Using a tri-axial accelerometer to quantify the locomotive patterns before and after 60 days of bed-rest

Master Thesis presented

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Abstract

The effects that microgravity induces to the human body are well known. Unfortunately, how to completely counter them is not yet clear. One method among others is very effective to mimic and simulate these effects to study them on Earth – the bed-rest study. To date, the best countermeasure known to preserve the physiological functions during a spaceflight or during bed-rest is physical exercise.

This thesis aims to quantify, using a tri-axial accelerometer, the changes in locomotive patterns and levels of physical activity (PA) before and after a 60-day bed-rest and the effectiveness of a new training device – Sledge Jump System (SJS) – as countermeasure of bed-rest and, eventually, spaceflights.

23 male subjects, divided in two groups underwent a 60-day bed-rest period. They wore a tri-axial accelerometer on the waist for two consecutive weeks before and after this period. The *training group* (n=12) trained daily in the SJS, while the *control group* (n=11) did not perform any kind of activity during the whole period.

In the two weeks before and after the bed-rest period, measurements of gait and of PA were taken. To measure the gait parameters (walking, slow run, moderate run, climb up stairs and climb down stairs), one gait course was done before bed-rest to set baseline values and three more gait courses were done after the bed-rest period, one day (R+1), seven days (R+7) after and fourteen days (R+14) after re-ambulation to see the differences in gait parameters and recovery over time. For the PA levels, integrals over the two weeks before and after bed-rest period were calculated from the signal of the accelerometer. Different levels of PA were set based on baseline values.

The linear mixed-effects models showed a statistical difference ($p<0.05$) for the relative values in the time to complete the task, the number of steps, the average speed for the slow run in the *control group* during the R+1 measurements, and a decrease in the stride length for both groups. A significant increase ($p<0.05$) in time to complete the task, number of steps as well as a decrease in the average speed have been reported for both groups during R+1 in the moderate run. No significant changes ($p<0.05$) were found in the PA levels.

Results support other findings suggesting the benefits of physical exercise during immobilization, proving a partial effectiveness of the SJS for preventing the effects of bed-rest period.

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Contents

Introduction

The desire of humankind to explore what is still unexplored is innate in the human being; history offers us many examples of extraordinary men who pushed themselves to the borders of the known and beyond – to name a few, Christopher Columbus and Amerigo Vespucci who discovered America more than 500 years ago, and Marco Polo, who was one of the first Europeans to reach China. There are some parallels between these expeditions, known as some of the greatest discoveries of the human history, and the desire of humankind to discover and explore new planets. The human explorations of new planets will not only increase our knowledge about planet formation and evolution, but will also bring new discoveries and new technologies to our society, like the historical explorations brought in their days. In recent years, it has always been the more realistic idea to colonize the *Red Planet*, Mars. However, to accomplish this extraordinary result, a joint effort from different disciplines is required to achieve new goals and overcome new limits.

The fields of Space Medicine and Physiology are, especially nowadays, of extreme importance when talking about Space human exploration. In the last decades, Space exploration made enormous improvements, from the first man orbiting the Earth on April 12, 1961, to the International Space Station, which accommodates, nowadays, astronauts for an average time of six consecutive months (Clément, 2011). In the next decades, human Space exploration will play a key role in Space science, but unfortunately, the knowledge acquired until today on how to prevent the negative effects of microgravity on the human body is not enough to ensure a safe long-term space mission (Adams G. R., 2003; LeBlanc A. D., 2007). New discoveries will be important not only to understand and counter what happens to the human body when outside of the gravitational field of Earth, and thus to plan long-term space mission on other satellites or planets (e.g. the Moon or Mars), but also to understand the role of gravity in life process, and, for instance, how it has affected the evolution of the living organisms on this planet.

To date, one of the most effective methods known to reduce the effect of microgravity on the human body is physical exercise (Trappe S., 2009), and thanks to research in the field of exercise physiology and related disciplines, the knowledge of the effects of microgravity on human systems has significantly increased (McArdle W. D., 2010). Astronauts, in order to counter and prevent the effects of microgravity, spend many hours every day doing physical exercises. Unfortunately, this is still not enough. For this reason, researchers put a lot of effort in researching and understanding the mechanisms involved in microgravity's effect on humans, and space agencies all over the world are investing time and energy in new technologies and devices in order to find new solutions. The German Space Agency (Deutsches Zentrum für Luft- und Raumfahrt - DLR), along with the European Space Agency (ESA), is one of the leading agencies in the sector, contributing by offering their facilities and machines to researchers and students to conduct research and experiments in the field of Space Science.

In the last year, a 60-day bed-rest study has been carried out at DLR, with the collaboration and participation of many institutions, universities, and researchers all over Europe. Luckily, I had the opportunity to join the DLR - Space Physiology department and conduct my own research and thesis, in this study. The central purpose of the bed-rest study was, firstly, to evaluate the effectiveness of a new sledge jump system to use as a countermeasure to microgravity for astronauts, and secondly, to collect more data on the effects of simulated microgravity on human body. My small contribution in this work was the collection and analysis of data from accelerometers mounted on the waist of the subjects to detect and quantify the locomotive patterns before and after the bed-rest period.

1.1 Purpose and Aim

In this thesis, accelerometer data is used to investigate the effects of a 60-day bed-rest on the locomotive patterns of humans. This method offers several advantages. Firstly, it is a proven method to recognize physical activities (Montoye H. J., 1983), so it is very useful when talking about locomotive patterns such as running, walking, etc. Secondly, advancements in micro-electromechanical systems (MEMS) made this device very small and portable in size, low in price and in low-power format while still permitting to attain solid outputs (Mathie M. J., 2004a). The use of this device allows the recording of data during everyday activities and it can be easily worn on different sites of the body without being too bulky (Foerster F., 2000; Uiterwaal M., 1998).

In this work, a single tri-axial accelerometer mounted on the waist of the subjects was used to record data from different activities during the gait course (Evans A. L., 1991; Sekine M., 2000) before and after the bed-rest period. This device has been also used to estimate the level of physical activity prior and after the intervention period during normal daily-life. As recognized by some authors (Consolvo S., 2008; Preece S. J., 2009), using data from daily-life instead of trying to mimic the same conditions in a laboratory environment is of extreme importance for a real picture of the underlying mechanisms. Therefore, subjects were asked to wear the accelerometers for one week before arriving at the DLR and for one week after they left the laboratories. For the gait course, measurements were taken before the bed-rest period (Baseline Data Collection - BDC), and one day after the re-ambulation (R+1), seven days after the re-ambulation (R+7) and fourteen days after the re-ambulation (R+14).

1.2 Hypotheses

In light of what was mentioned in the above section, the following hypotheses were formulated:

I. Significant differences in the gait course parameters, between pre and post measurements (BDC and R+1) for both groups in the following points:
   - Number of steps, frequency of steps and time spent to complete each activity (walking, slow run, moderate run, climb up-stairs, climb down-stairs)
   - Average speed and stride length for walking, slow run and moderate run

II. *Training group* will recover faster than c*ontrol group* in terms of gait course parameters measured during R+7 and R+14 for regarding the point stated in the first hypothesis

III. Decrease in level of physical activity for both groups during in-house recovery (2 weeks after head-down tilt phase) compared to the BDC phase (2 weeks before head-down tilt)

Background

2.1 Gravity and micro-gravity

"*Every particle of matter in the universe attracts every other particle with a force that is directly proportional to the product of the masses of the particles and inversely proportional to the square of the distance between them*." states the gravitational law proposed by Sir Isaac Newton in 1687, when describing the force of gravity acting on Earth and on the whole universe. On Earth, the acceleration of gravity is approximately 9.8 m/s^2, while on other planets, stars and satellites it drastically varies. For instance, on the surface of the Moon, the acceleration of gravity is six times lesser than that on Earth, i.e., 1.6 m/s^2.

When talking about microgravity, we can interpret it in different ways, depending on the context as mentioned by Rogers (Rogers M. J. B., 1997). In this thesis, when the term "microgravity" is used, it will be referred to an environment where the gravity is near zero, or drastically reduced compared with the Earth's surface gravity.

2.1.1 Negative effects of micro-gravity on the human body

In a microgravity environment the linear acceleration forces head-to-foot do not act on the body. Thus, the normal biologic functions are compromised, creating several adaptions to such conditions. There are mainly two responses to microgravity – the short-term response and the long-term response. The short-term response occurs during the first few days of a mission. The most known adaption is called Space Motion Sickness (SMS); this syndrome usually occurs within the first 72 hours of a space mission and disappears on its own after the first few days of space-flight or with the help of medication. This syndrome is recognizable by difficulty in concentrating, disorientation, nausea, pallor, vertigo while standing and walking, vomiting, and blurred vision (McArdle W. D., 2010).

When thinking about a long-term space mission, efficient, working and healthy astronauts' systems and structures are essentials. Nowadays, the effect of the microgravity on the human body is well known, and unfortunately, it does not permit long-term space missions without taking any countermeasure. The major changes that can be observed in these systems: (i) cardiovascular and cardiopulmonary; (ii) hematologic; (iii) fluid, electrolyte and hormonal; (iv) muscle; (v) bone and (vi) neurosensory and vestibular (McArdle W. D., 2010) (Figure 12. See Appendix).

To name a few of these effects on the human body, the most evident effect of microgravity after landing back on Earth is the general reentry syndrome that includes nausea, vertigo and overall fatigue and the orthostatic intolerance. This intolerance to orthostatic position of the body is given by a postural decrease in cardiac filling and stroke volume and an inadequate brain perfusion (Blomqvist, 1990; Buckey J. C., 1996). From a cardiovascular point of view, during the first few days in microgravity we can observe a decrease in the total fluid volume with negative consequences in the total work done by the heart, producing a cardiac atrophy and being one of the causes inducing the orthostatic intolerance. As shown by Perhonen, et al. (Perhonen, 2001), cardiac output and stroke volume decrease during inflight period and during the first two weeks of bed-rest, and same decrease has been noticed in the left ventricular mass after six weeks of bed-rest. Another important system that is affected by microgravity is the skeletal system. The bone mass can decrease up to 20% after six months of exposure to microgravity in the lower limbs, continuing for months after landing (Clément, 2011), or as suggested by Oshima (Ohshima, 2010b), during a long-term space mission the average bone mineral loss in weight-bearing bones is about 1-2% per month. The mechanism of this reduction in bone mass is still not completely clear, but it can be associated to the lack of bone deformation due to the lack of gravitational forces acting on the skeletal system. To explain this principle, the model introduced by Frost (Frost, 1987) can help us. This model introduces a mechanism of adaptation of the bone tissue to the mechanical loads they are exposed. If a bone receives a strain (the ratio of elongation to the original length) in the range of 1000-2000 (normal range), the bone keeps its strength. If this range is exceeded, new bone material is built, or the trabecular bone is reorganized. If this stimulus is below the normal range, a deterioration of the bone occurs with a consequently reduction of the bone mass. This reduction can drastically lead to an increase in the risk of fracture once the astronauts return on Earth.

The loss in mass and function of the skeletal muscle system can be rapid and considerable even during the first few days of a mission (Tesch P. A., 2005), as reported by Ferrando et al. (Ferrando A. A., 1995), where a decrease of 3% in the thigh muscle was observed after only seven days of bed-rest. Moreover, Edgerton et al. (Edgerton V. R., 1995) showed that 11 days of microgravity can produce significant reductions in muscle fiber cross-sectional area, 16-36% smaller than pre-flight values in the *vastus lateralis* muscle. Another study has demonstrated that bed-rest and long-duration spaceflight can bring a reduction up to of 25% of the mass of the *triceps surae* muscle (Adams G. R., 2003). As a consequence of the muscle mass lost in microgravity, there is a commensurate loss in muscle function, that, in some cases, can be close to a 40% of deficit (Adams G. R., 2003). This muscle atrophy is greater mainly in two groups of muscles – those involved in activities like walking, standing and lifting objects on Earth, the so-called postural muscles and in the extensor muscles, or known also as anti-gravity muscles (Clément, 2011).

Funato et al. (Funato K., 1997) compared the velocity, the force and the power output of lower and upper limb movements using a single-joint dynamometer, showing that after 20 days of bed-rest the decrease in all the parameters studied was observed only in the lower limb (19.8-43.6%) and not in the upper limb. Alkner et al. (Alkner B. A., 2004a, 2004b) reported a decrease in the volume of the knee extensor muscles and plantar flexor muscles of respectively 18% and 29%. The force and the power decreased by 31-60% for the knee extensor muscles and by 37-56% for the plantar flexor muscles. The EMG activity for the knee extensors and the plantar flexors decreased by 31-38% and 28-35%, respectively.

The loss in strength reported in these studies cannot be explained by a loss in the maximal strength alone. Other factors, such as changes in the contractile properties of the muscle fibers and altered motor control must contribute in this loss. Portero et al. (Portero P., 1996) reported an increase in the fatigability after four weeks of head-down bed-rest (HDBR) more evident in the plantar-flexor muscles compared to the dorsi-flexor muscles. Kawakami et al. (Kawakami Y., 2001) used a supramaximal twitch interpolation over voluntary contraction during knee extension for studying neural activation. It was found that the voluntary activation was smaller after 20 days of HDBR. Comparing the changes in force and in the physiological cross-section area (PCSA), it was found that the changes in the neural activation were more related with the changes in force than the change in the PCSA itself.

Kubo et al. (Kubo K., 2004a, 2004b) studied the mechanical properties of tendons in the knee extensor and plantar flexor muscles after 20 days of bed-rest. The authors used ultrasonography during isometric contraction and relaxation, and to determine the tendon stiffness, the relationship between muscle force and tendon elongation was taken in consideration. Authors found out a significant decrease in the tendon stiffness in the knee extensors but not in the plantar flexors.

The loss in muscle mass, force, power, and function is not only confined to the musculoskeletal system, but it goes well beyond. First, the skeletal muscles cover an important role in maintaining homeostasis and second, the musculoskeletal system has a key role in ruling the loading conditions imposed on the skeletal system, and it is crucial for maintaining and regulating the bone mass (Al-Shanti N., 2009; Fitts R. H., 2001). Studies on older people demonstrated how muscle power is correlated with a better quality of life, activities of daily living and even mortality (Katuala J. A., 2008). Moreover, the energetic requirements of skeletal muscles also dictate the demand placed on the cardiovascular system, influencing important elements such as heart mass, stroke volume and capillarity density (Blomqvist C. G., 1983) (Figure 13).

2.1.2 How to counter the effects of micro-gravity

As mentioned before, for a successful long-term space mission, the entire crew must not suffer from the abovementioned symptoms, so countermeasures are needed in order to counter these effects. Nowadays, countermeasures are taken during all the stages of a mission: preflight, inflight and after-flight.

For instance, drugs are used to help minimize the SMS effect during the first days of the flight (Jennings, 1998; Paule M. G., 2004). Another example is the use of Lower-Body Negative Pressure (LBNP), used as a countermeasure to the cardiovascular response to microgravity (Johnson R. L., 1975). It applies a negative pressure to the lower limbs, so that the fluids in the vascular system floating in the upper region of the body are forced to shift into the lower body. Another important countermeasure taken inflight is the diet. An optimal dietary regimen may help in preventing the physiological maladaptation of astronauts to microgravity (McArdle W. D., 2010).

Among all the treatments used to reduce the effect of microgravity on the human body, the most effective countermeasure known to prevent loss in muscle strength and mass is the physical exercise. For this reason, members of the crew exercise for hours almost every day (Baldwin K. M., 1996; Trappe S., 2009). Over the course of the years, four exercises have been used the most on board of the ISS according to McArdle (McArdle W. D., 2010): (i) treadmill walking and running; (ii) cycling on an ergometer; (iii) leg rowing; (iv) upper- and lower-body dynamic resistance-exercise. These exercises are combined to counteract the loss in muscle strength and mass, and to preserve aerobic power and endurance. But despite the high number of hours spent in exercising, the astronauts still experience loss in muscles and bones tissue, caused by the absence of large forces acting on muscles and bones (Ohshima, 2010a). A combination of different countermeasures is used to reduce the effects of microgravity. For instance, LBNP and exercise are combined to have bigger benefits. Murthy et al. (Murthy G., 1994) compared five minutes of exercise in supine position with a LBNP (-100mmHg) with a five minutes exercise in an upright position and found that the combination ‘exercise + LBNP’ can mimic the same stress for the legs muscles and also a greater cardiovascular stress than the upright position exercise. Watenpaugh et al. (Watenpaugh D. E., 2000) showed how effective 40 minutes of supine exercise in a LBNP chamber (-52mmHg) is during 15 days of HDBR.

Despite all these countermeasures and treatments for solving the problem of microgravity on human body, astronauts still suffer from the related symptoms during spaceflights. In order to ensure safer spaceflights and efficient tools for astronauts’ health, new and better solutions are needed.

2.2 How to simulate micro-gravity effect on Earth

On Earth, different strategies are used to simulate a microgravity environment. These experiments allow researchers to use different modalities to vary the experiment conditions and variables before a real mission in the outer space and thus, deciding which procedures fit better for a particular mission. There are mainly three approaches for mimicking microgravity. The approach depends on the subject in the study. For non-living things, a microgravity environment can be created during free fall. This can be achieved by letting objects fall from towers and tubes for a short time. The same condition can be achieved by placing objects in sounding rockets, thus during the free fall after reaching the maximum altitude a microgravity condition can be recreated (McArdle W. D., 2010).

Another approach used with living and non-living objects is the parabolic flight. In this method, the aircraft flights describe several parabolas which cause the sense of microgravity. As reported by McArdle (McArdle W. D., 2010) when reporting this technique utilized by NASA with the KC-135 aircraft which during the experiments goes up rapidly with an angle of 45° and subsequently goes down rapidly following a parabolic path, with an angle of 45°. During this maneuver, in the parabolic phase, a near-zero-gravity effect is produced for about 30 seconds. The author reports also that during the ascending and descending phase, hyper-gravity (2 to 2.5g) is experienced. This is achieved thanks to the acceleration and deceleration forces produced in the pull-up and pull-down phases. Up to 60 parabolic maneuvers can be done within a single parabolic flight, for a total weightless time of 30 minutes per day.

The third approach includes different strategies to mimic microgravity conditions when studying its effects on humans and animals. One of these methods is the wheelchair confinement (McArdle W. D., 2010). It has been seen that a prolonged wheelchair period can produce postural hypotension in paraplegics (Convertino V. A. , 1991) that can be compared to what astronauts experience during long-term missions. The same conditions can be recreated using the technique of water immersion, where the body is in a situation of weightlessness relative to the surrounding environment. Thus, a redistribution of blood volume occurs with a central hypervolemia as a consequence (Arborelius M., 1972; Gauer O. H., 1970). There are two types of water immersion – dry and wet immersion. In the dry immersion, the skin is not directly touching the water, but a thin sheet protects the subject, while in the wet immersion technique, as suggested by the name, the subject is directly immersed in the water without any protection between the skin and the water (McArdle W. D., 2010). During water immersion, subjects and astronauts have to perform hand-eye coordination tasks to recreate similar conditions to those that can be found when performing extravehicular activity (EVA) during space missions (Graveline D. E., 1961; McArdle W. D., 2010).

2.2.1 Bed-rest

The last technique utilized for mimic the effects of microgravity on the human body is the bed-rest (BR). This technique has been used long before the era of space flights. During the nineteenth century, bed-rest was used as medical treatment, resulting in adverse consequences due to the confinement in bed. Only in 1948, a group of researchers (Dietrick J. E., 1948) studied the effects of bed-rest for 30 days on healthy people, finding out an increase in the calcium excretion and a lost in bone density, demonstrating the side effects of immobilization in bed. These results found application later, also in space research, where astronauts do not experience the effects of the acceleration of gravity, living in a state of inactivity – especially for the lower limbs which do not need to support the astronaut's body weight, losing bone calcium, just as it happened to the first subjects who underwent a 30 days bed-rest period. Thus, using the bed-rest became the model of choice for studying the effects of microgravity on human body and also for testing countermeasures (Pavy-Le Traon A., 2007).

In the early '70s, the idea of a HDBR started to take place after cosmonauts returning from long-term space missions complained about difficulties in sleeping due to a sensation of slipping off the foot of the bed. To remedy this sensation, the medical staff of the cosmonauts started to raise the foot of the bed until it was perceived as horizontal by the cosmonauts and they could go back to sleep. After this event, Russian researchers came up with the idea that maybe, what was perceived in space was similar to what cosmonauts perceived while lying head-down on Earth (Pavy-Le Traon A., 2007). Thus, the HDBR was ideated and born. After several attempts to choose the optimal inclination at -15°, -10° and -5°, researchers (Atkov O. Y., 1992) decided that -6° was the best compromise for comfort, magnitude of response and acceptability. The same fluid shift can also be observed in outer space (Clément, 2011). Thus, in the last two decades, HDBR has been used for almost all the studies (Pavy-Le Traon A., 2007).

HDBR can reproduce almost all the physiological changes that are experienced by the astronauts during long-term space missions. Nicogossian (Nicogossian, 1994) showed a comparison between changes induced by space flight and changes induced by bed-rest, and changes after bed-rest and after returning on Earth. These effects are shown in the Table 1.

	Space	HDBR	Post-flight	Post-HDBR
Height	+ ±1.3 cm	+ ±1.0 cm		
Body mass	- 3-4%	- 2-4%		
Maximal aerobic capacity	Not measured	- 25%	- ±12%	- 20-25%
Plasma volume	- 10-15%	- 10-15%		
Bone density	- 1.6% monthly	- 0.5-1% monthly		
Urinary calcium	+	+		
Absorption of *Ca* from gut	-	-		
Renal stone risk	+	+		
Muscle mass	-	-		
Muscle strength	-	-		
Insulin resistance	+	+		
Orthostatic hypotension			+	+
Balance/stability			-	-
Coordination/gate			Poor/wide	poor
Nausea/sickness/vertigo	None 35% Severe 7% Moderate 23% Mild 35%	Vertigo 10% Nausea rarely		

Table 1. Comparison of physiological changes induced by space flights, HDBR, and related consequences after landing and after HDBR. + increase; - decrease. (Adapted from: Space physiology and medicine. Nicogossian A. E. 1994, 3rd edition. Lea & Febiger A. Waverly, Philadelphia).

Even though bed-rest does not mimic the entireness of a space mission (for instance, the activities surrounding launch, the acceleration or the confinement and isolation in small living area are not reproduced, or the SMS does not occur), HDBR is the best model we have on Earth to simulate microgravity (Pavy-Le Traon A., 2007). Thanks to it, nowadays, the knowledge and the understanding about the physiological processes caused by living in microgravity are increased, and countermeasures can be studied and designed in order to ensure a safer stay in Outer space and to plan long-term space missions.

2.3 Physical activity and accelerometers

2.3.1 Physical activity

Physical activity (PA) is defined as any bodily movement produced by skeletal muscles which results in an energy expenditure (Caspersen C. J., 1985). It has been also recognized as one of the leading health indicators (LHI) by the U.S. government (organization: Healthy People 2020), and it is a useful tool when exploring human movements and the relationship to health status. A decline in the PA level can be considered as indicator in different symptoms related to functional impairment (Steele B. G., 2000), so it is essential to monitor and to measure it. Moreover, the energy consumed due to PA is accepted as an important factor for preventing some disease such as obesity, diabetes, cardiovascular disease, and muscle wasting (Warburton, Nicol, & Bredin, 2006). So, it can also be used as a good indicator for the health of astronauts when they return to Earth. Nowadays, many methods exist to measure the PA level. Some of them are subjective methods, such as surveys, diaries, and questionnaires. These methods, even if very inexpensive tools, are not consistent, because they depend on subjective interpretation of the data (W. K. R. Meijer G. A. L., Verhoeven F. M. H., Koper H. B. M., Hoor F., 1991). The other class of methods are objective. Techniques that are reliable and consistent, even if sometimes the outcomes can be misleading or the systems may not be practical for the daily-life measurement in a free-living environment. For example, when using a pedometer that detects the clear impacts made by steps when hitting the ground during locomotion, it can only record the number of steps, and not the intensity of the movement. Thus, an estimation of the energy expenditure will be inaccurate (Saris W. H. M., 1977). Another example is when using optical systems (devices that use lens and cameras to record the activities) that require a special instrumentation and environment setting. Thus the complexity of daily-life activities cannot be reproduced in laboratory conditions.

2.3.2 Accelerometers

Among the objective methods, accelerometers are preferred to use when talking about PA (Yang C., 2010). Accelerometers measure the rate of change of velocity along axes, or acceleration. Acceleration is a vector quantity, and it is measured in m/s^2 in SI unit. Another common unit for acceleration is "g"; 1g is equivalent to the acceleration caused by the gravitational force of the Earth at the surface of the Earth, that is defined as being equal to 9.80665 m/s^2 ("Resolution of the 3rd General Conference of Weights and Measures (GCPM)," 1901). Trying to explain the concept of accelerometers in simple words, one can image a mass on a spring. If the mass is stationary, it will experience the gravitational force acting upon it, and the displacement caused by the weight of the mass on a scale can be marked as 1g. If this mass is accelerated upwards or downwards, the spring will be lengthened or shortened accordingly. Measuring this displacement on a scale corresponding to acceleration is a way to estimate acceleration (Figure 14). This example describes a single-axis accelerometer. A bi- or tri-axial accelerometer can be made following the same principle using two or three single-axis accelerometers mounted on the three different axes (*x, y,* and *z*). The acceleration of the mass can be measured by converting mechanical motion into an electric signal. There are several types of accelerometers, but the most common, according to Yang (Yang C., 2010), are:

- *Piezoresistive accelerometers*: These devices have a feature whose resistance changes with stress. The changes of the resistance correspond directly to the changes in acceleration. These instruments are high quality, simple and low-cost and due to DC-responsiveness, they can measure constant acceleration such as gravity
- *Piezoelectric accelerometers*: Due to an ability of certain materials to generate current in response to mechanical stress or vibration (piezoelectric materials), these devices can detect the change in velocity measuring the voltage output given by a piezoelectric element bending under the applied acceleration of the mass

- *Differential capacitive accelerometers*: In these devices, capacitive plates are placed inside the instrument. The acceleration is measured calculating the change in capacitance between the electrodes. The advantages of this system are: low power consumption, fast response to motion and large output level

This device was used to measure gait velocity and acceleration during the 1950s (Saunders J. B., 1953), and subsequently, during the 1970s for measuring the human motion due to technological advances (Morris, 1973). Microelectromechanical Systems (MEMS) are mechanical and electro-mechanical elements that in the last four decades developed rapidly (Bao M., 1996), and nowadays allow, thanks to their very small size (in order of micrometers), to build small and reliable portable accelerometers. Nowadays, accelerometers have been universally accepted as helpful and effective instruments for wearable devices to measure PA in many fields, from clinical and laboratory settings to free-living environments (Lee I., 2005; Mathie M. J., 2004a). Inside a MEMS accelerometer, the principle of the differential capacitive is used, but instead of capacitive plates, a *comb-drive actuator* (Figure 15. See *Appendix*) can be found (Selvakumar A., 1998; Xie H., 2000).

Accelerometers are also used to classify movements and to extrapolate single features of the movement (e.g. stride length, number of steps, energy consumption) from the data (Bonomi A. G., 2009; Bouten C. V., 1994). The placement of the device on the human body contributes to the consistency of the outcome. Gemperle et al. (Gemperle F., 1998) provided a guideline of possible and optimal places on human body surface for wearable objects without being intrusive. The sensor placement indicates the locations where the devices are placed, and how these sensors are fixed to those locations. These devices can be positioned on different places on human body while activities are recorded. To name a few wearable zones from the list of Gemperle et al. (Gemperle F., 1998), an accelerometer can be placed on the rear of the upper arm, forearm, waist, thighs and foot, even though many scientist prefer to place the accelerometer on the waist (Bouten C. V., 1994; Karantonis D. M., 2006; Montoye H. J., 1983). This is because of a couple of reasons. The first being the closeness of the waist to the center of mass of the human body, so it means that a signal recorded in this position can represent very well the main human body movement, and a set of different principal daily life activities can be easily classified (Sekine M., 2000). The second is a practical reason – an accelerometer can be easily worn on the waist with a belt, causing less constraint and less discomfort when using the device in a daily-life environment.

Materials and Methods

3.1 Participants

24 healthy subjects took part in the study after thorough medical and psychological selections. They were split in two groups – *control group* (n = 12; age 28±5 years; height 180.4±5 cm; weight 76.3±7.8 kg) and *training group* (n = 12; age 30±6 years; height 181.2±6 cm; weight 77.1±6.7 kg) (Table 2). To accommodate all the 24 subjects in the DLR facilities, two campaigns named *Reactive Jumps in a Sledge Jump System as a Countermeasure during Long-term Bed Rest* (RSL) 1 and RSL2 were carried out, each hosting 12 subjects. During the second campaign, one subject dropped out due to unspecified problems, resulting a *control group* of 11 subjects. A total of 23 subjects competed the study. Physical characteristics of the subjects are presented in Table 2 and Table 3 (See *Appendix*).

3.2 Study design

Subjects wore the accelerometer for two consecutive weeks before the start of the bed-rest, for the so called Baseline Data Collect (BDC) phase, and the two weeks after the end of the bed-rest, called Rehabilitation (R) phase. They were asked to wear the device for as long as they could, and they were allowed to remove the accelerometer during night, when taking a shower or when they had to undergo specific analyses, tasks or experiments where the use of the accelerometer was not allowed. The accelerometer was recharged overnight to allow full data acquisition for the entire following day.

During BDC phase, from BDC-14 to BDC-1, all the subjects performed one gait course for setting the baseline values of different activities (for details see section *Gait*

Course). The gait course was performed again after the end of the bed-rest at three different times, to evaluate the differences between the BDC phase; one day after re-ambulation (R+1), seven days after re-ambulation (R+7) and fourteen days after the end of the bed-rest period (R+14).

At the end of the BDC phase, bed-rest period, or the so-called Head-Down Tilt phase (HDT) started. During this period, all the subjects underwent 60 days of strict 6° head-down tilt bed-rest. In this phase, subjects were not allowed to stand up or even raise the shoulders from the mattress, to ensure a continuity in the exposure of the artificial microgravity.

The t*raining group* underwent an almost daily workout on a special device to simulate reactive jumps under different gravity conditions (see section *Sledge Jump-System*) while the c*ontrol group* did not perform any activity for the entire HDT period. In Table 4, an example of the daily-scheduled routine for some of the subjects during HDT phase can be seen.

3.3 Accelerometers

The tri-axial accelerometer (TA) used in this study is a rechargeable 3-axis self-recording accelerometer (X16-4, Gulf Coast Data Concepts, LLC. Mississippi, United States) (Figure 16. See *Appendix*). The hardware consists of a wireless recorder, 10.16 cm x 2.54 cm x 2.54 cm (4” x 1” x 1”), 36.85 g. It can record acceleration up to 16g and it is equipped with a 500mAh rechargeable lithium-polymer battery and a push button for starting and stopping the data recording. Data can be recorded at different rates (12, 25, 50, 50, 100, 200, 400 Hz). Data are stored as Comma Separated Values (.csv file format), and can be downloaded to a computer through the USB interface. For the study, different sample frequencies have been used (Table 3). As suggested by authors (Godfrey A., 2009; Najafi B., 2003; Winter D. A., 1976), in normal non-impact PA, the information of the gait patterns does not exceed 8Hz, thus the lowest sample frequency was 25Hz, while the highest was 100Hz. The recorded signals were imported in a personal computer and later processed (See section *Data analysis*). Different sample frequencies were chosen prior to the start of RSL1 by other researchers at DLR to verify at which frequency it was possible to have a better data recording. Thus, it was not possible for me to change it in the middle of RSL1 to record all the data with the same sample frequency.

The TA was placed around the waist, near the center of mass of the subjects, with the aid of a belt. The position of the belt was chosen based on the comfort of the subject while wearing it. In Table 3 (See *Appendix*), the placement of the belt for each subject can be seen.

3.4 Gait course

The activities chosen for the gait course were selected for their resemblance with normal daily routine. The activities were *walking*, *slow running* or *jogging*, *moderate running* (subjects were asked to run at a speed as they have to run for 10km), *climbing up stairs* and *climbing down stairs*. To complete all the tasks, around 25-30 minutes were required. The gait courses were carried out mainly in single subject sessions, except sometimes when two or four subjects were asked to perform the gait courses during the same session. When this happened, to be sure that the pace (walking, running, etc.) of subjects was not influenced by the pattern pace of other subjects, they were told to keep their own pace, even if it was faster or slower than the other subject. Moreover, while performing the activities, the second subject started with a delay with respect to the first subject to avoid any unconscious influence of the pattern pace. On only one occasion, during the BDC phase in RSL2 four subjects performed the gait course at the same time, probably influencing the task pace.

To perform every activity, the gait course was carried out in two places, on a flight of stairs, from the basement to the third floor of the DLR Space physiology department building to record the patterns while climbing up and down the stairs, and in a corridor to record the walking and the run patterns. The only instruction the subjects received from the instructors regarding the activities was to follow their own feeling about the speed and the pace. No other restriction or limitation was given.

The gait course was structured as follows: after reaching the starting point for the gait course, the subject together with the instructor walked to the basement. Once the basement was reached, the subject was made to wait 30 seconds so as to have a clear demarcation between activities during the data analysis. This task consisted of climbing up 84 steps or 8 flights of stairs (4 floors) plus the landing of the staircase, at any selected speed. Once the subject climbed to the third floor, a break of one minute was taken to let the subject recover from the effort and to have a clear signal on the data recorded when the climb up stairs was over and the climb down stairs started. Once the break was complete, the subject and instructor climbed down the stairs until the basement. Even here, the subject had freedom to choose the pace to use for going down. Once they reached the basement, another break was taken to be sure to have a difference in the signal output when climbing down stairs and when not. After the break, the instructor and the subject walked to the corridor to perform the walking and the running test. The subject had freedom to choose the pace during these tests as well. From the starting point the subject walked to the end of the corridor. Once he reached the end, he rested for around 30 seconds and then slowly ran back to the start of the corridor. Once he reached back to the start point, the subject walked again to the end of the corridor, took a break of 30 seconds and then performed the moderate run to the starting point. The length of the corridor was 85.7 m. For the measurements taken during RSL2 this distance was always covered, but the same cannot be said during measurements taken in RSL1. During this phase, due to different instructors, the end of the corridor was not always considered the same. Further explanation will be given in the chapter *Discussion*. The entire sequence, was repeated a second time (Figure 17). For the entire course of the measurement, the subject was never left alone; at least one instructor was always with him. After every activity, a break of 30 seconds or more was taken to be sure that when reading the data output, it was clear when the activity finished and when started. This is possible because during the breaks the subjects were asked to move as less as possible to have a flat line as output in the resting period.

3.5 Sledge Jump System

The device used during the training sessions of the 60-day bed-rest by the *training group* was a new sledge jump system (SJS) developed by Novotec Medical GmbH (Pforzheim, Germany) together with the Sport Department of the University of Konstanz (Figure 18. See *Appendix*) that allows a more natural movement pattern while performing the jump on the sledge compared to older sledge jump systems (R. R. Kramer A., Gollhofer A., Gehring D., Gruber M., 2010). This device has been chosen because of its functionality and capability to mimic the natural movement of the reactive jump, as well as producing high peak ground reaction forces (GRF), high rate of force development (RFD), short ground contact times (GCT) and a high leg stiffness, allowing the storage of energy in the eccentric phase of the jump and the release in the following concentric phase (Asmussen E., 1974; Gollhofer A., 1991). The reactive jump has been proved to be the best exercise having the highest peak GRF and RFD among the tested exercises (Ebben W. P., 2010). In a previous study, Kramer et al. (R. R. Kramer A., Gollhofer A., Gehring D., Gruber M., 2010) showed how this device matches all these parameters, creating high forces in a short time period that are essential to create high strains and high strain rates on the bone tissue and increasing the bone strength (Suominen, 1993). The idea to use the reactive jumps in the SJS as a countermeasure to the 60-day bed-rest comes from several factors. Ebben et al. (Ebben W. P., 2010) in his study concluded that reactive jumps can be the best choice for osteogenic stimulus, so it can be beneficial for both skeletal system and musculoskeletal system providing high forces in the leg muscles and consequentially also to the bone structures. Moreover, not only are the muscles and bones stressed, but the neuromuscular system when performing reactive jumps is challenged as well. The movement presents a highly dynamic movement and it needs, besides a perfect activation and coordination of the muscles involved, an activation of different sensory inputs (e.g. Golgi tendon organs, visual and vestibular feedback and muscle spindles) (Dietz, 1992; Gollhofer A., 1991).

The SJS consists of mainly four parts: a tilting table and a lightweight sledge (5kg) attached to two rails, one for each side of the device, that allow the horizontal slip of the sledge along the structure (Figure 19). The tilt table can be adjusted continuously while performing the exercise, between 0 (horizontal position) and 90 degrees (vertical position) to allow a freedom of movement to the joints involved in the action, so that the subject is not restricted to a more superficial and assisted jump. Four straps, two around the shoulders and two around the thighs, attach the subject to the sledge. The last part that composes the SJS is the cylinders system. Two low-pressure cylinders, each with a capacity of 500N, pull the sledge against the force plate. Thus, any force between zero and 1000N can be selected by adjusting the pressure of each cylinder. The force generated by the cylinders is used to create different load conditions acting on the upper-body of the subject in a shoulders-to-feet direction. This part is just a glimpse of the article "*A new sledge jump system that allows almost natural reactive jumps.* By *Kramer et. al (2010). Journal of Biomechanics*", where a more precise and detailed explanation of the SJS can be found.

3.6 Data analysis

The analysis of the data was done using MATLAB (MATLAB R2015a, The language of Technical Computing, The MathWorks, Inc., Natick, Massachusetts, United States) and Microsoft Excel (Microsoft Corporation, Redmond, Washington, United States). Signals were filtered using a fourth order low-pass Butterworth filter with a cutoff frequency of 2.5Hz. A low-pass filter allows only low frequencies to pass that are set by the cutoff threshold, while higher frequencies are attenuated. To determine the limit of the low-pass filter, the type of movement that the device wants to record (Uiterwaal M., 1998) and the acceleration components on the waist (considering vertical, anteroposterior and mediolateral acceleration) must be taken in consideration. Moreover, different cutoff frequencies were tested to determine at which frequency corresponded the best steps estimation, resulting 2.5Hz to be the best choice, with a percentage of error equal of 1.65±0.52%.

Once the data were filtered, every activity within the gait course was isolated to allow a faster analysis. Subsequently, different approaches were used to calculate the variables for each activity.

number of steps (N_{step}): the magnitude of the signal from the three axes was calculated to convert acceleration to a scalar quantity. To remove the acceleration due to gravity, considered as a constant effect, the mean from the data was subtracted so, that the data are centered on zero when plotted. A special function in MATLAB, called '*findpeaks'* was used to calculate the number of steps. When using this function, a threshold must be set to determine whether a peak can be considered as a step or not. To set the threshold, the standard deviation of the magnitude of the signal with removed gravity was taken in consideration. Steps are counted from every peak higher than the standard deviation. To avoid two or more peaks too close to each other to be counted as two different steps, it was assumed that it was not possible due to the nature of the exercise that more than one step could be made in less than 0.29 s. An example of steps detection can be seen in Figure 20.

This method was evaluated with a preliminary study done within the workers of DLR. Three subjects performed the gait course (carrying out every activity and every pause) counting the number of steps for each activity and writing them down on a paper while wearing the accelerometer. The data recorded and analyzed with the method described above showed an accuracy of 96.2±0.59% compared with the steps counted by subjects.

time to complete task (T_{task})*:* this variable was calculated isolating each activity from the gait course and measuring the starting point and the ending point. The rest period between activities during the gait course was made to make this step easier; every activity was marked by a flat line before and after its execution. In Figure 21 it is shown how a gait course appears when plotting the magnitude of the signal from the three axes.

step frequency ($Freq_{step}$)*:* given by dividing the N_{step} of an activity by the T_{task} of the same activity ($Freq_{step} = N_{step} / T_{task}$).

stride length (L_{str})*:* calculated dividing the length of the corridor by the N_{step} (L_{str} = *length of the corridor* / N_{step}).

average speed (S_{avg})*:* calculated by multiplying the $Freq_{step}$ by the L_{str} ($S_{avg} = Freq_{step} * L_{str}$). Moreover, it can be calculated dividing the length of the corridor by the T_{task} *(S_{avg} = length of the corridor / T_{task}).*

physical activity levels: to calculate this, raw data were filtering first using a fourth order low-pass Butterworth filter with a cut-off frequency of 20Hz (Bouten C. V., 1994), and subsequently filtered with a fourth order high-pass Butterworth filter. Successively, all the data points of the signal have been converted into positive values, so that all the absolute values of the entire signal are taken. Once the signal has been converted into positive values, the magnitude of the signal is calculated. The next step, is to integrate the signal. The signal was integrated in 10-second epochs i.e., the signal was integrated every 10 seconds. This process was done for the entire data acquired from the accelerometers during the BDC and R phases, for a total of four weeks.

For each subject, different thresholds to determine the different activity intensities was set based on their own level of PA. For setting these thresholds, the gait course made during BDC phase was taken as baseline, and the thresholds were set taking in consideration four points: (i) threshold for inactivity, everything below the lowest integrated point during walking activity considered as *no-activity*; (ii) threshold for low-intensity activity, everything below the lowest integrated point during slow running activity considered as *low-intensity activity*; (iii) threshold for medium-intensity activity, everything below the lowest integrated point during moderate running activity considered as *medium-intensity activity*; (iv) everything above point (iii) was considered as *high-intensity activity.* Once all the thresholds were set, counting the points within each range gave an estimation of the PA during the time window taken in consideration. Doing so, it is possible to have a percentage of the type of physical activity within the data set. If all the data recorded from the two weeks before and two weeks after are analyzed, it is possible to calculate the percentage of activity or inactivity of the subjects. In Figure 22 an example of the integration analysis with all the steps made is shown.

Integrating the signal to estimate PA levels has been suggested by Chen (Chen K. Y., 2005). The authors state advantages and disadvantages of this method, where the advantages come from its simplicity, the ease of processing for hardware and software needs and the simplicity of the general understanding. The disadvantages will be discussed later in the chapter *Discussion*.

3.7 Statistical analysis

Statistical analyses have been done using SPSS Statistic (IBM SPSS Statistic for Windows, ver. 23.0. Armonk, NY: IBM Corp.). Linear mixed-effects models (LMM) were used to analyze the effects of group, time and time*group interaction on the locomotive patterns and physical activity levels before and after the 60-day bed-rest. The choice of the LMM helped us to cope with missing data from the subjects without reducing the sample size.

The dependent variables studied are: time to complete the task, number of step for the task, step frequency during the task, average speed during the task, stride length and physical activity levels. For each variable, other sub-variables were studied: w*alking, slow run, moderate run, climbing up-stair and climbing down-stair* for the variables number of steps, time to complete the task and step frequency. While only the sub-variables *walking, slow run and moderate run* were taken into account for the variables average speed and stride length. Thus, 22 variables were analyzed independently.

For each of the 22 variables, two statistical analyses were made. The first statistical analysis (for the first hypothesis) was done using time as factor and two data from BDC and R+1 for the repeated measurements. In the second analysis, the data points in the time factor were from the datasets BDC, R+1, R+7 and R+14 (for the second hypothesis).

The last statistical analysis (for the third hypothesis) used the entire dataset collected during BDC phase and R phase.

During the LMM analysis, time, group, and time*group models were used as fixed factors, while subjects were used as random factor. When significant time effects were found, a post hoc test with Bonferroni correction for multiple comparisons was performed to test at which time the differences were significant.

One more statistical analysis was carried out using the relative values instead of the absolutes. In this analysis, an LMM analysis was done following the above-mentioned criteria. Moreover, a one-sample t-test was done to compare the difference of the means from the baseline relative value (set always to 1) and an independent-samples t-test to compare the mean of the two groups.

Results

4.1. Gait course results

The values (mean and SD) of the gait parameters measured during the four sessions of gait course are shown in Table 5 and Table 6 (see *Appendix*) for the absolute values, and Table 7 and Table 8 (see *Appendix*) for the relative values. The effects of 60-days -6° HDT bed-rest and the efficiency of the SJS as countermeasure were analyzed with respect to spatial and temporal gait parameters. From Figure 1 to Figure 10, the effects of bed-rest and SJS sessions on the walking, slow run, moderate run, climb up stairs and climb down stairs patterns are shown. To indicate differences between BDC phase and R phases in the relative values, the results are expressed as percentages of the BDC phase for each parameter, where 1 is considered as the baseline value, and everything above or below 1 in the post measurements indicates a change in percentage.

Walk parameters: the gait parameters of walking (T_{taks}, N_{step}, S_{avg}, L_{str}, $Freq_{step}$) were not significantly affected by the bed-rest, showing no statistical differences between pre- and post-measurements. Only a groups difference was found ($p < 0.05$) regarding $Freq_{step}$ between R+1 and BDC regarding the absolute values (Figure 1).

When analyzing the relative values, statistical differences ($p < 0.05$) in the T_{taks} and in the S_{avg} can be found in both groups. Regarding the T_{taks}, an increase of 10% and 4%, for the *control group* and *training group*, respectively, appears in the R+1 measurment. This increase persists also during the measurment taken during R+7. Concerning the S_{avg}, the *control group* had a decrease during R+1 of 9% against the 5% decrease for the *training group*. Both the decreases are statistically significant ($p < 0.05$) with respect the BDC value (Figure 2). No groups difference has been observed while performing this task.

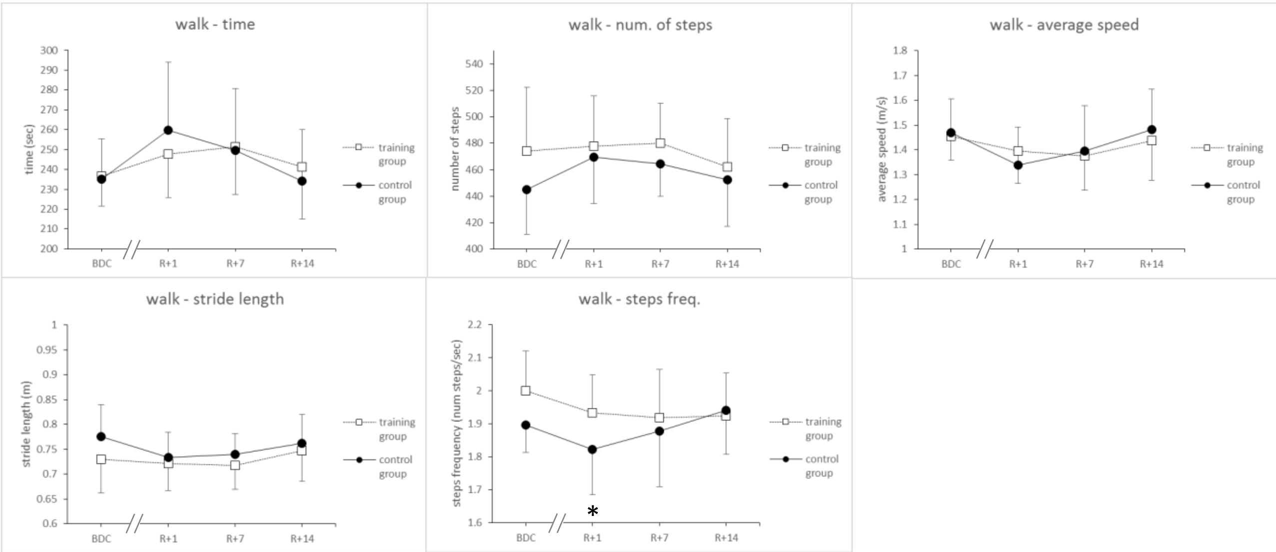

*Figure 1. Walk time (top left), number of steps (top center), average speed (top right), stride length (bottom left) and steps frequency (bottom center) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, absolute values. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement. † significant (p < 0.05) time*group effect.*

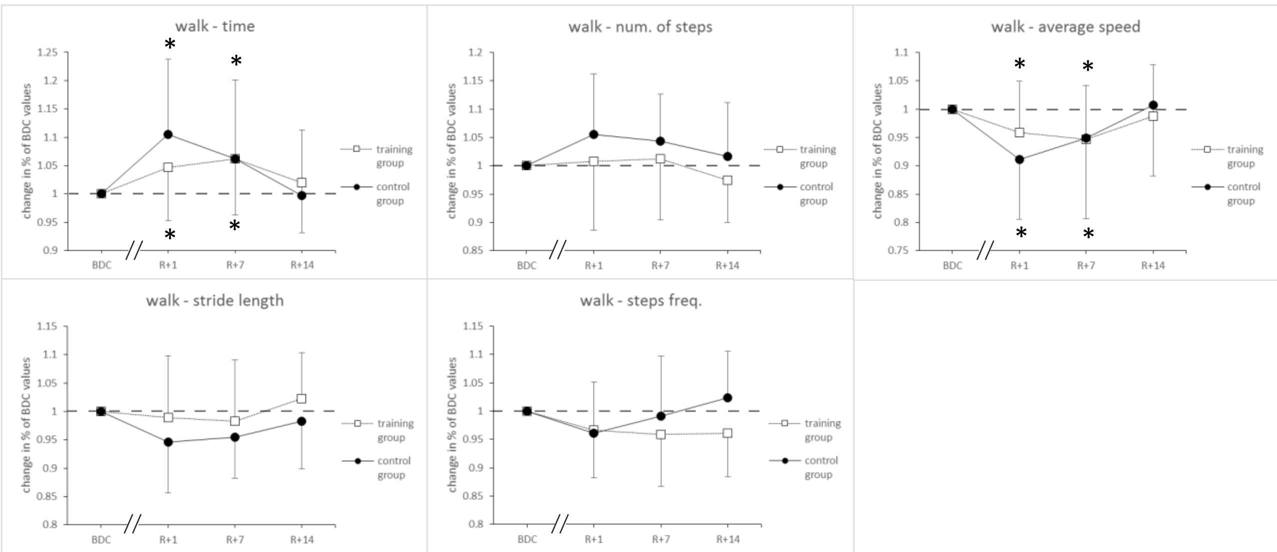

*Figure 2. Walk time (top left), number of steps (top center), average speed (top right), stride length (bottom left) and steps frequency (bottom center) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, relative values. The changes are expressed in percentage of BDC values (mean ± SD). * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

Slow run parameters: for the absolute values, the statistical analysis showed that bed-rest had significantly ($p < 0.05$) modified certain parameters. The slow run showed a significant increase during the measurement R+1 in T_{taks} ($p < 0.05$) in both groups, with an increase of about 13% with respect to BDC measurement for *control group*. This can be seen in the decrease in S_{avg} (of 14%) in the *control group*. The analysis also showed a time*group effect ($p < 0.05$) for T_{taks} and for S_{avg} during slow run. Other two parameters have significantly ($p < 0.05$) changed for both groups, showing no groups differences, the N_{step} and the L_{str}. During gait courses at day R+7 and R+14 no significant differences ($p < 0.05$) were found in any of the parameters for both groups (Figure 3).

The relative values show bigger differences regarding the groups' difference that can be found in the T_{taks}, in the N_{step} and in the S_{avg}, with a statistical decrease ($p < 0.05$) for the *control group* in these tasks. The statistical differences between groups disappear during the R+7 measurement, indicating a recovery of the *control group*. Statistical differences ($p < 0.05$) were found in the other two tasks for both groups. A decrease in the L_{str} during R+1 measurement, as well as an increase in the $Freq_{step}$ in R+7 measurement (Figure 4).

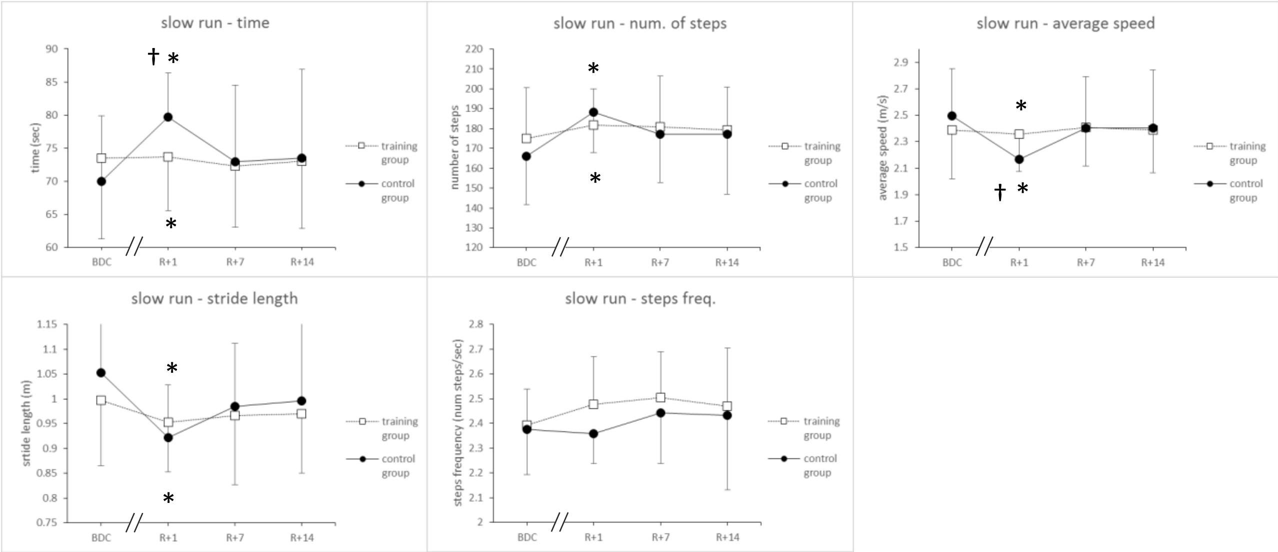

*Figure 3. Slow run time (top left), number of steps (top center), average speed (top right), stride length (bottom left) and steps frequency (bottom center) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, absolute values. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement. † significant (p < 0.05) time*group effect.*

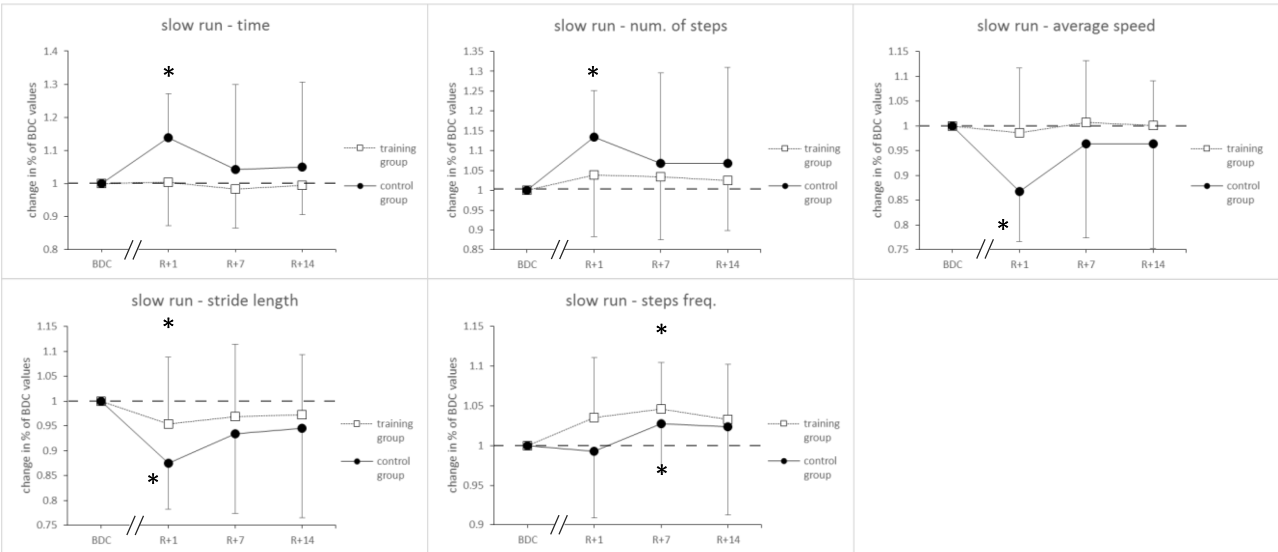

*Figure 4. Slow run time (top left), number of steps (top center), average speed (top right), stride length (bottom left) and steps frequency (bottom center) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, relative values. The changes are expressed in percentage of BDC values (mean ± SD). * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

Moderate run parameters: the statistical analysis on the absolute values showed a difference between groups ($p < 0.05$) in $Freq_{step}$ during R+1, with a decrease in the frequency for the *control group*. This difference disappeared during R+7. One of the most affected parameter, during this activity is the N_{step} for the *control group* with a 10% increase ($p < 0.05$), and for the *training group* with an 11% increase ($p < 0.05$) during R+1 measurement. Other parameters showed no statistical difference ($p < 0.05$) from BDC measurements (Figure 5).

The statistical analysis on the relative values showed a statistical ($p < 0.05$) increase in T_{taks} for both groups that persist until the measurement taken in R+14. The second parameter that was seriously affected by the bed-rest period is the N_{step}, with a statistically increase ($p < 0.05$) of about 10% for both groups in all the post-measurements (R+1, R+7, R+14). S_{avg} showed a significant decrease ($p < 0.05$) during R+1 measurement for both groups, disappearing during R+7 measurement (Figure 6).

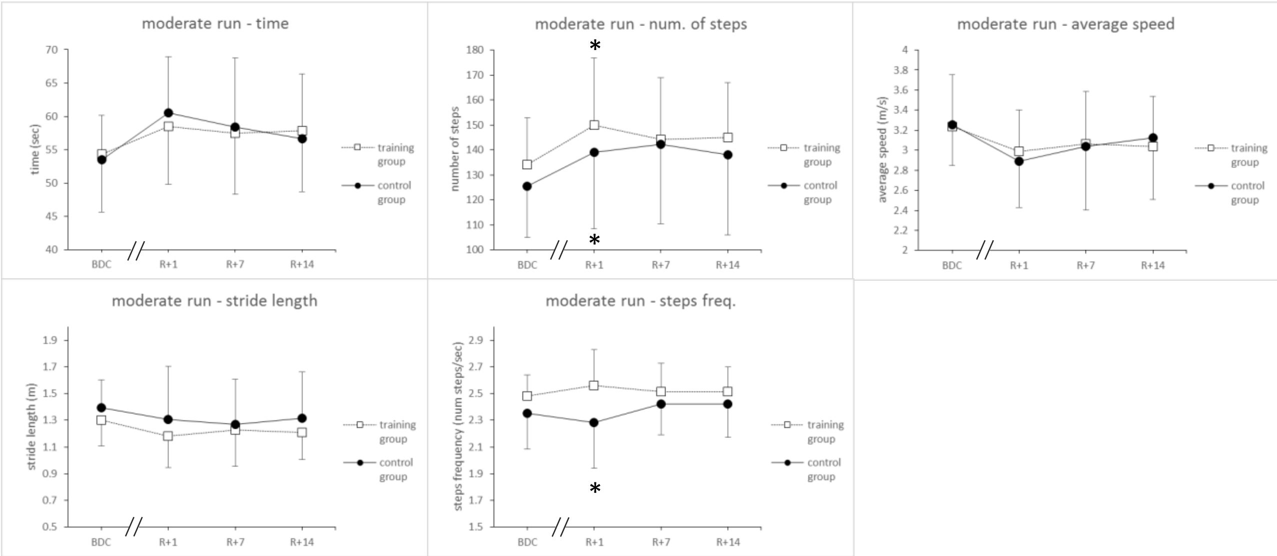

*Figure 5. Moderate run time (top left), number of steps (top center), average speed (top right), stride length (bottom left) and steps frequency (bottom center) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, absolute values. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement. † significant (p < 0.05) time*group effect.*

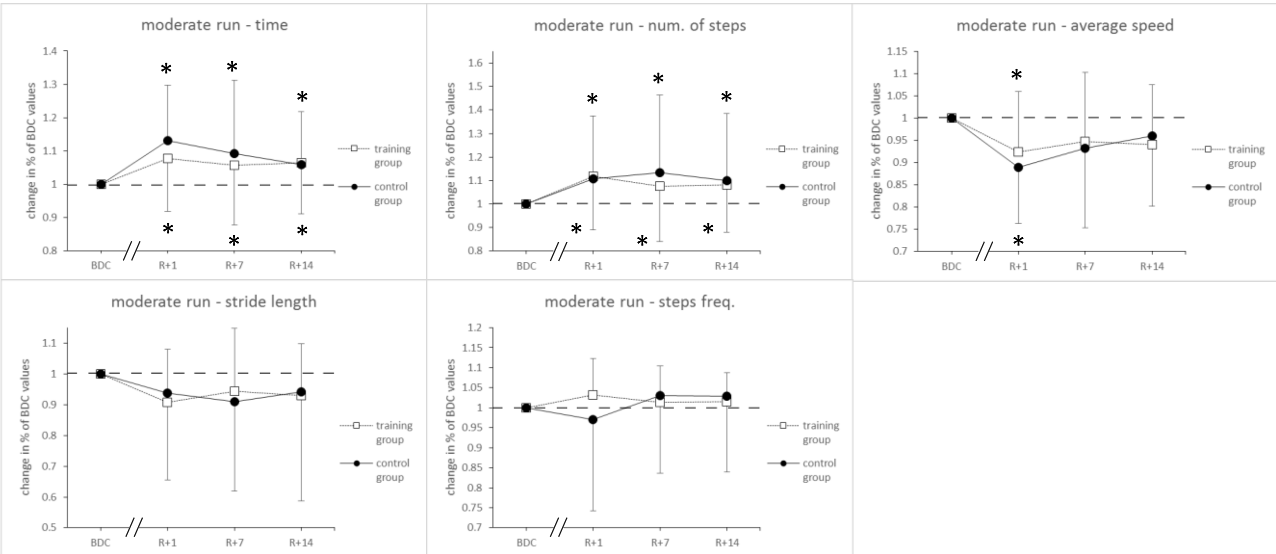

*Figure 6. Moderate run time (top left), number of steps (top center), average speed (top right), stride length (bottom left) and steps frequency (bottom center) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, relative values. The changes are expressed in percentage of BDC values (mean ± SD). * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

Climb up stairs: in this activity, when comparing the absolute values, only one parameter changed significantly ($p < 0.05$) from the BDC measurement. T_{taks}. Here, only the measurement R+14 statistically changes ($p < 0.05$) from the BDC value for both groups. While, in the same parameter, R+7 and R+14 measurements are statistically different ($p < 0.05$) from R+1 measurement. Regarding N_{step}, statistical difference ($p < 0.05$) was found between R+1 and R+14 measurements for both groups. A groups difference was found to be significant ($p < 0.05$) in $Freq_{step}$, with a decrease for the *control group* compared with the *training group* (Figure 7).

Talking about the relative values, only a statistical difference ($p < 0.05$) was found during T_{taks} between the measurements taken in R+1 and R+14, with a decrease in R+14 compared with R+1 (Figure 8) for both groups.

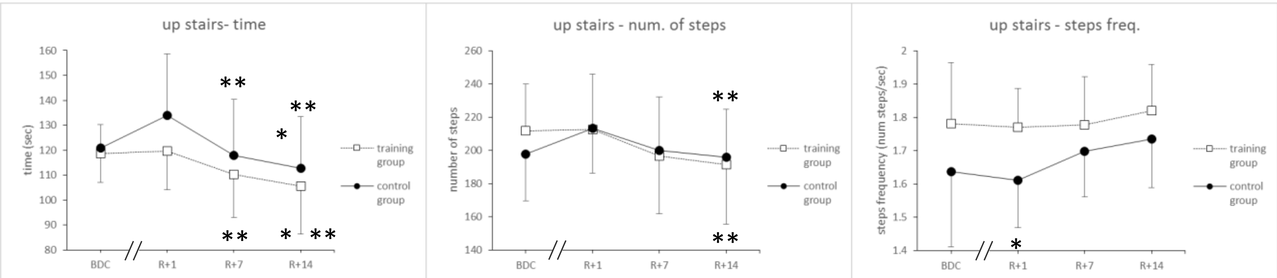

*Figure 7. Climb up stairs time (left), number of steps (center), average speed (right) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, absolute values. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement. † significant (p < 0.05) time*group effect.*

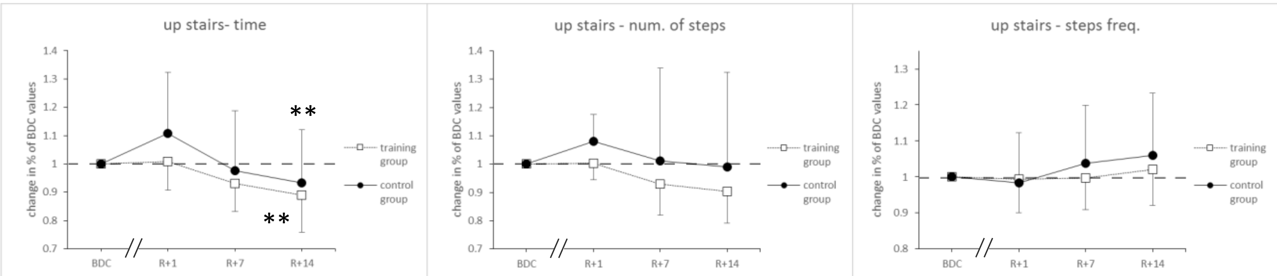

*Figure 8. Climb up stairs time (left), number of steps (center), average speed (right) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, relative values. The changes are expressed in percentage of BDC values (mean ± SD). * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

Climb down stairs: the statistical analysis showed a statistical difference in only two parameters for this activity regarding the absolute values, the T_{taks} and the $Freq_{step}$. They were found to be significantly different ($p < 0.05$) in R+1 measurement compared with BDC measurement in both groups, with no differences between groups (Figure 9).

The analysis on the relative values showed a statistical decrease ($p < 0.05$) from R+1 to R+14 in both groups, going back to the BDC values in the T_{taks} parameters. A significant decrease ($p < 0.05$) for the *control group* has been found in the $Freq_{step}$ during R+1 measurement Figure 10.

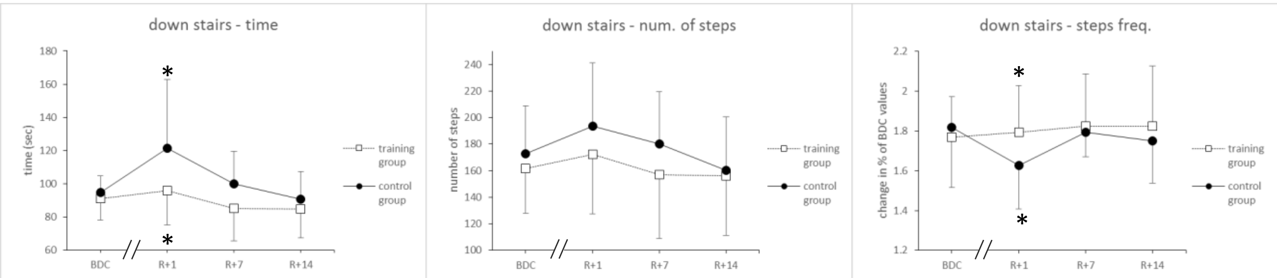

*Figure 9. Climb down stairs time (left), number of steps (center), average speed (right) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, absolute values. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement. † significant (p < 0.05) time*group effect.*

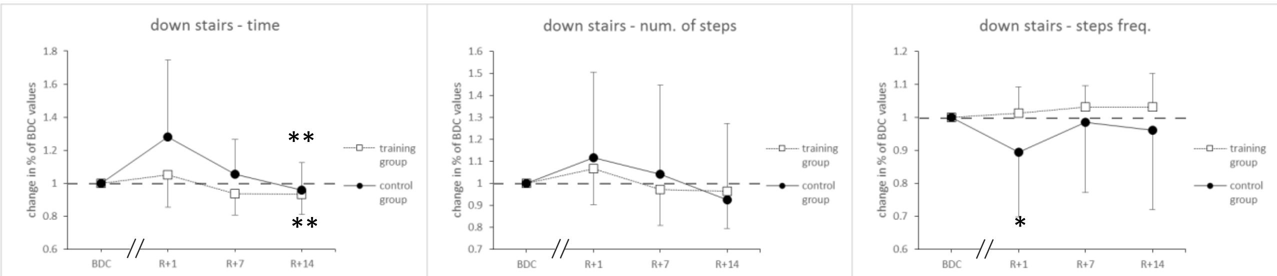

*Figure 10. Climb down stairs time (left), number of steps (center), average speed (right) during BDC and R phases (BDC, R+1, R+7 R+14) in both groups, relative values. The changes are expressed in percentage of BDC values (mean ± SD). * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

In this section only the statistical differences found with both analyses (using two data points, BDC and R+1; and using four data points, BDC, R+1, R+7, R+14) have been summarized. For some analyses, it so happened that while using the first type of statistical analysis to see whether a significant difference between BDC and R+1 occurred and significant differences were found, those statistical differences disappeared using the second analysis, for checking the differences between four data points (BDC, R+1, R+7, R+14), or vice versa. When it happened, for reporting the results between BDC and R+1, priority was given to the analysis with two data points. For a complete overview of all the results, from Table 5 to Table 8, together with Figure 1 to Figure Figure 10 can give an exhaustive explanation.

4.2 Physical activity results

Before showing the results of this section, a few of words are worth mentioning. The period taken into consideration for the analysis goes from BDC-14 to BDC-1 and from R+0 to R+14. In this period all the subjects were confined in the facilities of DLR (*:envihab*) for the pre and post period of bed-rest. For the analysis, the data was structured in this way: the percentages corresponding at *low intensity*, *medium intensity* and *high intensity* of PA have been merged together to have a more consistent value, otherwise values for *high intensity* PA were around 0.05% to 0.3% and values for the *medium intensity* PA around 0.07% to 1% of the entire period in the *:envihab* (see section *Limitations* for a possible explanation for percentages so low). Thus, the analysis was carried out having two variables, the *no activity levels* and the *activity level* of PA. Moreover, to not flatten values of every single day, the averages over seven days were taken instead of the averages over fourteen days, so the period has been split in four time points (from BDC-14 to BDC-8, from BDC-7 to BDC-1, from R+0 to R+7, from R+8 to R+14). The results are expressed in percentage, where 100% is the total recorded signal for the period BDC-14 to R+14.

The statistical analysis showed a non-significant difference ($p < 0.05$) between pre and post 60-day HDT bed-rest for both variables, *no activity levels* and *activity levels*. *No* *activity levels* in both groups remained similar after 60-day bed-rest, with values around 93%. As well as for the *activity levels* variable that after the intervention period, the values remained around 6% for both groups. Table 9 and Figure 11 give a detailed overview of the results.

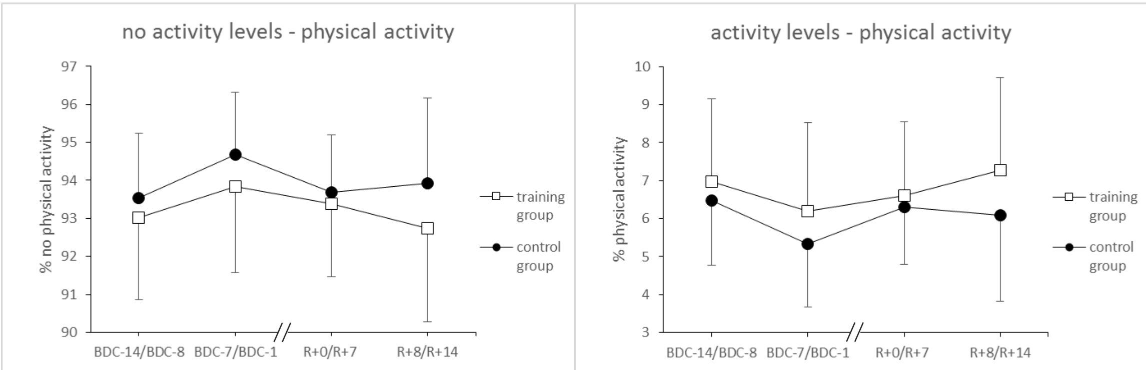

Figure 11. Percentage (mean ± SD) of no activity levels *(left) and* activity levels *(right) during the in-house recovery in both groups. * significant difference (p < 0.05) from BDC measurement.*

Discussion

HDBR is well known to mimic most of the physiological changes that occur while being in space, for instance the redistribution of the body fluids or the loss in muscle strength and mass and the bone demineralization, or the decrease in plasma volume. Even though these changes are well known, the changes in the gait analysis are not well defined yet.

Some authors (Bloomberg J. J., 1997; Dupui P., 1992; Mulavara A. P., 2010) investigated the changes in the locomotion and on the balance after spaceflight and bed-rest, finding irregularity in gait and balance parameters. These irregularities, can be explained by an alteration of the motor ability induced by a muscular atrophy together with a deterioration of the antigravity muscles (Sandler H., 1986). It has been seen that during BR or spaceflight, the decrease in the muscular activity plays a key role in the deconditioning of the muscular system (Thornton W. E., 1977). In particular, the antigravity muscles of the legs are the most affected, reducing in size and in performance when testing strength and motor capabilities (Pavy-Le Traon A., 2007; Sandler H., 1986). When studying immobilization using body cast for 6-8 weeks, Dietrick et al. (Dietrick J.E., 1948) reported that the bigger decrease in strength was seen in the muscles associated with the locomotion; the *tibialis anterior* lost 13.3%, the *gastrocnemius* and *soleus*, together lost 20.8% and the *biceps femoris* lost 6.6%. Locomotion is not just a simple task, but is the result of different coordination abilities – eye-head coordination, head-trunk coordination and trunk-lower limb coordination. In another study, Mulavara et al. (Mulavara A. P., 2010) showed that astronauts after spaceflight had an increase of 48% in the time to complete the functional mobility test – a test where the subjects are required to walk and avoid obstacles. This increase is explained by an increase in the reliance on the visual cues and a reduction in the signal from the graviceptors (Mueller C., 1994; Oman C. M., 2000; Reschke M. F., 1998) as well as a reduction in the proprioceptive inputs during standing and moving (Reschke M. F., 1998; Roll R., 1998). Other authors, showed that post-flight, a change in the spinal circuitry function is observed, with an alteration of the H-, otolith-, spinal- and stretch- reflex (Harris B. A. Jr, 1997; Watt D. G., 1985) and a reduction in muscle strength and mass (Fitts R. H., 2000).

The results of this study find a confirmation in what was said before and it can, in part, support other results from previous bed-rest studies (Haines, 1974; Viguier M., 2009), where bed-rest period caused a decrease in gait parameters and balance. The results of this study showed a negative effect of the bed-rest study on the gait parameters, particularly on the running pattern and the effectiveness of the SJS as countermeasure for some of the activities made during the gait course. On the other hand, the results from the physical activity levels analysis did not showed any interesting results.

5.1 Results from the Gait Course data

The results obtained from the analysis of the data of the gait course partially confirm the initial hypotheses, where a decrease in the parameters of all the activities were expected in R+1, and a faster recovery predicted for the *training group* compared with the *control group* in the two weeks following the HDBR.

If considering the relative values, regarding the walk parameter, the SJS has been able to preserve the *steps frequency*, the *number of steps* and the *stride length*, while it has not been effective in preserving the *time to complete the task* and the *average speed* in both groups. The effects of the bed-rest in the parameters affected seem to persist even in R+7 measurement, disappearing during R+14, suggesting a uniform recovery for both groups.

When slow run is considered, it is clear how the SJS could preserve some of the parameters in the *training group*, while the *control group* suffered from the bed-rest period. This can be explained by the effectiveness of the SJS, as suggested by Kramer et al. (R. R. Kramer A., Gollhofer A., Gruber M., 2012), where four weeks of training in the SJS can increase the rate of force development, the leg stiffness, peak forces and ground reaction force normalized to normal hops. An unexpected outcome is the recovery; it has been faster in this activity than in the walk activity. In R+7, the *control group* completely recovered the parameters affected by the bed-rest. Unexpectedly, the *steps frequency* increased, in both groups only during R+7 measurements, going back to normality during the week after. The most affected parameter is the moderate run, especially when considering the *time to complete the task* and the *number of steps*. In those two parameters, both groups suffered from the bed-rest period, with an incomplete recovery; the increase in the parameters persist for the two weeks after the bed-rest, without going back to the previous values. This could suggest that maybe, the SJS is not the best countermeasure for preventing the running pattern, mainly due to its nature. Subjects were trained for jumping and not for running. Thus, when coordination and strength are required for a specific task, such as running, it cannot completely satisfy this. In addition, the *average speed,* decreased for both groups in R+1, and recovered in the following week. These modifications observable after HDBR in the locomotive patterns can be explained by a combination between a loss in muscle strength and mass (Fitts R. H., 2000) and a distortion of the sensorimotor system in one or more of the levels of the motor control loops involved in the stabilization. These levels are represented by the sensorial receptors that collect data of the body movements and displacement, the perception and elaboration of the strategies from the brain and the final command to the muscles after the brain has analyzed the data (Komi, 2003). It is not new that HDBR causes impairment of the sensory receptors, including visual receptors (Drosdova N. T., 1970; Haines, 1973), vestibular receptors (Kotovskaya A. R., 1981) and cutaneous pressure- receptors of the foot sole (Kozlovskaya I. B., 2007). Due to the muscular atrophy and loss in strength, the muscular receptors are also altered, in particularly those of the antigravity muscles (Trappe T. A., 1999).

When focusing on the relative values of climbing up/down stairs, it can be noticed that they remain almost unchanged for all the parameters in both groups, except for the *steps frequency* while going down stairs. It showed a decrease for the *control group* during R+1, showing a full recovery during R+7 measurement. This shows that the capability to climb up and down stairs is almost not affected by bed-rest. One possible explanation can be found in the effort to complete the task. Usually when climbing up or down stairs at normal pace, not much effort is required (if subjects do not suffer from any physiological disease). Thus, even in a condition of disability brought by the BR period, increasing the effort to complete the task could let the task be accomplished without showing any disadvantage.

One of the reasons why statistical differences were observed only in certain parameters and not in all could be explained by the fact that the tasks performed were not sub-maximal tasks, as already explained for climbing up and down stairs tasks; the subjects were not asked to make a considerable effort to compete the action. It is reasonable to think that even if the subjects had a decline after the HDBR period, in the ability to perform and finish the task, this decline could be easily overtaken by putting more effort to accomplish it, and thus having a higher energy expenditure. Unfortunately, the energy expenditure was not considered as one of the features of the gait course for different reasons that will be explained later in this chapter. This lack of sub-maximal tasks in the gait course can be considered to be a limitation when we want to measure intensity of activities before and after an intervention period. Or moreover, because of the inhomogeneity of the groups that showed a big inter-subject variability, had flattened possible statistical differences (Dixon W. J., 1983). Some subjects had a huge decline in the ability to perform the task when compared with baseline values, while other subjects did not show any differences, regardless of the group. This variation can be also associated with the gene influence. It is known that for the same strength training, different subjects react in different ways; Folland et al. (Folland J., 2000) found that *angiotensin-converting enzyme* (ACE) genotype changes the adaptations of the musculoskeletal system to training. For this reason, more importance has been given to the relative data than the absolute data to reduce the inter-subject variability, and have a better understand of the studied parameters.

Another limitation factor that could have influenced the data can be explain by the fact that the gait courses have not been supervised by the same person, due to some problem in the logistical organization of the gait courses. This could bring some differences in the execution of the task and, consequently, in the consistency of the data. Especially during the early phase of RSL1, when more than one instructor supervised the gait courses.

For further research, it can be recommended to choose a set of sub-maximal activities for the gait course that can give an exhaustive picture of the situation, avoiding situations like the climbing up and down stairs, where no statistical differences were found maybe due to the specificity of the task. One more recommendation can be to integrate another device, such a portable and non-intrusive electrocardiograph (ECG) to record also the activity of the heart during the activities and thus having more information regarding the intensity and the effort done to accomplish the given task. The last recommendation that can be given in order to have a solid data collection, is to always have the same supervisor for every gait course, so that even during the data analysis it will be clear what has been done and in what order.

5.2 Results from the Physical Activity levels data

The role of PA as one of the health indicators has been recognized, but nowadays, thanks to better methods to record and to quantify it, our knowledge on this topic are increasing. Thus, a valid instrument that gives reliable output is needed, and the accelerometer demonstrated itself to be a trustable device because of its compactness, durability and reliability. Proving objective measurement of the intensity and frequency of the movements.

When talking about PA, many authors (Bouten C. V., 1994; Cotes J. E., 1960; Wong T. C., 1981) have reported a strong linear relationship between the body acceleration and the Energy Expenditure (EE). However, this linearity has been found only for low intensity activity such as walking. For example, Bouten et al. (Bouten C. V., 1994) found a correlation of 0.96. Other authors (Haymes E. M., 1991), when trying to estimate the linearity between EE and acceleration overestimated the EE by 1.5 $kcal \cdot min^{-1}$ in walking and by 3.6 and 3.7 $kcal \cdot min^{-1}$ when running at 4 and 5 mph, respectively, with a linearity of 0.86 and 0.29 for walking and running, respectively. Others authors (W. K. R. Meijer G. A. L., Koper H. B. M., Ten F., 1989) reported an underestimation of the EE under laboratory condition, and an overestimation of 30% when analyzing data from the field. During other activities, such as climb up stairs or down stairs, the estimation of EE is still not clear because of the difficulty in the correct detection of vertical movements (Ohtaky Y., 2005). Another factor that contributes to EE estimation is the speed, which is very difficult to estimate from the raw data of the accelerometers (Schimpl M., 2011). Others authors (Ohtaky Y., 2005; Puyau M R., 2002) used more complex and sophisticated methods, such as accelerometers combined with barometers or telemetry in a room calorimeter.

Because of the limitations mentioned for the EE estimation during different activities and the lack of special devices (such as barometers), in this work, a simpler method has been used to assess PA levels, so that a major overview of the entire state of PA can be seen, and not only extrapolated from activities, such as walking taken under laboratory conditions.

Concerning the results obtained from the PA levels analysis, no statistical differences were found, mainly due to the situation of the subjects during the two weeks before and the two weeks after the bed-rest period. The subjects were confined in the *:envihab*, where not many activities were allowed. For instance, they did not have the possibility to go for a run or a jog whenever and wherever they wanted, or the possibility to walk freely even inside the DLR facilities. So the subjects were mostly sedentary – indulging in activity such as watching TV, working with laptops, playing videogames, walking, sitting or lying on bed or couch for the entire in-house recovery period, except for the time of the experiments. All this could have brought to a very sedentary situation for all the subjects in the pre and post period that could not have been avoided. This situation can be seen as the major limitation regarding the PA levels recognition. One more limitation that could have interfered with the outcomes is the averaged period over seven days (from BDC-14 to BDC-8, from BDC-7 to BDC-1, from R+0 to R+7, from R+8 to R+14) of the two weeks of in-house recovery for the statistical analysis, leading to a flattening of the outcomes of the post bed-rest period.

Another factor that could have limited the outcomes is the method used to analyze the data. Even if, as mentioned before, this method allows to have a simple data processing, giving very straightforward outcomes and understandings, it also has significant limitations. Chen et al. (Chen K. Y., 2005) stated that using this process the details of the signal decrease for each time window, so it is recommended to use short epochs to have a higher resolution of bout durations. Using short epochs, say the authors, can also bring disadvantages. One of them is when calculating, for example, the EE, and a short epoch from 10 to 30 seconds can have lower physiological values. However, if we increase the length of the epoch that contain different activities made at different intensity, the entire dataset will be averaged and, as a result, only the intermediate intensity will be taken into consideration losing the different intensities. Thus, more importance has been given to the distinction of the intensities of different activities rather than having little physiological values and an epoch of ten seconds was chosen.

A suggestion that can be given for further research is the use of a more comfortable device in case it must be worn for a long period of time, like in this study. Many times, the subjects complained about the wearability of the device. Thus, a more comfortable and friendly device would be noticed less while worn and used with less unwillingness by participants.

5.3 Other features

Many others analyses can be done with the data acquired from accelerometers. For example, in the recent years, many authors started to classify movements using algorithms and many techniques have been developed.

For instance, Skotte et al. (Skotte J., 2014) developed a method to recognize different types of PA based on threshold values of standard deviation of acceleration signal and the derived inclination from two accelerometers mounted respectively at the right medial front thigh and at right side of the hip. The outcomes showed a very high (ca. 99%) sensitivity and specificity to discriminate between different standardized PA types (e.g. standing, walking, sitting, running and cycling) with the accelerometer mounted on the thigh. Other authors (Kiani K., 1997; Sharma A., 2008) used the Artificial Neural Networks (ANN) to train the machine for the detection and the distinction between different spontaneous motor activities, so that once the machine learned how to discriminate the activities, there is no further need of previous recording under laboratory conditions to set and distinguish the activities. Another strategy used to classify movements is the hierarchical binary tree (Mathie M. J., 2004b) where firstly, not so detailed classification of movements, calculated from the accelerometer signal, is made in the first levels of the tree and then more detailed classifications are made in the last levels of the tree, so that the movements are classified either to match required level of detail or to reach the limit of what can be obtained using the monitoring system.

Another interesting parameter that can be estimated from an accelerometer signal is the volume of oxygen (VO_2) consumption. Many authors proved the correlation between the VO_2 consumed and the accelerometer signal. Montoye et al. (Montoye H. J., 1983) came up with a uni-axial accelerometer and compared the output with the VO_2 consumed and the mercury switches. A variety of random physical activities were chosen because of their resemblance with everyday activities and then performed by subjects. The outcomes showed that the accelerometer output is highly reproducible and had moderate to high individual and group correlations with VO_2 (individual r=0.63-0.89, mean r=0.79, group r=0.74). Similar results are also confirmed by Eston et al. (Eston R. G., 1998), showing that a tri-axial accelerometer mounted on the belt, above the right hip, is the best predictor for the VO_2

consumption in a variety of children's activities compared with pedometers and uni-axial accelerometer. In his study, children walked and ran on a treadmill at 4 and 6 km/h in the walking activity and 8 and 10 km/h for the run. The gas exchanges were also measured with an on-line gas analysis every 30 seconds for each activity. The results show a correlation of r = 0.883 for treadmill activities and r = 0.926 for unregulated play activities, confirming the validity of this device to estimate VO_2 consumption during different activities.

In this study, those features have not been taken into consideration mainly due to the time and workload involved. Regarding the detection of movements with the ANN or the decision three, the initial idea was to use them to discriminate movements and activities performed before and after the bed-rest study, but due to a very different movement pattern in the days following the bed-rest period, this has not been possible. Moreover, carrying on all the data and statistical analysis for the new parameters on my own, plus the analysis already performed for the parameters showed in this work was out of my scope, letting me miss the deadline for the submission of the thesis. It is needless say that if more time would have been available, further analysis on these parameters would have been of extreme interest.

Conclusions

The study was carried out to verify the effects of a 60-day bed-rest on the locomotive patterns and the levels of PA in healthy subjects. Moreover, it wanted to know whether the PA is affected by the bed-rest period and in which measure, and verify if the SJS can be used as countermeasure during space flight to prevent or reduce the effects of microgravity on the human systems. The study sought to test the following hypotheses:

I. Significant differences in the gait course parameters, between pre and post measurements (BDC and R+1) for both groups in the following points:
   1. Number of steps, frequency of steps and time spent to complete each activity (walking, slow run, moderate run, climb up-stairs, climb down-stairs).
   2. Average speed and stride length for walking, slow run and moderate run.

II. *Training group* will recover faster than *control group* concerning gait course parameters made during R+7 and R+14 for regarding the point stated in the first hypothesis.

III. Decrease in level of physical activity for both groups during in-house recovery (2 weeks after head-down tilt phase) compared to the BDC phase (2 weeks before head-down tilt).

The main findings have already been summarized within the respective chapter (see *Results*). This part will only synthetize the findings to verify if they match with the initial hypotheses.

I. Significant differences in the gait course parameters, between pre and post measurements (BDC and R+1) for both groups.

When considering the relative values, the first hypothesis has been partially confirmed because not all parameters showed a significant difference between pre and post measurements taken respectively in BDC and R+1.

II. *Training group* will recover faster than *control group* concerning gait course parameters made during R+7 and R+14 for regarding the point stated in the first hypothesis.

The second hypothesis has been not confirmed even if the *training group* showed a better response compared to the *control group* to the bed-rest period for some parameters and some activities, showing no differences from the pre measurements, proving the effectiveness of the SJS in preventing from immobilization’s effects.

III. Decrease in level of physical activity for both groups during in-house recovery (2 weeks after head-down tilt phase) compared to the BDC phase (2 weeks before head-down tilt).

The third and last hypothesis has not been confirmed by the results; the level of PA remained unchanged, not showing any statistical difference between the BDC phase and the R+ phase for reasons that are explained in the chapter *Discussions*.

Further study should collect more data from the gait after a bed-rest study to compare other findings. Moreover others could focus more on the biomechanics of the gait, incorporating other methods together with the accelerometer, such as the motion capture system to study all the biomechanical aspects of the gait, or placing a portable and non-invasive ECG to integrate the two signals (ECG and accelerometer signals) to comparing them for different activities.

The findings support other studies that demonstrated the benefits of physical exercise while confined in bed or during a space mission to reduce the negative effects of microgravity on the human body, and partially prove the effectiveness of the SJS concerning to prevent the gait parameters.

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Appendices

8.1 Tables

	Num. subjects	Age	Height (cm)	Weight (kg)
Control group	11	28.09 ± 5.85	180.45 ± 5.04	76.35 ± 7.82
Training group	12	30.08 ± 6.43	181.20 ± 6.57	77.10 ± 6.78

Table 2. Mean ± SD. Age, height and weight divided by groups.

Subject	Age	Height (cm)	Weight (kg)	Group	Sample Frequency (Hz)	Belt position
A	25	185	84.3	Control	50	Left side
B	23	181	83.05	Control	25	Back
C	22	177	68.71	Training	50	Left side
D	21	176	70.14	Control	50	Left side
E	42	183	73.77	Training	50	Back
F	35	188.5	86.56	Control	25	Back
G	34	186	67.78	Training	50	Back
H	26	188	76.04	Control	50	Back
J	27	171	76.96	Training	25	Left side
K	27	178	79.95	Control	50	Right
L	29	169.5	67.34	Training	50	Left side
M	28	172.5	67.69	Control	50	Left side
N	24	190	80.48	Training	100	Left side
P	25	181	80	Training	100	Left side
Q	35	181	68.41	Control	100	Back
R	41	179	74.4	Training	100	Back
S	33	185	85.81	Training	100	Back
U	22	180	83.49	Control	100	Back
V	28	189	84.5	Training	100	Right side
W	28	176	76.49	Control	100	Back
X	31	178	79.49	Training	100	Back
Y	39	179	63.73	Control	100	Back
Z	25	186	86.01	Training	100	Back
Mean	29.13	180.84	76.74			
SD	6.10	5.77	7.14			

Table 3. Subjects, age, height, weight, group, sample rate and belt position for each participant of the study. SD, standard deviation.

RSL-Study (ESA LTBR Cologne) Saturday, 26 September 2015 32

study day	HDT16		HDT15		HDT14		HDT13		study day
wake-up order	3	4	7	8	1	2	5	6	wake-up order
subject	*E*	*F*	*G*	*H*	*J*	*K*	*L*	*M*	subject
6:30	Temp, BP	Temp, BP	Temp, BP	Temp, BP	Temp, BP	Temp, BP	Temp, BP	Temp, BP	6:30
6:45	BD	BD			BD	BD			6:45
7:00	Urine 29, BW	Urine 29, BW	Urine 28, BW	Urine 28, BW	Urine 27, BW	Urine 27, BW	Urine 26, BW	Urine 26, BW	7:00
7:15	activity				activity	activity			7:15
7:30		activity					activity	SBIS Stahn	7:30
7:45									7:45
8:00	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast	Breakfast	SBIS Stahn		8:00
8:15								activity	8:15
8:30							Breakfast		8:30
8:45								Breakfast	8:45
9:00									9:00
9:15					activity				9:15
9:30									9:30
9:45									9:45
10:00									10:00
10:15						activity			10:15
10:30	Snack	Snack	Snack	Snack	Snack		Snack	Snack	10:30
10:45									10:45
11:00						Snack			11:00
11:15									11:15
11:30									11:30
11:45									11:45
12:00									12:00
12:15									12:15
12:30									12:30
12:45									12:45
13:00	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	Lunch	13:00
13:15									13:15
13:30									13:30
13:45									13:45
14:00					activity				14:00
14:15									14:15
14:30				activity					14:30
14:45	activity								14:45
15:00						activity	CM TRAIN		15:00
15:15									15:15
15:30			activity						15:30
15:45		Snack						Snack	15:45
16:00	Snack		CM TRAIN	Snack	Snack	Snack	Snack	activity	16:00
16:15					Shower	Shower			16:15
16:30	CM TRAIN		Snack				activity		16:30
16:45		activity							16:45
17:00									17:00
17:15									17:15
17:30					activity				17:30
17:45									17:45
18:00						activity			18:00
18:15									18:15
18:30									18:30
18:45									18:45
19:00	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	Dinner	19:00
19:15									19:15
19:30	LOG (BCD)	LOG (BCD)	LOG (BCD)	LOG (BCD)	LOG (BCD)	LOG (BCD)	LOG (BCD)	LOG (BCD)	19:30
19:45									19:45
20:00					activity	activity			20:00
20:15					activity	activity			20:15
20:30									20:30
20:45					activity				20:45
21:00									21:00
21:15									21:15
21:30	Snack	Snack	Snack	Snack	Snack	Snack	Snack	Snack	21:30
21:45									21:45
22:00									22:00
22:15	Bedtime	Bedtime	Bedtime	Bedtime	Bedtime	Bedtime	Bedtime	Bedtime	22:15
22:30									22:30
22:45									22:45

Table 4. Example of a daily schedule for subjects.

Parameters	Control group			
	BDC	R+1	R+7	R+14
Walking				
time (s)	235.07(20.37)	259.64(34.33)	249.62(31.04)	234.25(25.68)
steps (num.)	445(34)	470(35)	465(25)	452(35)
avg. speed (m/s)	1.47(0.13)	1.33(0.15)	1.39(0.18)	1.48(0.16)
stride length (m)	0.78(0.06)	0.73(0.05)	0.74(0.04)	0.76(0.06)
step freq. (n. step/s)	1.90(0.08)	1.82(0.14)*	1.88(0.17)	1.94(0.13)
Slow run				
time (s)	69.98(9.85)	79.68(6.68)*	72.97(11.51)	73.50(13.39)
steps (num.)	166(24)	188(20)*	177(24)	177(30)
avg. speed (m/s)	2.49(0.35)	2.16(0.18)*	2.4(0.38)	2.4(0.43)
stride length (m)	1.05(0.15)	0.92(0.11)*	0.98(0.13)	1.00(0.18)
step freq. (n. step/s)	2.38(0.18)	2.36(0.12)	2.44(0.21)	2.43(0.30)
Moderate run				
time (s)	53.48(6.69)	60.49(8.43)	58.41(10.38)	56.63(9.75)
steps (num.)	126(20)	139(31)*	142(32)	138(32)
avg. speed (m/s)	3.25(0.4)	2.89(0.46)	3.03(0.63)	3.12(0.61)
stride length (m)	1.40(0.21)	1.31(0.39)	1.27(0.34)	1.31(0.35)
step freq. (n. step/s)	2.35(0.27)	2.28(0.34)*	2.42(0.23)	2.42(0.25)
Up stairs				
time (s)	120.88(9.3)	133.93(24.64)	118.05(22.29)**	112.75(20.82)*
steps (num.)	198(28)	214(27)	200(38)	196(40)**
step freq. (n. step/s)	1.64(0.23)	1.61(0.14)*	1.70(0.14)	1.73(0.14)
Down stairs				
time (s)	94.69(9.84)	121.35(41.43)*	99.97(19.34)	90.74(16.45)
steps (num.)	173(36)	193(48)	180(39)	160(40)
step freq. (n. step/s)	1.82(0.30)	1.63(0.22)*	1.79(0.12)	1.75(0.21)

*Table 5 - **control group.** Parameters measured during gait course in the four sessions (BDC, R+1, R+7, R+14) [mean (SD)] in both groups (control group, training group) expressed as absolute values. Post hoc test was done with Bonferroni's test. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

Parameters	Training group			
	BDC	R+1	R+7	R+14
Walking				
time (s)	236.75(15.36)	247.77(21.83)	251.43(23.96)	241.33(26.21)
steps (num.)	474(48)	478(38)	480(30)	462(36)
avg. speed (m/s)	1.45(0.09)	1.39(0.13)	1.37(0.14)	1.43(0.15)
stride length (m)	0.73(0.07)	0.72(0.05)	0.72(0.05)	0.75(0.06)
step freq. (n. step/s)	2.00(0.12)	1.93(0.11)	1.92(0.15)	1.92(0.13)
Slow run				
time (s)	73.47(12.19)	73.69(8.12)*	72.27(9.25)	72.98(10.09)
steps (num.)	175(26)	182(18)*	181(26)	179(22)
avg. speed (m/s)	2.38(0.36)	2.35(0.27)*	2.4(0.29)	2.39(0.32)
stride length (m)	1.00(0.13)	0.95(0.10)*	0.97(0.14)	0.97(0.12)
step freq. (n. step/s)	2.39(0.14)	2.48(0.19)	2.50(0.19)	2.47(0.23)
Moderate run				
time (s)	54.33(8.68)	58.52(8.74)	57.45(9.16)	57.82(9.15)
steps (num.)	134(19)	150(27)*	144(25)	145(22)
avg. speed (m/s)	3.23(0.52)	2.98(0.41)	3.06(0.52)	3.03(0.5)
stride length (m)	1.30(0.19)	1.18(0.24)	1.23(0.28)	1.21(0.21)
step freq. (n. step/s)	2.48(0.16)	2.56(0.27)	2.51(0.22)	2.52(0.18)
Up stairs				
time (s)	118.74(11.71)	119.66(15.61)	110.41(17.25)**	105.55(19.29)*
steps (num.)	212(28)	213(33)	197(36)	192(33)**
step freq. (n. step/s)	1.78(0.18)	1.77(0.12)	1.78(0.14)	1.82(0.14)
Down stairs				
time (s)	91.02(13.08)	95.67(20.73)*	85.14(19.64)	84.87(17.36)
steps (num.)	162(34)	172(45)	157(48)	156(45)
step freq. (n. step/s)	1.77(0.20)	1.79(0.23)*	1.82(0.26)	1.82(0.30)

*Table 6 - **training group.** Parameters measured during gait course in the four sessions (BDC, R+1, R+7, R+14) [mean (SD)] in both groups (control group, training group) expressed as absolute values. Post hoc test was done with Bonferroni's test. * significant difference (p < 0.05) from BDC measurement. ** significant difference (p < 0.05) from R+1 measurement.*

Parameters	Control group			
	BDC	R+1	R+7	R+14
Walking				
time (s)	1	1.10(0.13)*	1.06(0.13)*	0.99(0.11)
steps (num.)	1	1.05(0.10)	1.04(0.08)	1.01(0.09)
avg. speed (m/s)	1	0.91(0.10)*	0.94(0.14)*	1.00(0.12)
stride length (m)	1	0.94(0.08)	0.95(0.07)	0.98(0.08)
step freq. (n. step/s)	1	0.96(0.09)	0.99(0.10)	1.02(0.08)
Slow run				
time (s)	1	1.13(0.13)*	1.04(0.25)	1.05(0.25)
steps (num.)	1	1.13(0.11)*	1.06(0.22)	1.06(0.24)
avg. speed (m/s)	1	0.86(0.10)*	0.96(0.18)	0.96(0.20)
stride length (m)	1	0.87(0.09)*	0.93(0.16)	0.94(0.17)
step freq. (n. step/s)	1	0.99(0.08)	1.02(0.06)*	1.02(0.11)
Moderate run				
time (s)	1	1.13(0.16)*	1.09(0.21)*	1.05(0.15)*
steps (num.)	1	1.10(0.26)*	1.13(0.33)*	1.10(0.28)*
avg. speed (m/s)	1	0.88(0.12)*	0.93(0.17)	0.95(0.15)
stride length (m)	1	0.93(0.28)	0.90(0.29)	0.94(0.35)
step freq. (n. step/s)	1	0.97(0.22)	1.02(0.19)	1.02(0.19)
Up stairs				
time (s)	1	1.10(0.21)	0.97(0.21)	0.93(0.18)**
steps (num.)	1	1.08(0.09)	1.01(0.32)	0.99(0.33)
step freq. (n. step/s)	1	0.98(0.13)	1.03(0.16)	1.05(0.17)
Down stairs				
time (s)	1	1.28(0.46)	1.05(0.20)	0.95(0.16)**
steps (num.)	1	1.11(0.38)	1.04(0.40)	0.92(0.34)
step freq. (n. step/s)	1	0.89(0.19)*	0.98(0.21)	0.96(0.24)

*Table 7 - **control group.** Parameters measured during gait course in the four sessions (BDC, R+1, R+7, R+14) [mean (SD)] in both groups (control group, training group) expressed as relative values (% of change from BDC). Post hoc test was done with Bonferroni's test. * significant difference ($p < 0.05$) from BDC measurement. ** significant difference ($p < 0.05$) from R+1 measurement.*

Parameters	Training group			
	BDC	R+1	R+7	R+14
Walking				
time (s)	1	1.04(0.09)*	1.06(0.09)*	1.01(0.08)
steps (num.)	1	1.00(0.12)	1.01(0.10)	0.97(0.07)
avg. speed (m/s)	1	0.95(0.09)*	0.94(0.09)*	0.98(0.09)
stride length (m)	1	0.98(0.10)	0.98(0.10)	1.02(0.08)
step freq. (n. step/s)	1	0.96(0.08)	0.95(0.09)	0.96(0.07)
Slow run				
time (s)	1	1.00(0.13)	0.98(0.11)	0.99(0.08)
steps (num.)	1	1.03(0.15)	1.03(0.15)	1.02(0.12)
avg. speed (m/s)	1	0.98(0.13)	1.00(0.12)	1.00(0.09)
stride length (m)	1	0.95(0.13)*	0.96(0.14)	0.97(0.12)
step freq. (n. step/s)	1	1.03(0.07)	1.04(0.05)*	1.03(0.06)
Moderate run				
time (s)	1	1.07(0.15)*	1.05(0.17)*	1.06(0.15)*
steps (num.)	1	1.11(0.22)*	1.07(0.23)*	1.08(0.20)*
avg. speed (m/s)	1	0.92(0.13)*	0.94(0.15)	0.93(0.13)
stride length (m)	1	0.90(0.17)	0.94(0.20)	0.92(0.16)
step freq. (n. step/s)	1	1.03(0.09)	1.01(0.09)	1.01(0.07)
Up stairs				
time (s)	1	1.00(0.09)	0.92(0.09)	0.88(0.13)**
steps (num.)	1	1.00(0.05)	0.92(0.11)	0.90(0.11)
step freq. (n. step/s)	1	0.99(0.09)	0.99(0.08)	1.02(0.10)
Down stairs				
time (s)	1	1.05(0.19)	0.93(0.12)	0.93(0.12)**
steps (num.)	1	1.06(0.16)	0.97(0.16)	0.96(0.17)
step freq. (n. step/s)	1	1.01(0.07)	1.03(0.06)	1.03(0.10)

*Table 8 - **training group.** Parameters measured during gait course in the four sessions (BDC, R+1, R+7, R+14) [mean (SD)] in both groups (control group, training group) expressed as relative values (% of change from BDC). Post hoc test was done with Bonferroni's test. * significant difference ($p < 0.05$) from BDC measurement. ** significant difference ($p < 0.05$) from R+1 measurement.*

Parameters	BDC-14/BDC-8	BDC-7/BDC-1	R+0/R+7	R+8/R+14
	Control group			
No activity levels	93.52(1.7)	94.67(1.64)	93.68(1.51)	93.92(2.25)
Activity levels	6.47(1.7)	5.32(1.64)	6.31(1.51)	6.07(2.25)
	Training group			
No activity levels	93.01(2.16)	93.83(2.27)	93.39(1.93)	92.72(2.44)
Activity levels	6.98(2.16)	6.19(2.32)	6.60(1.93)	7.27(2.44)

Table 9. Percentages (mean ± SD) of physical activity levels divided in no activity level *and* activity level *in the period in-house recovery. * significant different (p < 0.05) from BDC measurement.*

8.2 Figures

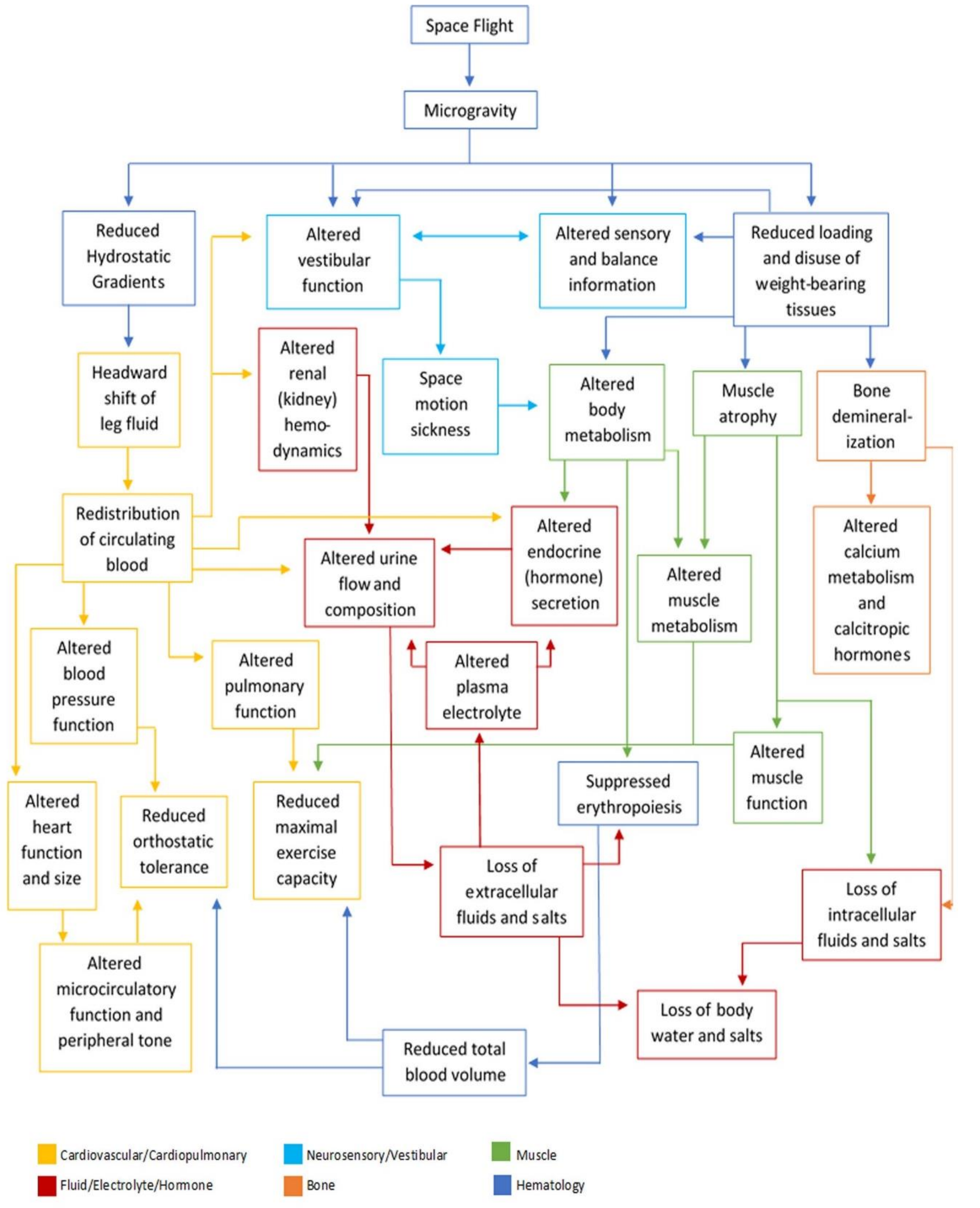

Figure 12. Scheme of the main physiological effects of the microgravity on the human systems. (From: McArdle W.D, Katch F.I., Katch V.L. Exercise Physiology: Lippincott Williams & Wilkins, 2010).

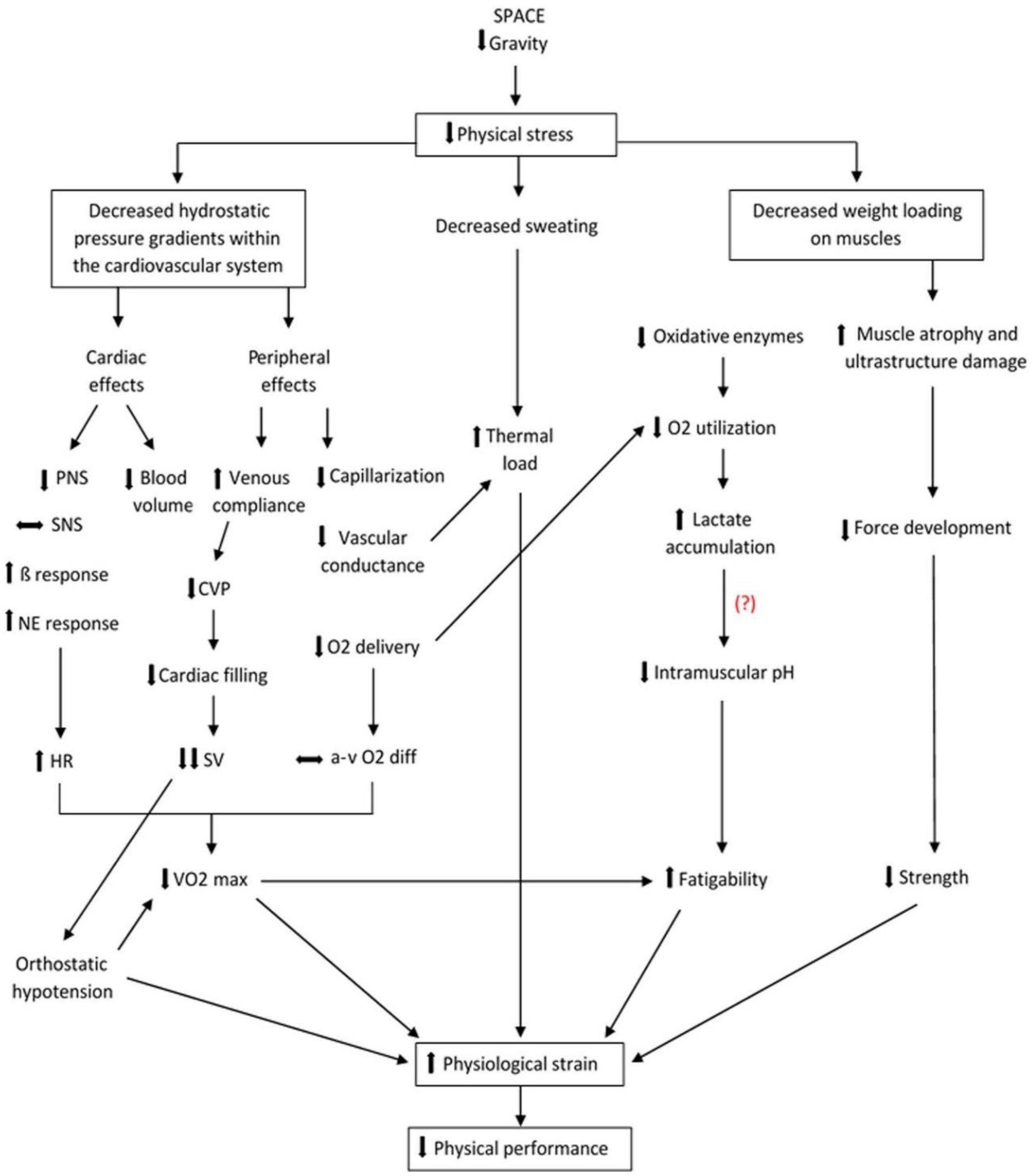

Figure 13. Relationship between muscular and cardiovascular system adaptations and the physical stress of the microgravity environment on the human body. As result can be observed an increase in the physiological strain and a decrease in the physical performance. PNS, peripheral nervous system; CNP, central nervous pressure; SNS, sympathetic nervous system; ß, beta-adrenergic; NE, ⬇ norepinephrine; HR, heart rate; SV, stroke volume; a-v O2 diff, arterious-venous oxygen difference; , decrease; ⬆ , increase; ⬇⬇ , large decrease; ⟺ , no change. (From Convertino VA. Effects of microgravity on exercise performance. In: McArdle W.D, Katch F.I., Katch V.L. Exercise Physiology: Lippincott Williams & Wilkins, 2010).

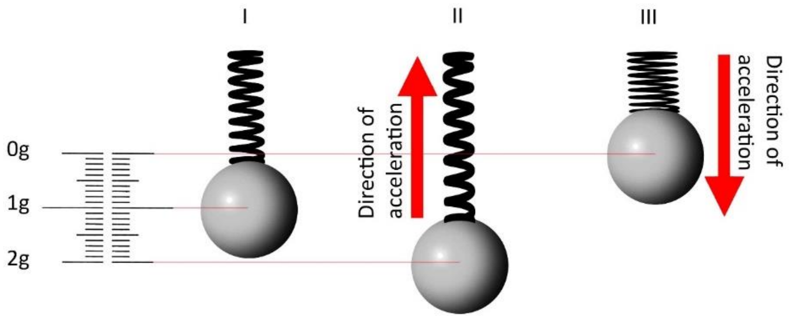

Figure 14. Illustration of the principle of an accelerometer. In illustration I, the mass is at rest and the scale shows 1g. In illustration II, the mass is accelerated upwards. In illustration III, the mass is falling in vacuum experiencing 0g. (From: Garimella R. How does an accelerometer work? A report submitted for "Project Seminar 1". University of Konstanz, *2015. Modified by Grassi M.).*

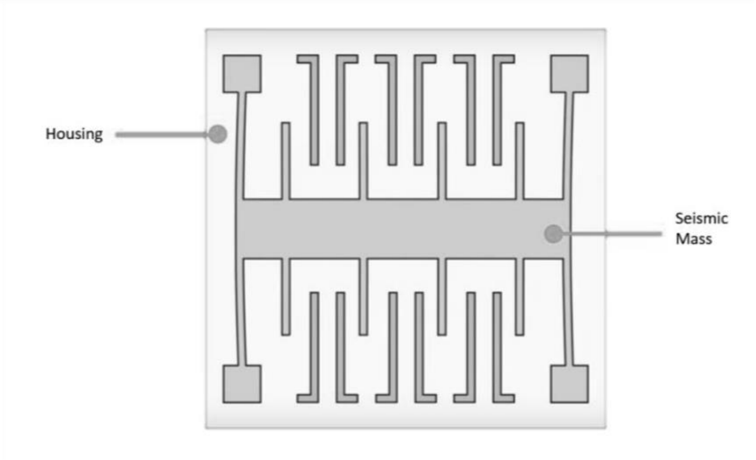

*Figure 15***.** *Schematic illustration of a* comb-drive actuator. *The seismic mass oscillates when accelerated, and the housing stays in position. The oscillations cause a change in capacitance between the comb-structure, which causes a potential difference. This voltage is proportional to the acceleration. (From: www-engineerguy.com).*

I.

II.

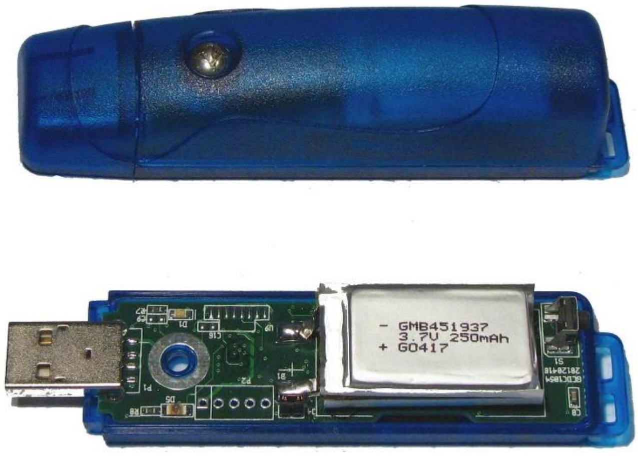

Figure 16. A picture of the X16-4 accelerometer. In illustration I. device appears ready to be used. In illustration II. can be seen the USB port for recharge the device and for the download the data and the battery slot. (Font: http://www.gcdataconcepts.com/images/x16-2_large.jpg. Modified by Grassi M.)

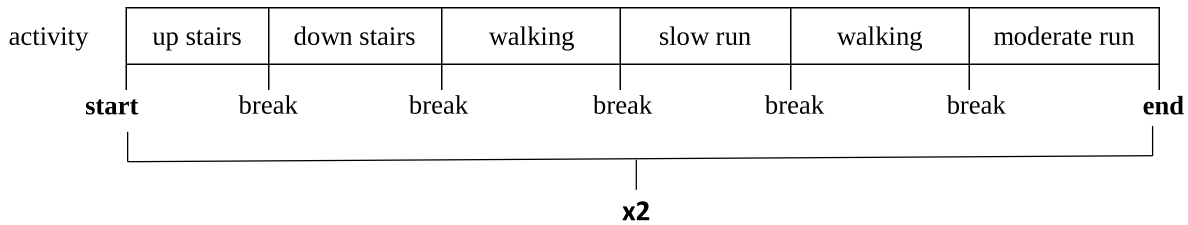

Figure 17. Schematize illustration of the gait course. The entire sequence has been repeated twice for each gait course. The break between each activity varied between 30 seconds and 2 minutes.

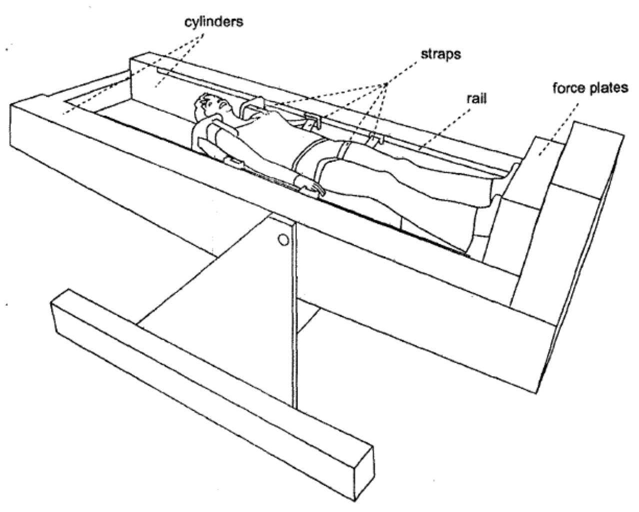

Figure 18. Illustration of the sledge jump system in a theoretical training session. The subject lies down in a horizontal position standing on two force plates (one for foot) while fixed with the straps to the wooden sledge. The subject together with the wooden sledge can only slide in the direction of the rails. (From: Kramer A. et al. A new sledge jump system that allows almost natural reactive jumps. Journal of Biomechanics, *2010).*

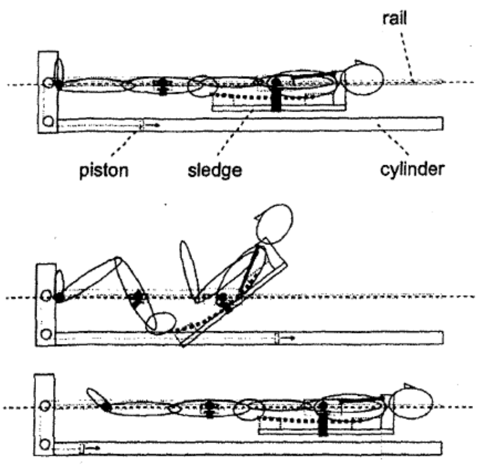

Figure 19. Illustration of a longitudinal section of the SJS. In the first draw, a schematic representation is displayed. In the second and third draws, the freedom of movement in the ankle, knee and hip joints, and the subsequent jump are represented (From: Kramer A. et al. A new sledge jump system that allows almost natural reactive jumps. Journal of Biomechanics, *2010).*

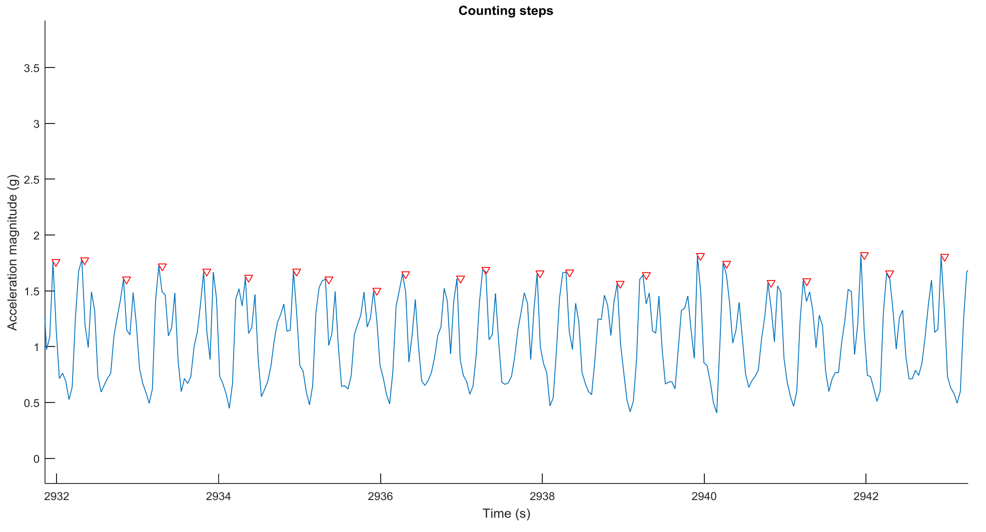

Figure 20. Exemple of steps detection using MATLAB. The red triangles indicate the peaks considered as steps.

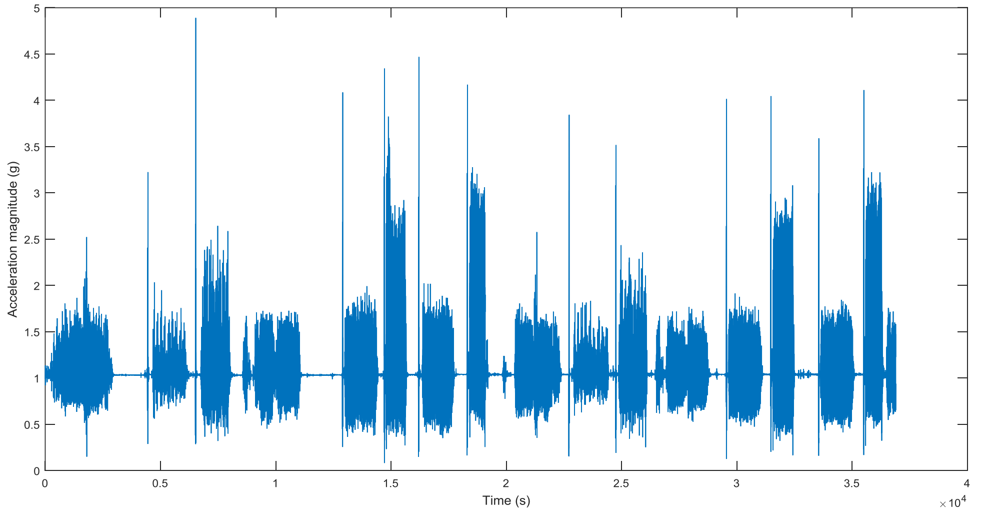

Figure 21. Example of a gait course when plotting the magnitude of the signals. To notice the clear separation between each activity given by the resting period between the activities.

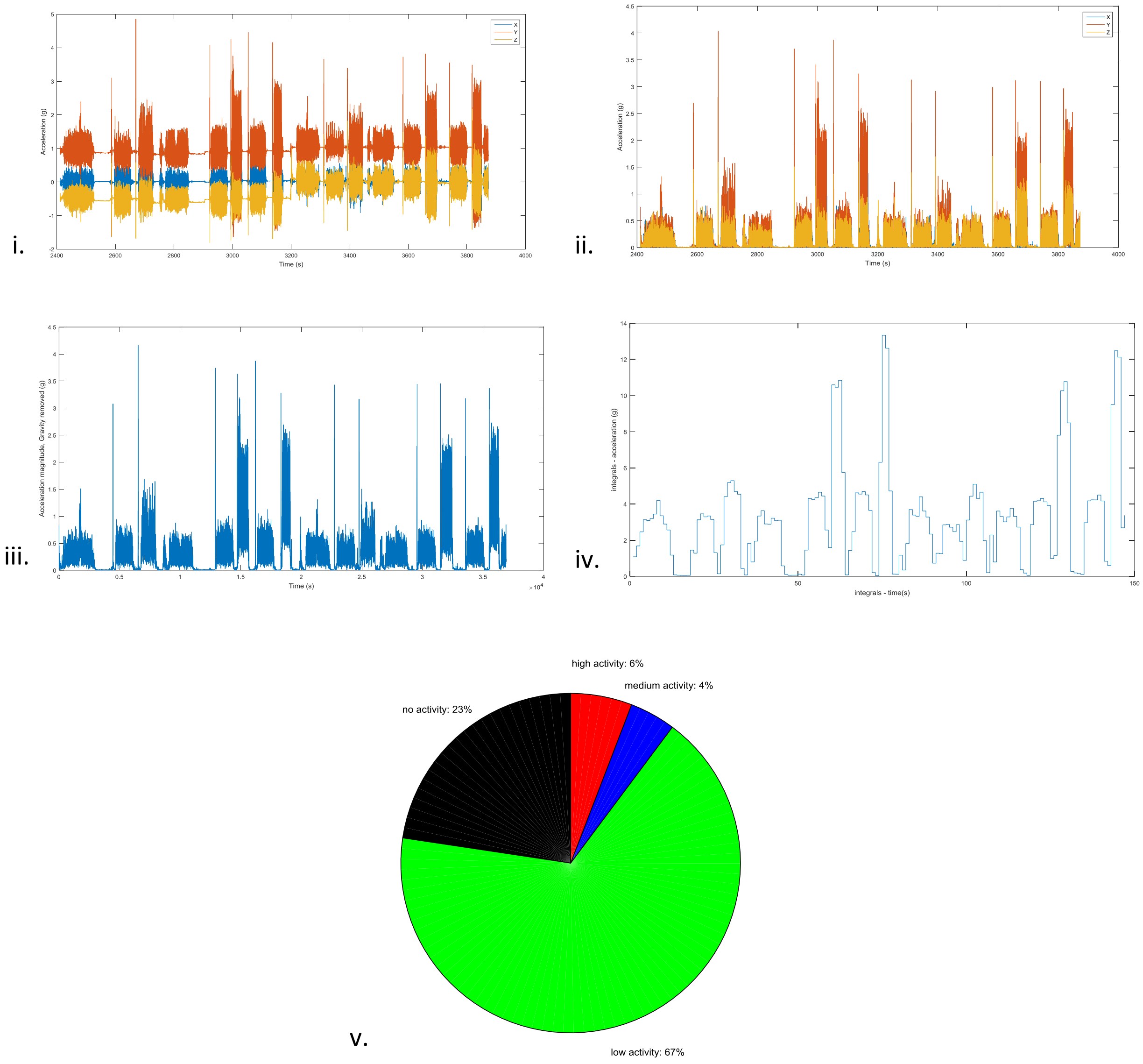

Figure 22. Representation of the analysis for calculating the level of PA. In the example, a gait course has been analyzed. i.filtered signal from three axes (X, Y and Z); ii. Convert the signal in absolute values; iii. Magnitude of the three axes; iv. Integration of the signal for every 10 seconds and representation of the different activity levels; v. pie-chart representing the percentage of the activity levels during gait course.