Life sciences

AUTHOR
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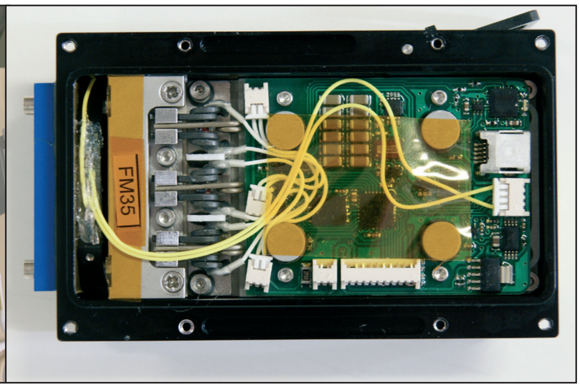
[Fig. 1]



[Fig. 2]

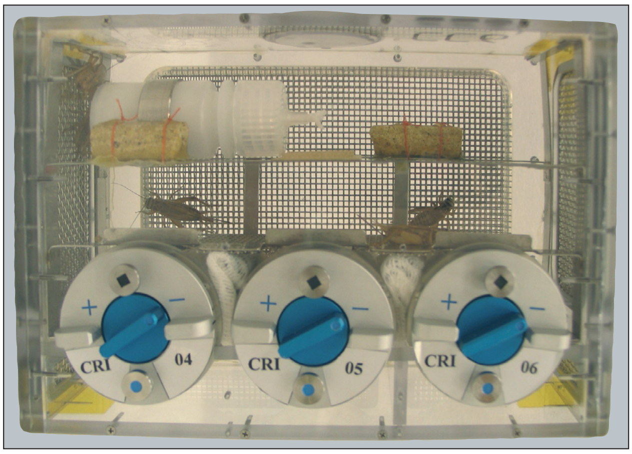
At the moment, space is bringing nations together which enables large-scale multilateral cooperation, of which the ISS is an example. We hope cooperation will increase in the future to answer the great challenge of a journey to Mars, which should provide us many answers on how the solar system works, and maybe even on the origin of life. Space exploration is in its infancy, and faces new technological, scientific and medical challenges. Overcoming them will be the dream of many a generation to come.

Gravity has shaped the plant and animal worlds for millions of years. If gravity did not exist, we would not need such a complex cardiovascular system, such as mechanisms of protection enabling to maintain a normal flow during orthostatism. This role already becomes obvious after fifteen days of microgravity, when major modifications of the cardiovascular, bone, muscular and nervous systems can be seen. Even at the cellular level, microgravity induces modifications of gene expression and modifications of the behaviour and morphology of cells. We spend most of our lives fighting against gravity.

The scientific approach –initiated by Claude Bernard and continuing with knockout animals– to better understand a system is thus to study the consequences of its exclusion. This fully justifies human and animal studies realized during space flights. The same applies to the plant kingdom (gravitropism). This is what the experiments on board Mir, the space shuttle or the ISS let us see. Concerning animal experimentation, let us note that animals will be essential on board automated stations (it is already the case on stations such as the Soviet Biocosmos, or the American Biosatellites) or future satellites (Bion and Biosputnik). Only aboard these platforms will we be able to study the effects of the absence of gravity and, more importantly, its effect on evolution.

It became clear early on that countermeasures were needed so that astronauts would not be subject to too many disorders in the station, where adaptation to space sickness is quick, but more importantly upon return (cardiovascular deconditioning, muscular atrophy, bone demineralisation, metabolic disorders). These disorders can become serious, this is why countermeasures are essential to balance the physiological effects of zero gravity. It is still impossible to know the effects of zero gravity on the organisation of life and in particular on humans. Environmental conditions such as temperature, luminosity and CO_2 levels are not well mastered, not to mention stress and workload. We also have to take into account inactivity which has similar effects to microgravity on the cardiovascular system, and on bones and muscles. Results obtained during flights, even if they are incomplete, enable to catch a glimpse of the importance of gravity in the development of life.

The life sciences scientific communities have at their disposal both space and ground complementary means to realize their experiments. In the coming years, the ISS will become



[Fig. 3]

the main means of experimentation for this field. It will also be an essential research facility for space medicine and the place of validation of technologies and procedures necessary for manned interplanetary missions. However, other means are also necessary to answer the priorities identified during the seminar of scientific prospective on microgravity sciences. These means, such as recoverable capsules, probe rockets, balloons, parabolic flights, and ground-simulation means are being set-up within national, European, and international frameworks.

Themes being studied include the muscle-skeleton system, the cardiovascular system, the neuro-sensorial system, nutrition and the energetic metabolism, plant gravitational biology, animal gravitational biology, radiobiology and psychology. Research in all these areas has applications in daily medicine. In preparation for the exploration of Mars, some themes considered as the limiting factors, such as radiobiology, psychology and life support, will need to be extensively studied.

[Fig. 4]

Fig. 1*: Inserts placed in the Kubik incubator. In order to study the effects of gravity on plants, CNES is conducting green biology experiments in zero gravity onboard the ISS in 2010.*
Fig. 2*: Inserts placed in the Kubik incubator.*
Fig. 3*: The experiment CRISP containing crickets. It aims to measure the influence of microgravity environment on the development of neurones in young cricket larva.*
Fig. 4*: Neurospat experiment being conducted at the Medes clinic.*

COSPAR 2010

Life sciences

Cardiovascular response to lower body negative pressure aboard the Mir space station.

Réponse cardiovasculaire au test du caisson à dépression à bord de la station spatiale Mir.

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Abstract

Orthostatic intolerance is often observed following spaceflight. Lower Body Negative Pressure (LBNP) mimics cardiovascular orthostatic adaptation. We hypothesized that long-term spaceflight alters differentially LBNP response to low and high level of stimulation. Changes of RR-Interval and blood pressure in response to LBNP were mainly observed at low level of stimulation indicating a change in sensitivity to blood volume instead of blood pressure.

L'intolérance à l'orthostatisme est souvent observée après un vol spatial. Le caisson à dépression (LBNP) reproduit les effets de l'orthostatisme au niveau cardiovasculaire. Nous avons posé l'hypothèse que les longs vols spatiaux altéraient différemment les réponses aux faibles et fortes dépressions du LBNP. Des variations des intervalles R-R et des pressions artérielles sont observées lors de faibles dépressions, indiquant un changement de la sensibilité au volume sanguin plutôt qu'à la pression artérielle.

Cosmonauts are exposed to cardiovascular changes induced by weightlessness. When they return to Earth they often experience orthostatic intolerance which is the main symptom of cardiovascular deconditioning [1]. Suspected causes of this symptom are changes of the autonomic nervous system at cardiovascular level. Indeed, weightlessness alters heart-rate variability and spontaneous baroreflex sensitivity [2]. However these alterations can also reflect the changes in heart rate and in blood volume observed during spaceflights. The Russian space agency used LBNP (by means of a device called "Tchibis") aboard the Mir space station (Fig. 1) to evaluate cardiovascular changes during spaceflight missions and to prepare the return of cosmonauts. This method of cardiovascular evaluation provides several levels of stimulation. A low level of stimulation (-25 mmHg) induces mainly activation of volume receptors that are sensitive to blood volume changes. While a high level of stimulation (-45 mmHg) involves both volume and baroreceptors. In this study we hypothesized that long-term spaceflight alters the cardiovascular response to LBNP.

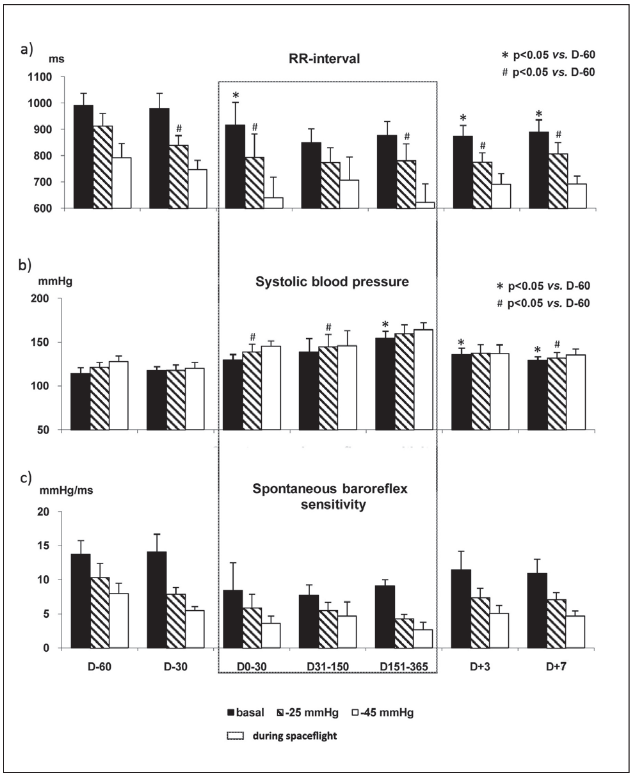
Before (at D-60, and at D-30), during (between D0–30, between D31–150, and between D151–365) and after (at D+3, and at

[Fig. 1]

D+7) spaceflight missions of different durations (two weeks to twelve months) aboard the Mir station, LBNP was applied on ten cosmonauts (nine males and one female, 42 yr ± 1 yr, 73 kg ± 3 kg, 1.76 m ± 0.02 m, mean ± SEM). The protocol consisted of 10 min at rest followed by 5 min at -25 mmHg, 1 min at -35 mmHg for adaptation and 5 min at -45 mmHg. Heart rate and Systolic Blood Pressure (SBP) were monitored by means of an electrocardiogram and a non-invasive beat-by-beat measurement system (Portapres® finger photoplethysmography) developed by CNES during the whole LBNP protocol. The mean of each cardiovascular variables described above was calculated for the five minutes at -25 mmHg and -45 mmHg. BaroReflex Sensitivity (SBRS) was evaluated by the spontaneous baroreflex sequence method. Results were analyzed by ANOVA for repeated measurements followed by t-tests.

The number of LBNP sessions was restricted because of the cosmonauts' timetable: four sessions for each period (D0–30, D31–150 and D151–365). As expected, RR-interval (RRI) tended to decrease during spaceflight mission. This effect was clear at -25 mmHg but not at -45 mmHg (Fig. 2a). However, shorter RRI at D-30 was already observed in comparison to D-60. SBP tended to increase during flight whatever the LBNP level (Fig. 2b) while SBRS tended to decrease (no significant differences) (Fig. 2c).

The low number of LBNP sessions represented a major limitation of this study. This limitation emphasized the large amount of cardiovascular problems during missions. However, our study is the first report of cardiovascular response to simulated orthostatic stress during real weightlessness. The significant decrease of RRI observed even before space-flight at -25 mmHg of LBNP indicates that stress and workload are partly responsible for the cardiovascular changes observed during spaceflight. The alterations of RRI and in blood pressure during flight observed at -25 mmHg of LBNP should not reflect the decrease of blood volume nor the baroreflex alteration because no flight effect was observed at higher level of LBNP. These results indicate a change in the sensitivity of low pressure baroreceptors which seemed more sensitive to blood volume changes during spaceflight missions.



[Fig. 2]

Fig. 1: *A cosmonaut during a LBNP session aboard the Mir space station.*

Fig. 2:

a) mean of RR-interval during LBNP session before (D-60, D-30), during (between D0–30, D31–150, D151–365) and after (D+3, D+7) spaceflight mission.

b) mean of systolic blood pressure during (between D0–30, D31–150, D151–365) and after (D+3, D+7) spaceflight mission.

c) mean of spontaneous baroreflex sensitivity during (between D0–30, D31–150, D151–365) and after (D+3, D+7) spaceflight mission.

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COSPAR 2010

Life sciences

Effect of the change in root statocyte polarity on free calcium distribution.

Changement de la polarité des statocytes sur la répartition du calcium libre.

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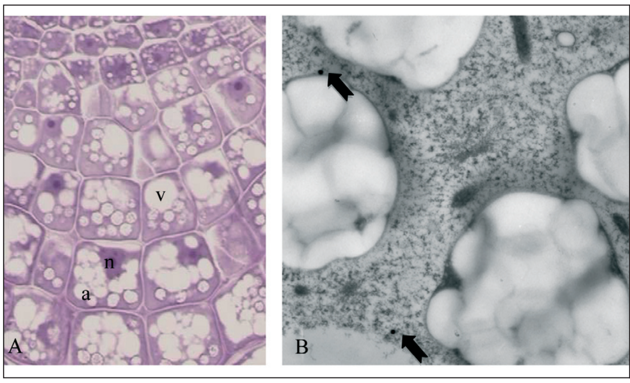
Abstract

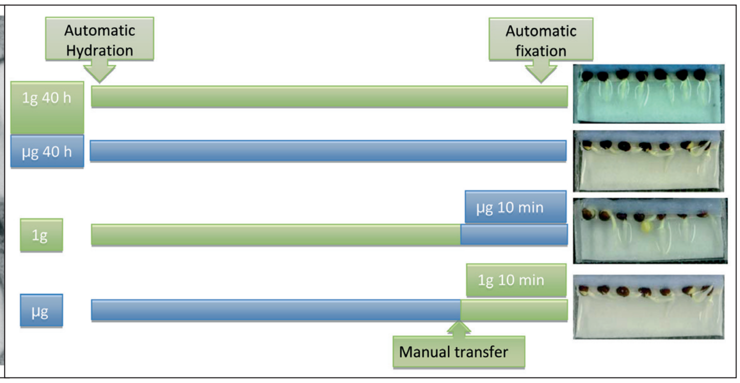
The root cap cells are the only cells that exhibit structural polarity with respect to gravity, providing interactions with amyloplasts and the cortical endoplasmic reticulum. There is no clear evidence that a change in these interactions could lead to a transduction gravity signal. The proposed scenario in the space experiment PolCa allowed to analyse the effect of these interactions on calcium distribution. The first results show that amyloplast displacements induce changes in calcium distribution.

Les cellules de la coiffe racinaire présentent une polarité structurale par rapport à la gravité. Cette polarité conduit à des interactions entre les amyloplastes et le réticulum endoplasmique. Peu d'études ont montré clairement qu'une modification de ces interactions conduisait à la transduction du signal gravité. Le scénario proposé lors de l'expérience spatiale PolCa permet de suggérer qu'un déplacement des amyloplastes induit des changements dans la répartition du calcium.

Plants have the ability to sense and to re-orient their growth in response to gravity. In roots, specialized sensory cells (called statocytes) perceive signal gravity and are the only cells that exhibit structural polarity with respect to gravity providing interactions with starch-containing plastids (amyloplasts) and the cortical Endoplasmic Reticulum (ER) [1]. Upon root reorientation, a displacement of amyloplasts is observed and is accompanied by a change in direct amyloplast-ER interaction in root cap cells. Even if amyloplasts are widely considered as gravity sensors, there is no clear evidence that a change in amyloplasts-ER interactions could lead to a transduction gravity signal. Previous space experiments clearly showed that amyloplasts interaction with ER is not necessary to lead to a root re-orientation, suggesting that amyloplasts displacement mediate transduction events through cytoskeleton reorganisation and calcium-dependant pathways [2] [3]. The main objective of the space experiment called PolCa is to dissect the effect of change in amyloplasts-ER interactions on calcium distribution.



[Fig. 1]



[Fig. 2]

Flight scenario

The PolCa experiment was performed on the ISS in the ESA Kubik instrument following the scenario presented in Fig. 1. Briefly, *Brassica Napus* seeds were set up on filter paper in culture chambers developed by CNES. One set of fixative chambers was filled with a fixative solution containing 2% paraformaldehyde, 0.5% glutaraldehyde and 3% potassium pyroantimonate in potassium phosphate buffer. Once in the ISS, the experiment was activated by an automatic hydration. The seedlings were submitted to four situations (1) continuously on 1 *g* centrifuge, (2) continuously in microgravity conditions, (3) seedlings germinated in microgravity conditions were transferred to centrifuge during 10 min (4) seedlings germinated on centrifuge were transferred to microgravity conditions during 10 min. After 40 hours of growth, the fixative was released automatically from the fixative chamber and containers were stored at 4° C. Once on Earth, containers were transported to the laboratory where they were opened. After having taken photos, roots were transferred to buffer medium and then progressively dehydrated and embedded in LR white resin. Ultrathin sections from root cap were obtained and observed with an electron transmission microscope.

Seed germination and root growth

We obtained 91% of seed germination illustrating the technical success of this experiment. The mean length of all roots was near 6 cm and there is no significant difference of root length between microgravity condition and 1 *g* centrifuge. The analysis of root orientation (Fig. 1) after 40 hours of growth on 1 *g* centrifuge showed that the roots are oriented in the direction of the centrifugation force. After having grown in microgravity conditions, roots developed a bending on root tips which seems to have a random origin.

Free calcium distribution

Electron transmission microscopy observations revealed that the presence of calcium precipitates of roots maintained in 1 *g* are mainly near amyloplasts but also in the nucleus (Fig. 2). This distribution is not significantly different from that observed in statocytes of roots grown in microgravity conditions.

Our first observations showed that calcium precipitates are affected following a transfer to microgravity conditions or to 1 *g* conditions. These situations induced amyloplasts' displacement and our results suggest that this displacement may play an important role in calcium signalling pathways.

We thank B. Eche and G. Gasset (GSBMS, Toulouse, France) for excellent technical assistance in the ground experiment as well as D. Chaput (Toulouse, CNES). We are grateful to the ESA team at ESTEC (Noordwijk, The Netherlands) and USOC teams for the preparation of the flight mission. The hardware was developed by COMAT (Toulouse, France). This work was supported by CNES.

***Fig. 1**:*
A) Semithin section of the central root cap from one sample grown in microgravity condition. The majority of amyloplasts are distributed in the upper part of the statocyte. a, amyloplast; n, nucleus and v, vacuole,
B) Ultrathin section showing the presence of calcium precipitates near amyloplasts (arrows).
***Fig. 2**: Schematic representation of scenario followed in the PolCa space experiment. Brassica Napus root orientation obtained after 40 h of growth in four different conditions. Roots grown in microgravity conditions clearly showed a deviation depending on gravity.*

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Life sciences

Psycho-environmental aspects of human adaptation in space analogs.

Aspects psycho-environnementaux de l'adaptation lors de simulations spatiales.

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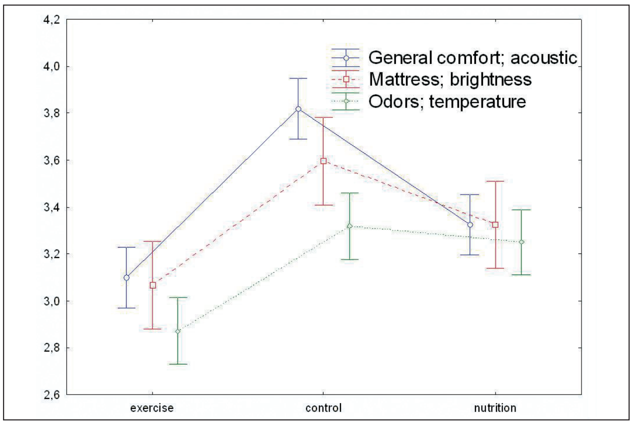
Abstract

The analysis of psycho-environmental factors shows indirect indicators of well-being and stress in isolated and confined situations, which are used as space analogs. The evaluation of environmental characteristics is correlated with stress levels, and the need for privacy reflects the level of perceived constraints. The interest of this approach is to provide tools that minimize social desirability bias.

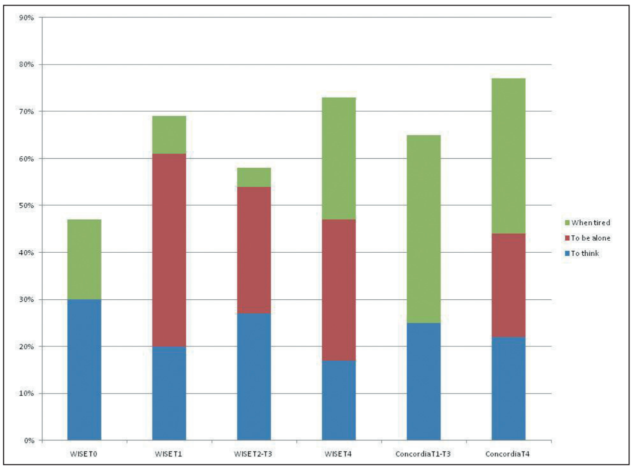
L'analyse des facteurs psycho-environnementaux met en évidence des indicateurs indirects du bien-être et du stress ressentis dans les situations d'isolement et de confinement utilisées comme simulations spatiales. L'évaluation des caractéristiques environnementales est corrélée avec le niveau de stress, et le besoin d'intimité reflète le niveau de contraintes perçues. Une telle approche est susceptible de proposer des outils de mesure minimisant le biais de désirabilité sociale.

The psychological approach of life in Isolated and Confined Environments (ICEs) usually focuses on behavioral and emotional maladjustments linked to stress. Most researchers postulate that these extreme situations constitute a source of acute stress, and consequently they omit potential positive aspects linked to such experiments. To maintain that the relations between socio-environmental constraints and negative reactions are direct and inevitable is a mistake [1]. In order to stress positive reactions in ICEs, Suedfeld & Steel (2000) [2] even speak about a "positive capsule psychology" (p. 229). A psycho-environmental approach points out both positive and negative reactions. It takes into account the whole situation, focusing on people's perceptions, related to stress as well as well-being.

The aim and interest of environmental psychology are to stress person-environment relationships as determinant factors of the well-being and the comfort (or discomfort) experienced by the subjects. It hypothesizes that the evaluation of the situation (*i.e.* the physical and social environment, the perceived goals linked to the situation, the role and status of the subject in this situation, *etc.*) plays a significant role in the adaptation process. Furthermore, the analysis of reactions to stressful conditions has shown that the perception of the situation as well as the perception of one's own means to cope with it constituted essential factors in the coping process. For instance, from a psycho-environmental point of view, monotony and under-stimulation constitute important features related to adaptation processes.



[Fig. 1]



[Fig. 2]

But on the other hand, an over-stimulation (linked to workload for instance) can also constitute a source of stress. Then, it seems that socio-environmental stimulations have an impact on person-environment relationships, and more precisely both on the evaluation of the environment, and on privacy regulations. Privacy arises as a mediating variable in well-being [3].

In order to test this impact of environmental features, we have elaborated questionnaires about the perception of these socio-environmental dimensions (evaluation of environmental features and privacy). These questionnaires were used during WISE (Women International Space Simulation for Exploration Study 2005-2006) and during a winter-over in the Concordia Antarctic station (2007). WISE concerns twenty four women, who stayed in a head-down tilt bed rest during 60 days. They were separated in three subgroups: control, nutrition and exercise. The Concordia team was constituted of fourteen men. Questionnaires were filled five times during WISE, and four times in Concordia. The WISE results have also been correlated with anxiety and stress measures.

Results show that socio-environmental factors are strongly correlated with well-being experienced by subjects who have to face isolated and confined situations. Two indicators confirm this hypothesis: the correlation with anxiety measures during WISE, and the evolution of the answers during the isolation period both in WISE and Concordia.

[Fig. 3]

During WISE, the three subgroups showed significant differences in anxiety and stress measures: the exercise group systematically had significantly higher scores in stress dimensions and lower scores in recovery dimensions, because of the important workload required by these exercises [4]. In the same way, this group also quoted environmental features as more negative than the other two groups did (see Fig. 1): they perceived more negatively the quality of their bed, brightness, odors, temperature, acoustic and general comfort than the other groups did ($p < 001$).

Privacy also raised a relevant issue: the questionnaire (inspired by Newell, 1998) included items about "why do you need a period of privacy?" and "how do you manage to get privacy?" These two questions are of interest when we look at the evolution of the answers during both the WISE and Concordia winter-over. This evolution reflects difficulties faced by the subjects. At the beginning of the isolation period, subjects specially needed privacy when they wanted to think or when they were tired. They never expressed the need to be alone. This need appeared afterwards, and then constituted the most frequent answer during WISE (Fig. 2). In the same way, during WISE, privacy didn't require at the beginning that "no one bothers me"; this need appeared with the second questionnaire's administration. In Concordia, this was never expressed, maybe because people had their own private space.

One important implication of these results is that well-being experienced in ICEs could be measured by indirect socio-environmental indicators, which point out quite well the perceived level of constraints: if someone evaluates his environment as very constraining and uncomfortable, this means that he does not live it in a positive way. Questions about environmental features are perceived as less personally involving by subjects, who are answering with more spontaneity than when we ask them about their mood or health states. The social desirability bias could then be bypassed using indirect indicators such as these ones. These tools are going to be used during the next Mars 500 study.

Fig. 1*: Global evaluation of comfort features by the three subgroups (exercise, nutrition and control) during WISE.*
Fig. 2*: Evolution of answers to the question "why do you most need privacy?" during WISE (five questionnaire administrations: T0-T4) and Concordia winter-over (four administrations: T1-T4). Columns from left to right: WISET0; WISET1; WISET2-T3; WISET4; ConcordiaT1-T3; ConcordiaT4.* ***Legend:*** *green: when tired; red: to be alone; blue: to think.*
Fig.3*: The Concordia station.*

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