# The human body in a microgravity environment: long term adaptations and countermeasures

O corpo humano em ambiente de microgravidade: adaptações à exposição de longo prazo e contramedidas

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***ABSTRACT:*** *Gravity has had a profound effect on human evolutionary development, shaping not only its mechanical dynamics but also its supporting mechanisms, including the cardiovascular, neural and musculoskeletal systems, which on exposure to microgravity undergo considerable adaptations, resulting in decreased bone, muscle and cardiac mass. Providing nominal countermeasures against the effects of microgravity is an on-going priority that requires an amalgamation of countermeasures, including exercise, centrifuges and loading suits. Suit technology, due to its low cost and mass has received increasing interest. The gravity loading countermeasure skinsuit (GLCS), utilises a bidirectional weave to create material strain that loads cumulatively towards the legs. Several components of current and future GLCS research are discussed in this paper. Recommendations for future research exploring long term use and potential transferable terrestrial benefits are explored.*

***KEYWORDS:*** *Microgravity, GLCS, exercise, space.*

***RESUMO:*** *A gravidade tem tido um profundo efeito no desenvolvimento evolucionário humano, moldando sua anatomia e fisiologia. Dessa forma, os sistemas corporais, quando expostos à microgravidade, passam por adaptações consideráveis, como redução da massa osteomuscular e alterações na fisiologia cardiovascular. Proporcionar medidas específicas contra os efeitos da microgravidade é uma prioridade atual, que requer um somatório de ações, como exercícios físicos diários, centrifugação e o uso de trajes especiais. O traje de contramedida por recarga da gravidade (GLCS) utiliza uma costura bidirecional que cria uma deformação no material, a qual gera uma carga que se acumula, progressivamente, em direção aos pés. Esses trajes vêm ganhando especial interesse por serem de baixo custo e de fácil utilização, bem como por possuírem uma massa pequena, que facilita seu transporte e armazenamento. Diversos aspectos dos estudos realizados com o GLCS são discutidos neste artigo. Recomendações para pesquisas futuras sobre os efeitos do uso*

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*crônico do GLCS na microgravidade e de sua potencial transferência para utilização em condições terrestres também é apresentada.*
***PALAVRAS-CHAVE:*** *Microgravidade, GLCS, exercício, espaço.*

## 1 Introduction

The human body is a complex innervation of chemical, mechanical and neural pathways designed to allow the body to adapt to situational changes and environmental stressors to maintain homeostasis. By studying the mechanisms behind adaptation, scientists and medical professionals are better able to differentiate between pathological and physiological states, determine control mechanisms and design countermeasures to maintain optimum functionality.

Exposure to microgravity, whether simulated or actual, has been shown to result in reductions in ventricular mass (Eckberg *et al. 2010*), blood volume (Eckberg, 2003), breathing frequency (Cox *et al.* 2002), balance control (Meck *et al.* 2004), nervous system sensitivity and reserve (Fritsch *et al.* 1994), arterial tone (Baevsky *et al.* 2007), bone mass (Zwart *et al.* 2004), immune function (Williams *et al*,, 2009), muscle mass (Fitts, Riley and Widrick, 2000) and space motion sickness (Blaber, Bondar and Kassam, 2004). This can lead to operational difficulties and health consequences, both in space and upon return to a gravitational body (including Earth or future missions to the Moon/Mars).

This paper aimed to integrate information from the ISS, MIR Skylab and Neurolab missions, as well as several parabolic and lab studies, to provide an overview of alterations that occur with long term (>1 month) exposure and its functional consequences on performance, countermeasures (both current and in development) and potential terrestrial applications from advances in microgravity countermeasures research.

## 2 Adaptations

Three main physiological problems occur in microgravity: changes in the neural afferent input; absence of weight bearing on the musculoskeletal system; and loss of hydrostatic gradients affecting cardiovascular distribution (Kotovskaya, 2011). While acute responses to microgravity (<2 weeks) appear to be highly reversible on return to Earth (Sides *et al.* 2005), longer term adaptations (>1 month – we said 3 months above) and in particular bone deterioration, muscle loss and cardiovascular deconditioning, present major problems for the operational planning of long term exploratory missions, i.e. Mars (Young, 1999). While research from the neurolab missions (Homick *et al.* 1998) has indicated that the neural system undergoes both short-term (through changes in pressure and locomotion) and long-term (changes in ultradian rhythms) reprogramming due to alteration in afferent input (Baevensky *et al.* 1998), it has not been shown to be detrimental or unstable in space (Ferretti and Capelli 2009).

## 2.1 Cardiovascular

During the 2008 International Cardiovascular Workshop for the International Space Life Sciences Working Group, at International Space University (ISU), Strasbourg, France, five key cardiovascular areas relating to microgravity were highlighted: inaccurate assessment of cardiovascular performance (Moore *et al.*2010); cardiac rhythm problems; impact of prolonged exercise countermeasures; reduced physical performance; and supine-standing test intolerance (Convertino, 2009). No known severe cardiovascular rhythm problems have arisen in space (Sides *et al.* 2005), although there is an observed decrease in the amplitude of the electrocardiogram T-Wave in the cardiac rhythm (ECG; Bogomolov, Grigoriev and Kozlovskaya, 2007).

Cardiovascular fitness is a fundamental component for both astronaut safety and space operations. For example, in an emergency situation requiring disembarkation from a vehicle and the wearing of a launch/re-entry suit, a minimum of 2-2.7L.min$^{-1}$ $\dot{V}O_{2\ MAX}$ level of fitness would be required, with $\dot{V}O_{2\ MAX}$ being a measure of the maximal amount of oxygen a person can use within one minute and being an indication of health and fitness (Moore, Stenger and Platts, 2010). For extravehicular activities (EVA) 0.7-1.7L.min$^{-1}$ $\dot{V}O_2$ is required to perform operations, primarily from the upper body (Moore *et al*, 2010).

Cardiovascular control centres located in the medulla, integrate sensory feedback, feed-forward and predictive neural vectors by gathering receptor input from baroreceptors in the carotid and aortic bodies (Meck *et al* 2004), mechanoreceptors and metaboreceptors in skeletal muscle (Edwards *et al.* 2007; Fisher *et al.* 2010), chemoreceptors in the higher brain centres and carotid bodies (Meck *et al.* 2004) proprioceptors in sensory organs and muscle spindles (Armstrong, Mcnair and Taylor, 2008) and environmental skin receptors (temperature/pressure). Through this integration an affecter response is generated in the autonomic nervous system (ANS), which comprises of two branches; the sympathetic (SNS) or "accelerator" and parasympathetic (PNS) "brake" systems. These modulate the heart rate (HR) and contractile force, and can be measured via heart rate variability (HRV). For a comprehensive review of this technique the reader is directed to the Task Force Paper, 1996.

On exposure to microgravity there exists a timeline to adaptations. Initially there is a loss of gravitational pull causing fluid redistribution of blood into the upper-body, resulting in a reflex adaptation in venous/arterial return through neuro-hormonal regulation (Baevsky *et al.* 2011). This leads to greater activation of cardiac-mechanoreceptors, baroreceptors (BR), which results in a short-term (1-3 days) increase in braking of the heart from the PNS. This increase in PNS activity is short lived as in response to fluid shifts, plasma volume falls (16%), resulting in less stretch on the BR, particularly in the carotid sinus but not excluding the aortic arch, and resulting in a drop ~20 % in the operational point (relative buffering capacity) of the BR (Fritsch *et al.* 1992). After a few days there is an increase in the SNS after initial remodelling (>5days) has occurred (Christensen et al 2005), increasing systolic blood pressure through an increase in the release of peripheral vasoconstrictors i.e. vasopressin, to maintain homeostasis and preserve cerebral perfusion (Meck *et al.* 2004). After 2 weeks there is a reduction in arterial stiffness and an increase in venous cross sectional area of ~70% (Grigoriev *et al.* 2011), consequentially stabilising and reducing diastolic blood pressure. Systolic blood pressure remains partially raised to the order of a few mmHg, potentially due the continued lack of inhibitory PNS activity and the possible reduced activation of metaboreceptors in muscle afferents, which project type III and IV afferent fibres sending excitatory input to the medulla in the face of Robust activation (Fisher *et al.* 2010).

Very little research exists into the long term adaptation of cardiac control with only one astronaut, Valeri Polyakov, being exposed to more than 1year (438 days). Using ballistic-cardiography (BCG) to monitor ultradian rhythms, which are purported to reflect higher brain centre activation (Baevensky *et al.* 1998), it was reported that after 250 days there was an increase in both - HR, neural control and cardiac contractility associated with a rise in ultradian rhythms. This was surmised to represent an adaptation in neural control centres. While it is inconclusive whether this was the case, it has been shown that the neural pathways have plasticity and the capacity to regenerate (Engineer *et al.* 2011), and glial cells in the brain can also myelinate neurons to improve neural conduction through a neural sheathe (Thomson, 2006). This could mean that the body can adapt to space by facilitating an "upgrade" in neural transmission to drive the CV system.

Post-flight orthostatic intolerance (OI) is a current problem among astronauts upon return to Earth, regardless of flight length (more prevalent after >1 week exposure). This arises from a disruption in homeostatic mechanisms that attempt to maintain blood pressure in the face of orthostatic stress (Blaber *et al.* 2004). Confusion exists regarding the predisposing factors that contribute to the development of OI, with some individuals being more at risk than others. This has led to postulations that those with reduced neural control and fitness pre-flight are more susceptible post-flight. Additionally there is a sex-specific difference in the stress response; men raise blood pressure through an increased SNS to raise peripheral vasoconstriction, whilst women increase cardiac output through an increased HR via parasympathetic control (Blaber *et al.* 2004). A study by Rana *et al.* (2007) found gene-gender differences in blood pressure regulation with women coding with β1 and α2a genes controlling blood vessels and men with β2 and α2a affecting angiotensin in kidneys. While the mechanisms behind the susceptibility to post spaceflight OI are still not fully understood, it has been shown that women are 5 times more vulnerable (Summers *et al.* 2010). The interpretation of this is clouded by the relatively low number of female astronauts relative to men (N= 517 W=52, M=465).

### 2.2 Musculoskeletal system

The disappearance of weight bearing on the musculoskeletal system has severe practical implications, both in space and on return to a planetary body with sufficient gravity. If bone loss continues in areas including the spine and trabecular head, with current research suggesting a 1-2% decline in bone mineral density per month, the damage could be irreversible (Shackleford *et al.* 2004). This increases the risk of osteoporotic fractures on Earth and affects the planning for missions to reduced gravity environments, e.g. Mars (Vainiopaa *et al 2007*).

Muscle loss has been seen to decrease predominantly in the postural muscles or antigravity muscles. Studies from MIR have shown declines after 112–196 days in space in the calf plantar flexors between 6-20%, a decrease in leg muscle volume of 19% in the gastrocnemius and soleus and 10% in the quadriceps (LeBlanc et al, 2000). Muscular strength also decreases, with one astronaut reporting to have lost 54% of single leg power after 21 days of space flight (Annonutto *et al*, 1998). Though the majority of this strength loss appears to be correlated with muscular atrophy, it was shown a 21% drop in maximal voluntary contraction ability of the plantar flexor muscles when corrected for mass was actually a 4% relative drop in strength (Fitts, Riley and Widrick, 2001). This alteration of the neuromuscular system in the lower limb musculature can have significant knock-on effects on locomotion, posture and spatial disorientation (Reschke *et al.* 1998).

## 3 Countermeasures

Exercise countermeasures prove effective at attenuating the decline in cardiovascular performance, but no known data exists on their continued use in space. Extreme environmental adaptation often requires technological intervention to assist in countering environmental effects. Currently, in space, a multifaceted countermeasure program is employed to optimise astronaut health and operational efficiency (Kozlovskaya and Grigoriev, 2004). For an in-depth review of current space countermeasures employed, the reader is referred to the following articles (IMBP, 2010; Kozlovskaya *et al.* 1995; Williams *et al*, 2009).

### 3.1 Lower body negative pressure

Lower body negative pressure (LBNP) provides an effective cardiovascular countermeasure. Using a vacuum tube isolated to the participants hips, it replicates a gravitational gradient by pulling fluid down to the legs, exposing the baroreceptors and vascular sensory network to signals similar to Earth (Boda *et al.* 2000). However, it requires 53mmHg (usually set at 40mmHg) to provide 1 body weight, which can be extremely uncomfortable and does not fully attenuate the occurrence of supine-standing test intolerance (Hargens *et al. 1996).*

### 3.2 Exercise

Exercise countermeasures form a crucial element of the astronaut training regime designed to attenuate the loss of bone, muscle and cardiovascular function associated with disuse in space (Convertino and Sandler, 1995). On Earth, exercise has been proven to increase bone mass, increase muscular strength and provide important cardiovascular and metabolic adaptations (Vainiopaa *et al.* 2007). In bed rest studies, patients who performed resistance exercise (80% of 6-10 rep max) were able to preserve their muscle mass (Narici and de Boer, 2011). In a similar study it was also demonstrated that supine resistance exercise improved the bone mineral density of the calcaneous, spine and hip by 1%, 3%, and 1%, respectively (Shackleford *et al.* 2004). In a typical week, NASA and European astronauts will complete 2 hours of split 1 hour sessions of exercise, consisting of 4-6 treadmill (TVIS) sessions a week, 2-3 cycle (CEVIS) sessions and 6 resistive sessions (ARED; Moore *et al.* 2010). The Russian system uses similar protocols of 2 hours of physical activity, consisting of 3 intense days and 1 rest day, utilising a treadmill (TVIS), bike (VB-3) which can do arm and leg cycling at an average intensity of 130Watts, and a special resistive loading device (NS-1; Kozloskaya and Grigoriev, *2004).* Upper body strength is a crucial component in microgravity as there is a shift of use from the lower body to the upper body to carryout work based tasks and locomotion (Reschke *et al.* 1998). Local fatigue of the upper body has been a rate limiting factor during extra vehicular activities (EVA) throughout the shuttle missions (Sawka and Pandolf, 1999), and thus, upper body resistive and ambulatory exercises are important in the countermeasure program for astronauts. Enhancement of exercise countermeasures would result in a significant step forward to improving the safety of long term space exploration (Williams *et al.* 2009). Though it is has been demonstrated that current countermeasures provide sufficient stimulus to maintain cardiovascular stability in space, there is still the question of reduced musculoskeletal loading (Hughson *et al. 2012)* and additional countermeasures have been proposed that use gravity loading on the body to stimulate muscle and bone.

### 3.3 Centrifuges

Artificial gravity, though still in development, has been successfully used in various centrifuges to create a gravitational gradient. This provides loading on the musculoskeletal system at the foot level and a shift in hydrostatic gradient, which could conceivably be applied continuously if a centrifuge of sufficient size could be constructed (Young, 1999). Centrifugation could be used as a countermeasure for long term flight, but brings with it issues of cost, engineering and a physiological issue of cross –coupling that can cause spatial disorientation, depending on a number of factors in centrifuge protocol (Lackner and DiZio, 2000).

### 3.4 Pingvin Suit

Another way to induce loading and simulate a gravitational effect is to apply a compressive loading down the body. This has been previously accomplished through resistive exercise and also through specialised loading suits. The Russians were the first to experiment with this concept and still currently use the TNK V-1 Pingvin or "Penguin" suit (Figure 1). The Penguin suit allows static axial loading of 70% during treadmill running and static and dynamic loading up to 40kg while walking, when combined with specially designed shoes (Kozlovskaya and Grigoriev, 2004). It was shown that those cosmonauts that adhered to the integrated suit and treadmill exercise had a lower amount of bone mineral density loss at the lumbar vertebrae (0-3%), while those who did not adhere had a substantially higher loss (6-10%). A further study on 4 bed rest participants demonstrated that 10 hours a day of 10kg loading from a Penguin suit was sufficient to preserve the size of soleus muscle (Ohira *et al. 1999*). These findings suggest that the suit is an effective countermeasure, both with and without integrated exercise. However, issues exist with the suit design, with it being uncomfortable and thermally unviable if worn for the recommended 8 hours, often hindering further exercise performance (Marwaha, 2010). Additionally, it loads in three stages, the shoulder, hips and with bungee cords attached to the feet, which are often repeatedly undone due to comfort issues (Waldie and Newman, 2011). This design does not effectively replicate gravity nor does it place sufficient or appropriate loading on the body.

### 3.5 Gravity loading countermeasure skinsuit

The gravity loading countermeasures skinsuit (GLCS), designed at MIT, Massachusetts, USA, is the first known suit to utilise a specialised, tailored material strain to replicate the gravitational loading on the body when on Earth (Waldie and Newman, 2011). The skeletal loading on the body when standing at Earth's gravity is not constant at every joint but is cumulative; at the feet you have the entire bodyweight, at the hips the upper torso, while the neck supports only the head. While the Penguin suit loads a specific weight up to 40kg in three places only, the GLCS uses a bidirectional weave to stretch and load in hundreds of stages. Using body segment data, it can be calculated and made to load at specific joints, i.e. the hips, to a higher degree of load and efficacy than the Penguin suit (Waldie and Newham, 2011). The GLCS has been proposed to be easy to wear and thermally comfortable, with only minor discomfort reported by some individuals.

Pilot studies at King's College London (Figure 2) have shown it to be both thermally tolerable and viable for integration into cycling and resistance based exercise, whilst providing a passive loading regime of ~0.8G (Carvil *et al., 2013).* In addition, with a skin pressure between 4-10mmHg in comparison to the 50mmHg of the Penguin suit, it is vastly more appropriate for short and long term wear as the risk of occlusion and compartment syndrome issues are significantly reduced (Marwaha, 2010).

By integrating exercise and the gravity loading countermeasure skinsuit, this could provide greater musculoskeletal stimulus via both passive and active loading. It has previously been shown that integrating exercise with centrifuges (Kotovskaya, 2011), Pengvin suits (Bogomolov *et al.* 2007) and LBNP (Boda *et al*. 2000) improves the effectiveness of these countermeasures.

Current countermeasures on the ISS also include treadmill walking. Further assessment of the locomotive properties of the skinsuit and how it modifies a treadmill based exercise protocol, both on Earth and potentially in other gravitational environments e.g. Mars and Moon, are required due to the ambulatory restrictions in mobility found in previous studies on the suit (Carvil *et al, 2013)*. As yet unpublished reports from a single case study (Carvil *et al, 2013;* figure 3*)* appear to indicate the suits capacity to augment the HR-$\dot{V}O_2$ relationship by increasing the oxygen utilisation for a given HR at different simulations of g (Mars – 1/3G and Moon – 1/6G). This could have intriguing consequences for improving CV strength during long term explorer class missions, as well as having the potential to augment athletic training on Earth. However, further analysis of the locomotive properties of the suit while both running and walking need to be undertaken in a wider sample to verify this.

### 3.6 Additional

The ability of loading suits to provide a low cost, low mass countermeasure has received greater attention in the last year, with three new concepts being revealed. The Dynasuit utilises (line space) biofeedback, physiological monitoring and artificial muscles to allow for real-time, passive and integrated loading on the musculoskeletal and cardiovascular system (Leiter et al, 2012). The V2, "Variable Vector Countermeasure Suit", encompasses human system integration and monitoring, fly wheels and gyroscopic motion to provide an integrated countermeasure platform via reactive force generation (Duda and Newman, 2013). The Torso Compression harness utilises a posterior directed compressive load on the spine, to add a resistive component to aid in the reduction of lower back pain through improving the spine stabiliser muscles in microgravity (Sayson *et al*, 2013).

## 4 Conclusion

The human body goes through a complicated, almost pre-programmed adaption that results in a reduced functional capacity that mirrors the environmental situation experienced in microgravity. This result in fluid shifts that desensitise cardiovascular receptors, reduced input from afferent fibres (muscle spindles), cardiac capacity, muscle and bone mass. On return to 1G environment this leads to functional consequences, such as increased risk of fractures, decreased strength and orthostatic intolerance. While promising research indicates that the body can adapt to microgravity, it is imperative that this research continues to identity the signalling pathways involved and potential ways to countermeasure these adaptations, with the potential to bring benefits for terrestrial based conditions, such as age related muscle degeneration, stress fractures and bed rest. Several countermeasures have been developed which have already reaped benefits in space and enhanced terrestrial understanding. Further research is recommended regarding improvements to countermeasures, such as the GLCS, involving a larger participant base to investigate the long term training effects of suit technology and its integration into exercise, validating its potential benefits for both terrestrial and microgravity use.

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