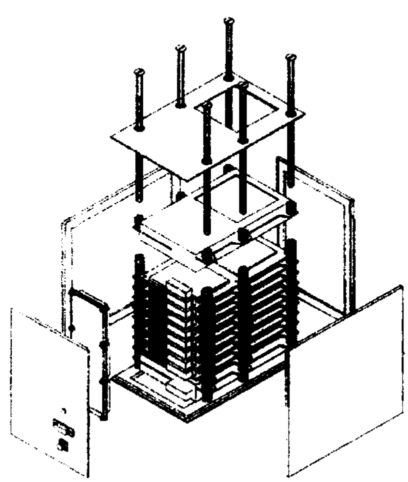

Fig. 2. A schematic view of the AST for the RS ISS

One AST, with the addition of two scintillators to extend its triggering capabilities, will be launched on the Russian segment of the ISS in the early 2002 (Figure 2).

b) Electrophysiological recordings

The system for electrophysiological recordings will feature 32 channels plus 4 channels for Electroretinograms acquisition. Newly developed electrodes will be mounted on an elastic cap in pre-determined positions (10-20 systems plus additional electrodes over the occipital cortex). The electrodes will allow for operation without the use of conductive paste/gel, and with minimum (or null) amount needed of surface preparation and impedance minimization.

c) The Visual Stimulator

To monitor the status of the visual system, a dedicated visual stimulator as well as procedures for visual testing according to the international laboratory standards will be used. The visual stimulator is an adapted Virtual Reality system, which allows for computer controlled 3D color viewing and include the possibility of stereo audio input (see Figure 1). The stimulation routine for the baseline ALTEA experiment will use luminance and contrast gray scale stimulation, exploiting only parts of the potentialities of this system. Design of more complex experiments, involving different stimulation procedures is in progress and encouraged.

d) Data acquisition

Particle passage information will be stored together with the continuous EEG, with a common time reference. The visual stimulator, synchronized with the acquisition system, will be driven by a dedicated card which will include the stimulation software.

PROCEDURES

The basic experiment includes proper training of the astronauts on ground, acquisition of baseline database, measurement in orbit and again on ground after landing; most of the data analyses will be performed off line.

A typical schedule of the experiment is presented in the following.

A) *Astronauts Training.* B) *Ground measurements* (prior to launching): i) Set-up testing; ii) Electrodes positioning (10 min); iii) Stimulation paradigm (5 min). C) *Onboard measures*: i) Set-up testing; ii) Electrodes positioning (10 min); iii) Stimulation paradigm (5 min); iv) Dark adaptation (15 min); v) electrophysiological recording and particle assessment during a full orbit (90 min). D) *Ground measurements* (after landing): i) Set-up testing; ii) Electrodes positioning (10 min); iii) Stimulation paradigm (5 min).

The stimulation paradigm is being designed in order to assess the status of the visual system following known electrophysiological models in the most compact way. We are aiming at a procedure shorter than five minutes. On board measures (C, above) will be repeated in different moments of the orbital permanence of the astronaut to follow the dynamics of the visual system status from immediately after launch to the end of the permanence in space. All measurements will be performed in relatively stable vigilance level, under proper control and monitoring.

EXPECTED RESULTS

The experiment ALTEA will allow the first complete electrophysiological investigation of the visual system in space. The quantitative dynamics of the functional parameters and the correlations of the electrophysiological activity with the passages of particles, that can be described in type, energy and trajectory in areas of the cortex that can be localized, will assess the hazard risk during long manned flight for what concerns functionality of the visual system. The electrophysiological investigations will cover all cortical regions permitting to extend these findings to other cortical areas.

ALTEA as facility will allow to set up all those experiments asking for simple or complex visual and/or auditory stimulation with concurrent EEG acquisition/particle detection. As an example, experiments aimed at assessing the level of cognitive performance during long flights might be envised.

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