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‘Post-mission Exercise (Reconditioning)’ Topical Team

FINAL REPORT

Recommendations for Future Post-mission Neuro-musculoskeletal Reconditioning Research and Practice

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EXECUTIVE SUMMARY

Scope

This report outlines the work undertaken by the ESA Post-Mission Exercise (Reconditioning) Topical Team to ascertain and provide details of evidence based postflight reconditioning programmes, looking beyond current practices in readiness for future longer duration missions. The report covers gaps in knowledge and proposes how terrestrial rehabilitation practices, and research and development, may have lessons for post-space mission reconditioning. Information is presented to help protect astronauts from the potential long-term effects of their occupation, i.e. periodic but regular deconditioning and exposure to microgravity, and how these factors might impact the long-term risk and incidence of osteoporosis, osteoarthritis, and other conditions related to deconditioning or premature ageing. The report culminates in conclusions and recommendations for the future activities the European Space Agency and the wider space community might pursue in preparation for long duration exploration missions.

Objectives

The Topical Team aimed to produce recommendations for future post-space mission reconditioning research and practice. Inflight countermeasure (CM) programmes do not prevent deconditioning completely and structural and functional deficits in many of the body's physiological systems are still present on return from long duration spaceflight. The musculoskeletal and neuromuscular (neuro-musculoskeletal, including neuromotor control) systems are especially affected and have a strong relevance to the practice and effectiveness of reconditioning. Until an inflight solution is found that prevents space deconditioning entirely, the need exists to optimise post-mission reconditioning to correct neuro-musculoskeletal changes and reduce the risk of musculoskeletal problems, and promote return to pre-flight function, as well as ensure good long-term health.

The objectives of the work to be pursued by the Topical Team were as follows:

1. Identify acute and chronic neuro-musculoskeletal problems experienced by astronauts as a result of undertaking short and long-term space missions.
2. Identify risk factors affecting successful reconditioning following spaceflight.
3. Identify and document existing strategies for correcting deconditioning related to neuro-musculoskeletal problems.
4. Anticipate challenges to reconditioning likely to result from longer (exploration) missions.
5. Document potentially useful reconditioning strategies to prevent and/or treat these long duration mission-derived challenges.
6. Produce a report including recommendations for research prioritisation to enhance postflight reconditioning of ESA astronauts.

The approach taken to achieve these objectives and produce the deliverable, this report, involved developing a collaborative team of scientists, medical operations experts and astronauts. Tasks involved identifying knowledge gaps, including a systematic literature review and consulting with those who experience and witness effects on astronauts, and then exploring ways to fill these gaps, using optimal research methodologies for optimal designs and outcome measures in astronaut research studies. The report also indicates how evidence based terrestrial practices could be adopted directly for the benefit of postflight reconditioning, given that some research questions are not possible to test in the astronaut population.

Science / Operations Collaboration

The breadth of expertise of the authors of this report spans several scientific and clinical disciplines, including physiotherapy, medicine, sport and exercise science, physiology, psychology, statistics and research methodology. Patient and public involvement (PPI) is fundamental to the feasibility and success of terrestrial medical research. Therefore, the involvement of astronauts and operations experts was considered integral to this report, as well as to future research aimed at improving the efficiency, effectiveness and impact of reconditioning activities. Astronaut experiences and views provide valuable insight into how their care might be optimised, and aids decision making concerning research priorities. The pre-, in- and postflight medical issues reported in this document illustrate aspects where past crew health management was lacking and that current and future practice can benefit from considering the perspectives of astronauts themselves and those working closely with them.

Knowledge Gaps

Responses to microgravity, inflight CM and postflight reconditioning after missions to the International Space Station (ISS) are better understood for some of the body's systems and functions than others. For example, aerobic performance can be well maintained with effective CM and can recover rapidly postflight but muscle weakness, particularly of postural muscles protecting the back, is still a significant problem on return to Earth.

The gaps in knowledge which will need to be 'spanned' to adequately embark upon Long Duration Exploration Missions (LDEM) involving planetary surface excursions, e.g. on Mars, are explained (Chapter 3) and specific research questions posed (Chapter 5). A potential new challenge is a reduced CM programme during transit (e.g. due to limited equipment space; need to conserve resources; reduced motivation for compliance with exercise on prolonged, isolated missions than current ISS missions etc.). Crewmembers may therefore be required to undertake a reconditioning (preconditioning) programme specifically to prepare for planetary surface excursions, either in orbit or on the surface, to ensure safe, effective performance of tasks. It is expected, therefore, that the challenges to the human body and effects of micro- and reduced gravity will be greater after longer duration missions, but the magnitude, duration and emphasis of effects on the different systems and specific parameters are difficult to anticipate. It is also not possible to know whether any cumulative effects will occur after repeated long duration missions, which could compromise the long-term health of the astronaut, so research will be vital to understand recovery processes after reconditioning between missions.

Filling Knowledge Gaps

Solutions proposed for filling the knowledge gaps focus on reversing musculoskeletal deficits and improving performance using physical and psychological strategies. Accurate, routine reporting and monitoring of musculoskeletal and psychological status will be vital to understand the body's adaptations to long duration spaceflight and postflight recovery. Delphi studies are suggested to capture practices of medical operations specialists and to determine future study designs from experts in different areas of terrestrial rehabilitation research. Long-duration bed rest offers an opportunity to conduct exercise reconditioning research more systematically.

Translation of evidence-based clinical and research practices from terrestrial rehabilitation and sports settings, which are not possible to investigate in astronauts, may provide valuable lessons for postflight reconditioning. Parallels with terrestrial populations include clinical conditions involving deconditioning (e.g. low back pain, neurological disorders and critical care patients) and elite sports training (preconditioning and reconditioning exercise programmes to optimise performance, prevent injury (including overuse microtrauma and acute trauma) and promote musculoskeletal health, and psychological strategies to enhance motivation and adherence to exercise programmes). The benefits of exchanging knowledge and expertise between the space and terrestrial environments are reciprocal. Terrestrial scenarios are discussed briefly in this report, whilst more detailed accounts will be published in a special issue of the *Manual Therapy* rehabilitation journal (Appendix D).

Potential solutions to the difficulties in human space medicine research are proposed by considering methodologies that can draw from robust terrestrial designs and practices, and alternative approaches to address the unique aspects of space science which demand special consideration (e.g. small numbers and the need for accurate, reliable outcome measures).

Conclusions

The identified effects of microgravity and factors that affect the efficacy of post-mission reconditioning include:

- Loss of muscle mass and strength, as well as neuromuscular changes.
- The vulnerability of the muscles of the lumbopelvic region.
- Risk of bone fractures and spinal injuries due to bone loss and changes in spinal structures.
- Effects on cartilage, which are unknown and have yet to be explored (research in progress)
- The effect of the Advanced Resistive Exercise Device (ARED). This CM has reduced declines in physiological and physical function but not entirely mitigated them, e.g. muscle strength can still be reduced by 20%; orthostatic tolerance and neuromuscular control are still poor for the first few days and performance of functional tasks requiring dynamic control is adversely affected.
- Motivation to comply with the exercise programme and adhere to exercise after supervised reconditioning.
- Continued access to reconditioning facilities and support during the postflight period.
- Competing commitments and available time for reconditioning.

A systematic review of exercise CM during bed rest, focusing on the lumbopelvic muscles showed that:

- Lack of consistency in outcome measures limited the ability to make meaningful comparisons between studies and between CM interventions
- No CM intervention has thus far been successful in limiting or preventing all musculoskeletal changes seen in the lumbopelvic region, including spinal morphology, muscle physiology and function.

The current ESA postflight reconditioning programme is based on principles from the best evidence available from space (currently minimal) and terrestrial research:

- Early intervention is centred on retraining motor control, balance and posture
- Exercises progress to trunk strengthening once lumbar postural control is restored
- More strenuous general resistance and cardiovascular training follow.

Potential reconditioning strategies need to be investigated to prevent and/or treat the effects of longer duration exploration missions (LDEMs), involving surface planetary excursions, e.g.:

- Knowledge is needed of short-term effects of LDEMs to determine factors that will influence the ability to perform postflight reconditioning and the effectiveness of exercise programmes
- Programmes are required that use physical and psychological strategies for postflight reconditioning are required upon return to Earth
- Preconidtioning to prepare for planetary surface excursions are also needed.
- Intelligence on any long-term effects of repeated LDEMs, (e.g. osteoporosis, osteoarthritis) must be gathered.

RECOMMENDATIONS

The following recommendations for future post-mission reconditioning research and practice are presented in relation to the objectives and are detailed further in Chapter 10. Research priorities will need to be determined by involving relevant space and terrestrial communities of scientific experts (basic and rehabilitation sciences) and users (astronauts and Medical Operations specialists) in an initial Delphi study. The Delphi research method involves gaining consensus on a specific topic from relevant experts through a series of surveys (Section 8.2.6).

It is recommended that research be conducted on:

1. Effects of spaceflight on neuro-musculoskeletal function *(Objective 1)*

- More crew focused research is needed;
  - on adaptation processes to improve inflight CM and postflight reconditioning strategies
  - on the possible long-term effects of space travel (e.g. osteoporosis, osteoarthritis)

2. Postflight effects *(Obj 1)* **and risk factors impacting on reconditioning** *(Obj 2)*

- Routine (anonymised) systems are required to capture data on musculoskeletal problems
- Use astronaut-specific personalised outcome measures
- Use novel technologies to assess muscle status inflight to help improve inflight CM to reduce postflight deficits.

3. Improving existing reconditioning strategies after ISS missions *(Obj 3)*

- Multi-agency studies (quantitative and qualitative) are required for international consensus and guidance on reconditioning practice, and future research priorities
- Develop optimal reconditioning programmes - account for safe reloading; exercise dose, duration, rest periods, timing; functional activities of daily living; psychological factors.
- Obtain views of astronauts (using qualitative methods)
- Synthesise and build on existing evidence from relevant terrestrial populations in clinical specialties (e.g. back pain, neurology) and elite sports training
- Evaluate effectiveness of current and new post-ISS programmes.

- Minimise injury and ensure safe exercise for postflight reconditioning programmes
  - Establish re-loading protocols that minimise tissue damage (e.g. joint cartilage, intervertebral discs, muscle injuries)
  - Use movement screening tools to assess quality of movement pre- in-and postflight
  - Develop tailored exercise programmes to re-educate movement control to protect joints from abnormal or excessive loading during exercise.

- Improve functional performance evaluation in postflight reconditioning
  - Include functional tests relevant to activities of daily living.

- Improve motivation strategies for complying with and adhering to postflight reconditioning
  - Investigate links between behaviours pre-flight, inflight, and postflight
  - Utilise astronaut experiences to inform motivation enhancement strategies
  - Understand the therapeutic alliance to enhance reconditioning outcomes
  - Draw from motivation and adherence strategies in elite sports.

4. Anticipating challenges to reconditioning from longer (exploration) missions *(Obj 4)* **and developing reconditioning and preconditioning strategies in preparation for planetary surface explorations** *(Obj 5)*

- Develop inflight exercise CM that are less time-consuming, functional, enjoyable and target multiple physiological systems simultaneously
- Establish inflight monitoring procedures to inform preconditioning programmes and determine readiness for safe and effective planetary surface excursions.
- Develop equipment/hardware for inflight preconditioning programmes.
- Bed rest studies to develop inflight preconditioning exercise programmes
- Develop non-technology based preconditioning exercise programmes
- Develop technologies for inflight monitoring of e.g. orthostatic intolerance, sensorimotor function and functional performance using sensors with feedback to astronauts
- Develop non-technology based exercises as contingency for equipment failure
- Develop optimal postflight reconditioning exercise programmes
- Identify and prevent potential barriers to ongoing health behaviours for designing mission specifications and generating policies

CHAPTER 1: INTRODUCTION

1.1. The Goal of Postflight Reconditioning is:

> To trigger and complete physical re-adaptation processes to Earth gravity after long-term exposure to reduced gravity during space flight, to return astronauts to their pre-flight status.

For future exploration class missions, an additional phase of postflight reconditioning will be required following deep space cruise to destination, to enable surface exploration. Such reconditioning will need to incorporate specific functional exercises to prepare crewmembers for safe and effective undertaking of mission objectives. Hence, this aspect of conditioning is termed preconditioning (Figure 1.1). Optimal reconditioning and preconditioning programmes have yet to be established.

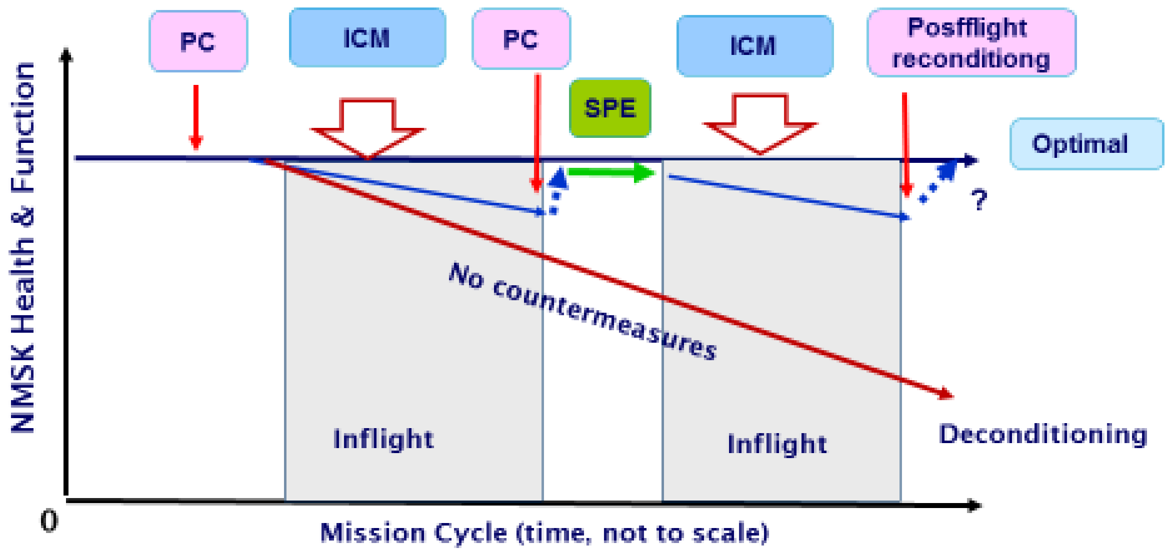

Figure 1.1: Optimal conditioning of astronauts over one long duration mission cycle involving surface exploration
NMSK = Neuro-musculoskeletal System
PC = Preconditioning; ICM = Inflight Countermeasures;
SPE = surface planetary excursion

1.2 Purpose and Content of the Report

The negative effects of microgravity on musculoskeletal structures, physiology and function are well documented for space missions up to six months (Buckey 2006; Clément 2011; Smith et al. 2012). Advances in technology and inflight exercise programmes have largely mitigated these effects but not entirely, as impairments are still present on return to earth, e.g. loss of muscle strength can be as much as 20% (Gopalakrishnan et al. 2010). As missions increase in duration and extend to unfamiliar environments beyond Low Earth Orbit (LEO) and involve planetary surface excursions (Long Duration Exploration Missions; LDEM) e.g. on Mars, challenges to the human body and requirements for effective postflight reconditioning need to be better understood by learning from existing knowledge and further research.

The term ***reconditioning*** is used rather than ***rehabilitation***, as astronauts are not patients with pathology but rather have made normal physiological adaptations in response to exposure to time in space (adaptation occurs in these circumstances as an aspect of muscle plasticity which is the ability of a tissue or organ to adapt to a given environment e.g. 1G or µG). Indeed, feedback from an astronaut was that rehabilitation implied recovery from addictive behaviours, whereas ***reconditioning*** was a more appropriate term.

Whilst normal adaptation takes place in space, on returning to Earth (or landing on the Moon or Mars), these changes could be seen as “maladaptation” and thus need to be minimized by inflight CM. Postflight recovery requires the astronaut to readapt to gravity on Earth to achieve normal function as safely and as rapidly as possible. Reconditioning therefore needs to consider both the short-term requirements to return the astronaut to activities of daily living and readiness for future missions (Figure 1.1), as well as the astronaut’s long-term health (Figure 1.2).

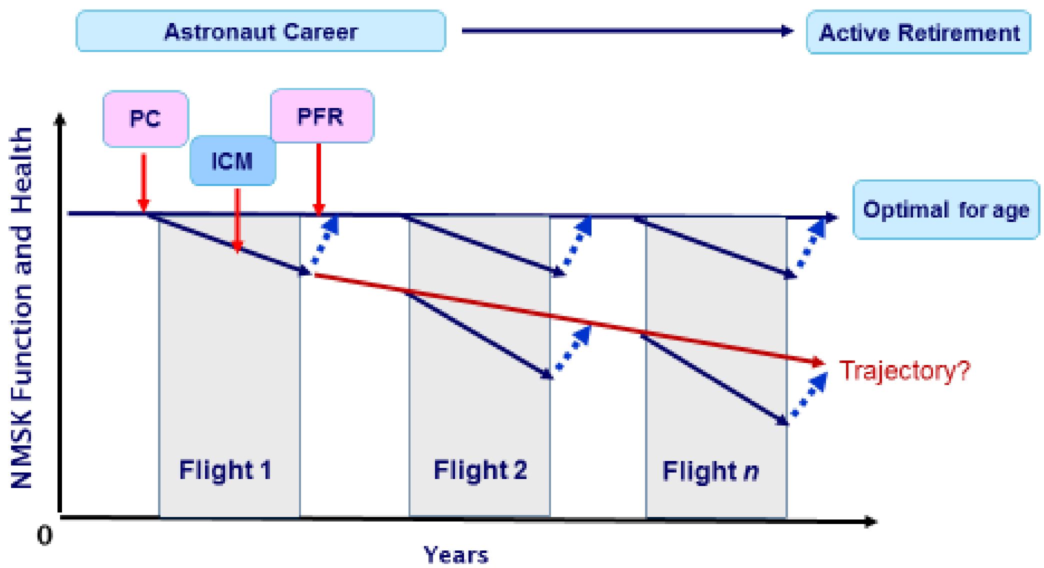

Figure 1.2: **Potential long-term neuro-musculoskeletal (NMSK) function** and health of crewmembers over repeated long-duration mission cycles
PC = Preconditioning; ICM = Inflight Countermeasures
PFR = Postflight reconditioning

The present Topical Team for Post-mission Exercise (Reconditioning) was tasked with setting priorities for research to develop optimal postflight reconditioning programmes for astronauts returning from future long duration exploration space missions. Both the short-term and longer-term reconditioning requirements for crewmember health have been considered.

Gravity plays a fundamental role in physiotherapy, particularly in re-educating posture and its control through antigravity muscle activity (Massion 1998), and use of gravity in graded manual muscle strength testing methods (Hislop et al. 2013). The acceleration levels experienced by astronauts range from up to 9Gx (felt briefly, horizontally through the chest) during Soyuz ballistic re-entry, to 1Gz (9.81 m/s^2) on Earth (feetward) to 0G (microgravity) in orbit with variable reduced gravity experienced on planet surfaces, e.g. lunar gravity 0.17Gz (1.63 m/s^2) or on Mars 0.38Gz (3.71 m/s^2). Effective and safe performance during surface planetary excursions on Mars following long duration flights at 0G will require preparation through specific exercise programmes on board prior to landing, which the authors of this report have termed preconditioning (a term also used in sport, as are ***prehabilitation*** and ***preactivation***).

The ability to conduct definitive studies of postflight reconditioning using conventional research designs, such as randomised controlled trials (RCTs), is restricted by factors such as insufficient numbers, availability of astronauts (which can be restricted for follow-up testing for reasons such as distance of home base from study location) and the use of non-standardised exercise programmes between agencies. Knowledge is largely gleaned from bed rest studies and by drawing on similarities with conditions seen in terrestrial populations, e.g. low back pain (LBP), where the distribution of trunk muscle atrophy is similar to that in microgravity (Hides et al. 2007; Pool-Goudzwaard et al. 2015). Another field suitable for comparison with the effects of microgravity is that of ageing (Biolo et al. 2003) but the greater challenges ahead that result from longer missions and new environments may benefit from drawing on challenges faced by, and rehabilitation strategies used in, other terrestrial clinical conditions involving deconditioning, such as neurological and intensive care conditions. At the other end of the spectrum, reconditioning of astronauts may benefit from adopting the physical and psychological strategies for achieving optimal performance used by athletes in elite sports. To enable these parallels to be drawn and broaden the knowledge base relevant to postflight reconditioning, the Topical Team recruited additional experts in relevant fields to contribute as authors of this report (see authors in Appendix A). More detailed accounts of the reciprocal benefits of these parallels are published in a Special Edition of the rehabilitation journal *Manual Therapy*, including a systematic review conducted as a basis for this report in relation to lumbopelvic rehabilitation (Winnard et al, 2016 in Appendix D).

An advantage of drawing on evidence from terrestrial populations is that knowledge is typically more advanced than that from space research, due to availability of larger study populations and more stable environments, enabling robust research designs. However, the present report explores research methodologies for optimal designs and outcome measures in astronaut studies as well. It also indicates how evidence based terrestrial findings could be adopted directly for postflight reconditioning practice, given that some research questions are not possible to test in the astronaut population, due to the difficulty in employing complex designs requiring large numbers to test dose (intensity) effects of exercise over different postflight time periods.

A key feature of the present report is the involvement of astronauts and Medical Operations specialists in the Topical Team to gain their unique perspectives of the challenges that influence postflight reconditioning. Throughout the report, the need for input from astronauts and operations specialists at all stages of future research is stressed, mirroring the practice of PPI now considered vital in terrestrial research in some countries (http://www.nihr.ac.uk/funding/pgfar-patient-and-public-involvement.htm). This approach ensures research questions are relevant to users (astronauts and those involved in their care) and that studies are designed to develop protocols that are feasible to produce findings that will have an impact on everyday practice and the long-term health of astronauts.

This report therefore proposes recommendations for future research and practice for postflight reconditioning based on current knowledge from scientific literature on astronaut and bed rest studies, and relevant terrestrial populations, as well as insights from the perspectives of astronauts, space Medical Operations and terrestrial clinical experts. The content of the report is intended to inform priority setting for research, provide information that could be used in the calls for research and provide a useful resource for researchers investigating those topics.

CHAPTER 2: TOPICAL TEAM OBJECTIVES

The objectives of the work to be pursued by the Topical Team were as follows:

2.1 Identify acute and chronic neuro-musculoskeletal problems experienced by astronauts as a result of undertaking short and long-term space missions.

2.2 Identify risk factors affecting successful reconditioning following spaceflight.

2.3 Identify and document existing reconditioning strategies for correcting deconditioning related to neuro-musculoskeletal problems.

2.4 Propose the anticipated challenges to reconditioning likely to result from longer (exploration) missions.

2.5 Document potentially useful reconditioning strategies to prevent and/or treat these long duration mission-derived challenges.

2.6 Produce a report including recommendations for research prioritisation to enhance postflight reconditioning of ESA astronauts.

CHAPTER 3

CURRENT KNOWLEDGE OF THE EFFECTS OF TIME IN SPACE AND COUNTERMEASURES ON THE NEURO-MUSCULOSKELETAL SYSTEM AND FLUID STATE

3. Introduction

The environment at the surface of the Earth is highly distinctive. It has nurtured the evolution of life over millions of years and in turn life has refined itself to thrive in these exclusive conditions. Therefore, since the beginning of human exploration above and below the surface of the Earth, the primary goal has been the provision of conditions that approximate those normally provided by nature. In space, this is provided by life-support systems which keep the astronaut alive and by deconditioning CM which attempt to maintain terrestrial physical and physiological function.

The human body does, however, adapt to novel environments. This capability is such that the physical structure and function of many of the body's tissues, organs and systems alter to enable life to proceed in microgravity in an efficient and economical manner. The primary systems affected are the skeletal, muscular, neuromotor, neurovestibular, cardiovascular, endocrine and immune systems. Adaptations occur within hours to days for some systems, but can take weeks to months or even longer for others. Inflight exercise CM programmes mitigate these effects to an extent but deficits are still present on return to Earth and need to be better understood to inform effective reconditioning.

Details are provided hereafter concerning the effects of exposure to the space environment on the physiological systems that are pertinent to post-mission reconditioning. Findings from a Systematic Review of the topic are incorporated into the chapter. The effects of microgravity have been reported widely in the literature and in other ESA Topical Team reports (ESA SP1281, 2005, Belavy et al 2016), and as such are only summarised here. This chapter focuses on what is known about the status of the body after prolonged microgravity with and without CM, in both the postflight period (after short and long duration space missions) and after bed rest studies. The limited research on reconditioning after bed rest is then outlined.

3.1 Skeletal Muscle

In the absence of adequate CM, the decreased stimulus experienced during exposure to microgravity causes muscles to atrophy and alters muscle morphology, with a resulting loss of contractile mass and performance capability (Fitts et al. 2010). This loss reduces the speed and strength of muscular contraction and thus leads to detriments in overall force and power (Widrick et al. 1999). Alterations in muscle morphology for some muscles (e.g. soleus) are characterised as a transition from Type I slow twitch to Type II fast twitch fibre types, a shift away from aerobic and towards anaerobic capabilities (Fitts, Trappe 2010). This is similar to the fibre-type conversion that occurs in spinal cord injury patients (Lotta et al. 1991). Most of the muscle losses occur in anti-gravity muscles of the lower back, pelvis and lower limbs, with a predominance of effect on extensors over flexors throughout the body (Danneels et al. 2000; Hides et al. 2007).

3.1.1 Lower Limb Muscles

Strength reductions may be 2 to 5% per week depending on the site and function of the muscle, and CM use (Narici et al. 1989; Tesch & Berg 1998). Reductions in knee extensor maximum strength of 15% have been found after 2 weeks of spaceflight (Gopalakrishnan, Genc 2010) and 16% reductions in knee flexion strength are evident after ISS missions even with today's extensive CM programmes (English et al. 2015). Soleus peak power has been reported to be 32% lower after 6 months on the ISS (Trappe et al. 2009).

Bed rest studies suggest that, in addition to morphology and function changes, prolonged disuse in bed rest without CM resulted in altered molecular composition of the soleus neuromuscular synapse (Salanova et al. 2011). They have also shown an imbalance in redox mechanisms of postural skeletal muscle fibres (oxidative stress), which is a potential cause of the disuse-induced muscle stiffness and fatigue seen after extended muscle inactivity in various clinical settings (e.g., intensive care units; see Section 7.5), in bed rest, and also in astronauts in space (Blottner & Salanova 2015; Salanova et al. 2013). Reconditioning of redox mechanisms in skeletal muscle and neuromuscular properties (recovery of Homer signal proteins involved in synaptic transmission), as well as global changes in the disuse-sensitive skeletal muscle proteome (contractile to metabolism to signalling) and related gene transcripts (transcriptome) have been achieved by resistive vibration exercise (RVE) during and after bed rest (Salanova et al. 2015; Salanova et al. 2014). The novel findings from such ground-based spaceflight analogue studies may help to find optimal CM protocols for functional and structural (close-to-normal physiological) recovery postflight to nearly pre-flight conditions.

Bed rest studies also indicate that for some muscles, in particular postural, a return to normal function may take some time despite a return to normal activity and upright gravitational loading (Belavy et al, 2008). The composite data from Skylab, Mir and Shuttle flights suggest that the loss of lower limb muscle mass is exponential with the duration of flight (Fitts et al. 2000); however, with the addition of recent ISS findings it appears that this loss can be minimised for some crew during six months on ISS with the current on-board exercise CM programmes that incorporate ARED and the most recent treadmill, T2 (English, Lee 2015).

3.1.2 Paraspinal and abdominal muscles of the trunk.

Spinal extensor volume decreases have been reported to be greater than hip flexor (psoas muscle) decline in astronauts (LeBlanc et al. 1995). A single case study by Hides and associates (Hides et al. 2016a) revealed that the deep lumbopelvic muscles (transversus abdominus and lumbar multifidus) were atrophied after a six month mission on the ISS. These data are consistent with the findings of ESA operational measurements of crew on their return from ISS missions (personal communication – Lambrecht, ESA Physiotherapists). Although bed rest is not a perfect model for spaceflight where astronauts can move freely, similar patterns of muscle imbalance in the trunk muscles appear to occur in response to both conditions (Hides et al. 2016a; Adams et al. 2003; Pavy-Le Traon et al. 2007). While some muscles undergo the expected response of atrophy, such as the lumbar multifidus, erector spinae and Transversus Abdominis, other trunk muscles, such as the psoas, rectus abdominis and anterolateral abdominal muscles increase in size (Hides et al. 2007). Overactivity of the abdominal muscles was verified in a bed rest study (First Berlin Bed Rest Study [BBR-1}) using electromyography and activation of spinal extensor muscles changed from tonic activation to a more phasic pattern that persisted for at least six months after re-ambulation. These changes in muscle may impact the ability of the spine to distribute loads appropriately. Selective atrophy of spinal extensors and preservation of the flexors is also seen in terrestrial individuals with low back pain (LBP) when compared to healthy controls (Section 7.2.1). A recent study showed that 70% of astronauts suffered LBP inflight and for those with a history of LBP prior to spaceflight, inflight prevalence was 100% (Pool-Goudzwaard et al 2015). Most of this inflight LBP occurs early in the mission during acute adaptation and resolves within 7–10 days. This separates the short-lived adaptive back pain from the chronic degradative condition that can occur. The persistence of LBP postflight and the associated muscle deficits are not well documented. It is unknown how far the results of bed rest studies can be translated when interpreting microgravity-induced changes after spaceflight.

3.2 Bone

Bone is lost in space and individuals can lose as much as a quarter of their bone mineral density at selected skeletal sites within a 6-month mission (Vico et al. 2000). Bone is also lost in unloading paradigms that are used as ground based space-analogues, such as experimental bed rest (Rittweger et al. 2005) and experimental limb suspension (Rittweger et al. 2006). The greatest bone losses, notably, have been observed after spinal cord injury (Wilmet et al. 1995).

The skeletal system is weakened through this demineralisation and atrophy, primarily in the bones that are normally weight bearing on Earth e.g. the pelvis, femur and lower vertebrae (Lang et al. 2004). The dynamic turnover of bone is altered towards a predominance of bone resorption by the absence of the static loading present in 1G (Smith, Heer 2012), and by reductions in the dynamic loading applied by impact and muscular contraction (Yang et al. 2015).

During a meta-analysis of the effects of spaceflight on bone Sibonga and colleagues (Sibonga et al. 2007) highlighted that astronauts who participated in long duration flights aboard Mir and ISS showed consistent loss of regional bone mineral content, with 92% experiencing a minimum 5% loss in at least one skeletal site (e.g. the calcaneous or pelvis) and over 40% experiencing a 10% or greater loss in at least one site (e.g. lumbar spine or femoral neck). These losses occurred in spite of exercise regimens aboard the space stations (Sibonga, Evans 2007). More recently with the advent of the ARED on ISS, losses of bone mineral density in orbit have been reduced to acceptable levels in some subjects (Smith, Heer 2012) and in experiments incorporating bisphosphonates a prevention of loss has been reported (Leblanc et al. 2013). What still remains to be ascertained, however, is how bone structure is affected and what bearing this has on bone strength characteristics.

Without or with minimal CM, however, early spaceflight findings indicate that load bearing bones may lose 1 to 2% of their density per month for extended periods leading to clinically relevant conditions in less than a year or two (Lang, LeBlanc 2004; LeBlanc et al. 2000). Bone atrophy increases the hypothetical risk of fracture when returning to gravity conditions (return to Earth, planetary exploration or hyper gravity flight conditions) and the time of post-mission convalescence on Earth can be significant without the certainty of complete recovery (Carpenter & Carter 2010).

If recovery from bone loss is not complete it could lead to osteoporosis, which is known to be a predisposing factor for fractures (Kanis et al. 1994). The question arises whether bone loss incurred during spaceflight will recover on Earth (LeBlanc & Schneider 1991). For the femoral neck it has been demonstrated that bone mass recovers 1 year after space flight (Lang, LeBlanc 2004; Lang et al. 2006), albeit with greater bone diameter, and thus with structurally reduced energy absorbing capacity. In the distal tibia, recovery is in-complete at 1 year postflight (Personal communication, L Vico, University St Etienne), and it is currently being studied whether full recovery is reached at later stages. Evidence from clinical observations, however, suggests that full recovery of bone is linked to full functional reconditioning (Lang, LeBlanc 2004; Lang, Leblanc 2006; Rittweger et al. 2011). Moreover, full recovery of tibial bone loss has been demonstrated after 3-months of experimental bed rest (Rittweger & Felsenberg 2009).

Taken together, the available evidence suggests that bone loss in astronauts will recover as long as full functional reconditioning is achieved. Risk of fractures may not be substantially increased in bone-deficient astronauts when they are relatively young; however, enhanced risk of fracture must be expected when space-related bone loss persists into old age.

3.3 Stature

Reports from Shuttle and Skylab missions reveal that astronaut body-length may increase up to six centimetres during missions (Sayson et al. 2013) . Increases in stature are also noted during and after current ISS missions (Young & Rajulu 2011). This can have operational impacts as EVA suits and capsule seats are individually tailored using stature as measured on Earth. There may also be health impacts due to morphological changes, and it has been noted that many astronauts suffer from LBP for a period of time on return to Earth (English et al. 2015).

Due to the absence of gravitational loading in space, the intervertebral discs, particularly the nuclei pulposi, absorb more water than on Earth. This lengthens the spine and flattens its curves, and is associated with moderate to severe LBP in the early stages of space flight (Belavy et al. 2016; Kerstman et al. 2012). Reports of astronauts experiencing back pain in space have been consistent with Wing and colleagues (1991) reporting incidence proportins up to 68% and Pool-Goudzwaard et al (2015) reporting pain in 70% of those without a history of LBP and 100% of those with a history of LBP. It has recently been postulated (Belavy et al. 2016) that the condition of overhydrated discs comprises a major risk factor for herniated discs in astronauts on their return to earth, as illustrated by one of the astronaut case histories in this report (Section 4.2.1). In order to relieve acute LBP in space, astronauts apply different strategies, such as tucking themselves into a foetal position, taking pain killers, stretching themselves or trying to compress the spine through loaded exercise on the treadmill or ARED (Belavy et al. 2016; Kerstman et al. 2012).

Johnston et al. (2010) found that astronauts had a four-fold increased incidence of herniated disc pulposus within the first year following spaceflight, compared with matched controls. Sayson and Hargens (2008) suggested that LBP and disc injury in astronauts could be caused by a range of factors linked to spinal lengthening and reduced loading. Belavy et al. (2016) argued that the increased lumbar intervertebral disc herniation risk in astronauts was most likely caused by long term disc tissue deconditioning which results from swelling of the discs due to unloading during spaceflight.

3.4 Cartilage

Articular cartilage provides joint congruency and transfers and distributes forces, allowing for normal joint movement. Cartilage is presumed to respond to mechanical loading and this mechanism may play a key role in maintaining cartilage health (Andriacchi et al. 2004), 2004). Although the effects of microgravity on bone and muscle have been studied extensively, little is known about the effects of immobilization on human articular cartilage morphology and composition in humans in response to a longer stay in microgravity. However, the question of whether joints are still fully functional after several months in microgravity is essential for astronauts' health during space travel and especially for reconditioning after space flight.

Current knowledge of immobilization effects on articular cartilage are based on a few studies which have investigated the influence of mechanical unloading on articular cartilage in patient cohorts (Hinterwimmer et al. 2004; Hudelmaier et al. 2006; Owman et al. 2014; Vanwanseele et al. 2004; Vanwanseele et al. 2003).Unloading after spinal cord injury, ankle fractures or knee surgeries provides an opportunity to analyse the effects of no or absent/reduced cartilage loading on tissue integrity. In paraplegic patients after spinal cord injury, cartilage thinning of up to 25% after 24 months has been observed (Vanwanseele, Eckstein 2004; Vanwanseele, Eckstein 2003). Hinterwimmer and colleagues investigated the effect of 7 weeks of partial load bearing after an ankle fracture on articular cartilage morphology in different knee compartments (Hinterwimmer, Krammer 2004). The reported changes in articular cartilage thickness for the different compartments ranged from -2.9 ± 3.2 % for the patella to -6.6 ± 4.9% for the medial tibia. Hudelmaier and associates detected a reduction in patellar cartilage thickness of 14 % but no changes at the tibia in a patient affected by 6 weeks of immobilization after knee joint surgery (Hudelmaier, Glaser 2006).

Cartilage health of the lower limb joints has been investigated in microgravity analogue bed rest studies. Fourteen days of bed rest reduced cartilage thickness at the knee, as well as serum oligomeric matrix protein (COMP) concentrations (Liphardt et al. 2009). Furthermore, it has been shown that COMP, matrix-metalloprotease-3 (MMP[1] -3) and matrix-metalloprotease-9 (MMP-9), were sensitive to 5- and 21-days of bed rest. These results indicate that a cartilage response to unloading can be seen after as little as 1 to 2 weeks of immobilization (Liphardt 2015) Applied CM in bed rest studies, such as vibration training with (Liphardt 2015) or without (Liphardt et al. 2009) additional resistive exercise have not successfully compensated for the effects of immobilisation on cartilage metabolism. The effects of microgravity on cartilage health in humans are only just being investigated in ISS experiments.

3.5 Cardiovascular system.

With inactivity the cardiovascular system deconditions resulting in reductions in muscle mass, metabolic enzyme levels, and the size and quality of capillary beds and mitochondria. Decreases of circulating blood volume and ventricular stroke volume are also prevalent (Neufer 1989). The main effects of such deconditioning during spaceflight where exercise CM are sub-optimal, include decreases in maximal aerobic capacity, increased heart rate for any given level of exertion and orthostatic intolerance (Moore et al. 2014). The ISS CM programme appears to be relatively effective, however, in preventing significant in- and postflight changes of cardiovascular stability under low intensity physical conditions (Hughson et al. 2012).

Nine to 14 days of space flight have shown a 22% reduction in VO2max (maximum aerobic capacity) (Levine et al. 1996). Reports of 80% of astronauts returning from ISS experiencing greater than 6% loss of VO2max despite a rigorous CM programme are typical (Moore et al. 2010). These temporal cardiovascular fitness responses are typical of a 6 month ISS mission, as outlined below (Section 3.8.7). The loss of oxygen carrying capacity contributes to the observed limitation of exercise and work capacity seen under microgravity conditions (Convertino & Sandler 1995).

[1] MMPs are matrix degrading proteins

3.5.1 Fluid Shifts

On entry to microgravity body fluids, principally the blood, move from the lower to upper body. This shift leads to immediate changes in venous pressures across the body and minor, possibly transitory, alterations in arterial pressure where for instance reductions of between 8 and 10 mmHg for systolic, diastolic and mean arterial pressure have been noted (Norsk et al. 2015). Stroke Volume is increased (+35%) by an augmented preload to the heart, which when coupled with a relatively stable heart rate, can cause increases in cardiac output (+41%) (Norsk et al, 2015). Within days blood volume becomes substantially decreased. Some of these effects in the short to medium term may be linked with space adaptation syndrome, in particular space motion sickness and mild cognitive impairment.

Although mean arterial blood pressure and central venous pressures (Buckey et al. 1993 & 1996) appear to be only mildly less than terrestrial standing values, microgravity induced pressure equilibration across the body results in pressures in the upper body which are greater in space than experienced when standing on Earth. It is becoming increasingly evident that the association some of these changes have with intracranial pressure has the potential to indirectly affect intraocular pressure and vision (Mader et al. 2011).

Postflight alterations in baroreflex response slopes correlate with reductions in parasympathetic activity to the heart, an effect which is indicative of cardiovascular deconditioning (Hughson, Shoemaker 2012) and may play a role in orthostatic intolerance. Over a period of months in space the structure and function of the blood vessels of the lower body and the heart alter (i.e. decondition), resulting in a poorer ability to react to stress hormones and aid blood perfusion, contributing to excessive blood pooling in the lower body and thus also to orthostatic intolerance on a return to Earth (Verheyden et al. 2010).

3.5.2 Orthostatic intolerance.

The inability to assume and retain the standing position under +1Gz is a multifactorial consequence of cardiovascular deconditioning. Due to the risk of syncope (temporary loss of consciousness due to fall in blood pressure), it is a major risk specifically during re-entry in the Gz alignment through the atmosphere. The incidence of orthostatic intolerance increases with space mission duration (Lee et al. 2015), and has been seen to be as high as 64% for short missions (Buckey, Gaffney 1996) and up to 90% after long duration missions (Vorobyov et al. 1983). Factors that may be involved in the aetiology of this condition are blood volume (and the related reduction in red blood cell mass), baroreceptor function and cardiac and smooth muscle structure and function (Lee, Feiveson 2015).

3.6 Neurovestibular and Sensorimotor Deconditioning

The neurovestibular/muscular systems are acutely affected by the loss of the gravity vector resulting in transitory space motion sickness, decrements in oculomotor control, hand-eye coordination, spatial orientation, and cognition during space flight missions and a deconditioning of the proprioceptive system and associated structures for most crew (Center 2008). The systems decondition due to a chronic alteration in stimuli causing balance and gait control detriments (Carpenter et al. 2010), and motion sickness for many, immediately on return to a gravity environment.

NASA's Human Research Roadmap states that given that there is an alteration in vestibular/sensorimotor function during and immediately following gravitational transitions, manifested as changes in eye-head-hand control, postural and/or locomotor ability, gaze function, and perception (https://humanresearchroadmap.nasa.gov/risks/risk.aspx?i=88 X). There is a possibility that crew will experience impaired control of the spacecraft during gravity transitions and during landing or decreased mobility during gravity transitions and following a landing on a planetary surface (Earth or other) after long-duration spaceflight.

Astronauts can also suffer from disorientation, a loss of sense of direction and loss of postural stability (Miller et al. 2010). Upon return astronauts must readjust to gravity and can experience problems standing up, stabilizing their gaze, walking and turning, and retaining posture (Clement et al. 2013; Bloomberg & Mulavara, 2003; also Section 4.2.2 , 4.2.1 and Appendix C). The magnitude of sensorimotor disturbances after gravity transitions increases with microgravity exposure, which is of particular relevance to long duration spaceflight (Reschke et al. 1998). Such disturbances can impact operational activities including approach and landing, docking, remote manipulation, extravehicular activity and egress (both normal and emergency), and thus if not adequately handled, compromise crew safety, performance and mission success (Paloski et al. 2008). It is believed that this sensorimotor deconditioning results from inflight adaptive changes in central nervous system processing of information from the visual, vestibular, and proprioceptive systems (Paloski et al. 1992). The absence of muscular and joint proprioception has been shown to affect performance in several ways, and plays a key role in determining the spatial motor frame of reference (Bard et al. 1995). The loss in postural control has also been attributed to atrophy of the antigravity extensor muscles and spindle sensitivity (Forth & Layne 2008).

Some interesting novel findings suggest that the neurovestibular system is also linked via vestibulosympathetic reflexes to the musculoskeletal system (shown in an experimental animal model lacking neurovestibular input and ß-adrenergic receptor signalling). This could be an additional inflight CM protocol to ameliorate muscle and bone loss to circumvent impaired performance control observed in astronauts during spaceflight (Levasseur et al. 2004; Luxa et al. 2013; Ray 2001; Vignaux et al. 2015) and thereafter.

These changes, seen over hours, days, weeks and months, are a positive response to the space environment, in particular the absence of gravity. However, they are problematic if gravity is re-imposed during planetary excursions (increasing risk of injury), when Earth related achievement standards are necessary inflight e.g. during emergencies, or on return to Earth.

3.7 Current International Space Station Exercise Countermeasures Programme

3.7.1 The current inflight exercise CM programme followed by ESA is delivered primarily through the use of three exercise devices: a cycle ergometer, a treadmill and a resistance training machine, supplemented by the addition of other CM such as isotonic saline fluid loading immediately before departing ISS. The programme is divided into three phases; an Adaptation Phase (14–30 d), a Main Phase (120 d) and the Preparation for Return Phase (14–30 d) immediately before un-docking for re-entry. The Adaptation Phase provides the crew with the opportunity to familiarise themselves with the on-board exercise equipment and their programme. The Main Phase aims to provide a regular and appropriate physiological stimulus in an attempt to maintain aerobic capacity, muscle strength, neuromuscular control and bone mass/strength at pre-flight levels. The Preparation for Return Phase emphasises neuromuscular control and functional movement patterns to ease the transition back to a gravity environment. More details on the ISS inflight CM programme can be found in Appendix B.

3.8 Physiological systems positively affected by countermeasures in the ISS exercise programme and bed rest studies

The goal of postflight reconditioning is to correct any physiological deficits incurred during space travel and thus return a crewmember to their pre-flight status. As such, the focus of current reconditioning is driven by the deficits astronauts present with postflight, the presence and magnitude of which reflect the summation of the well-documented adaptive responses to long-duration spaceflight and the efficacy of the current inflight CM.

3.8.1 The Musculoskeletal System

3.8.1.1 Major Muscle Groups

In ground-based analogues of microgravity, exercise CM have proven to be largely effective in preventing deleterious changes in skeletal muscle during unloading, while nutritional interventions in isolation offer little protection (Blottner et al. 2014). Early inflight studies of skeletal muscle during ISS LDM, where crew had access to the TVIS, CEVIS and the iRED exercise devices suggested that, in combination, these devices resulted in better maintenance of muscle mass than the systems used on the Shuttle-Mir missions (LeBlanc, Schneider 2000). Despite this, they still observed a loss of muscle volume at the thigh (4-7%) and calf (10-18%), with greater losses in the soleus muscle compared with the gastrocnemius (Gopalakrishnan, Genc 2010; Trappe, Costill 2009), although some of this loss was as a result of cephalad fluid movement on entry to microgravity. During recovery from flight, Trappe and colleagues reported approximately 50% of the loss of muscle volume was restored by R+19, whereas overall reduction in muscle performance was sustained, and in several cases exacerbated on R+13 (Trappe, Costill 2009).

Comparable detailed studies of muscle function after LDM when crew have had access to a treadmill (T2), cycle ergometer (CEVIS) and, importantly the ARED, are limited, but published data suggest further improvements in muscle volume/function protection with the current CM programme:

- Gains (compared to previous losses in the pre-ARED era) in lean body mass (Smith, 2012);
- Less reduction in total body mass (Smith, Heer 2012);
- Smaller magnitude of losses in knee muscle strength vs. pre-ARED era (-7 to -15% vs. -9 to 20%, (Center 2008; English, Lee 2015).

Despite these improvements, however, there has been minimal positive effect on ankle and trunk strength (English, Lee 2015) and, on an individual level, many crewmembers continue to lose in excess of 20% muscle strength, which fails to meet the current permissible outcome limit for returning crewmembers.

3.8.1.2 Postural Muscles

As demonstrated by the sensitivity of the soleus muscle to space flight, postural muscles are considered to be particularly sensitive to prolonged unloading due to their tonic, continuous activation for normal function in gravity. Muscle atrophy is known to occur around the lumbar spine during spaceflight, but not in the cervical extensor muscles (LeBlanc, Schneider 2000) and crewmembers with access to ARED show marginally less decrease in spinal muscle extensor strength compared with the iRED era (Center 2008). However, despite this apparent improvement using

ARED, the most recent published data (albeit with small subject numbers) from ISS suggests that atrophy of key spinal stabilising muscles is still evident after LDMs (Hides et al. 2016a).

3.8.2 Bone Mineral Density

Although the combination of suitable aerobic training devices on ISS and appropriate CM programmes has been largely successful at countering the loss of aerobic capacity which occurs during LDMs, it has not been successful at countering inflight bone loss and despite the inclusion of weight-bearing exercise (T2) and moderate intensity resistance exercise (iRED), (Lang, LeBlanc 2004; Sibonga, Evans 2007). However, with the transition to ARED, recent preliminary evidence suggests that some crewmembers with access to ARED and with adequate energy and vitamin D intake display little or no difference between pre- and postflight measures of bone health (Smith, Heer 2012), with no difference between male and female astronauts (Smith et al. 2014). More recently still, ARED use has been seen to be associated with significantly less bone loss measured at the trochanter, total hip and pelvis than during the pre-ARED era, with a trend for better preservation at the lumbar spine and femoral neck (Sibonga et al. 2015).

3.8.3. The Spine

Ground-based analogues of prolonged microgravity in which the spine is no longer subjected to an axial load have provided evidence of an increase in stature, changes in spinal curvature and an increase in volume of the intervertebral discs (IVD) (Belavy et al. 2011; Cao et al. 2005). These changes may persist for a prolonged period following re-loading (Belavy et al. 2012; Belavy et al. 2011). In comparison, however, there is little inflight data to corroborate this. Stature certainly increases, but no differences in sagittal plane disc area or lumbar spine length are reported (LeBlanc et al. 1994) and only now are inflight studies of the effect CM programmes have on IVDs underway[2]. Considering initial data from these experiments, Sayson and colleagues (Sayson 2015) report the following observations:

- Variable (between crew and different spinal levels) IVD water content changes, but no significant changes in disc height;
- Decreased functional extensor endurance and decreased (-14 to -17%) cross-sectional area of lumbar and cervical muscles;
- Increased spine stiffness in flexion and increased spine straightening due to 11% reduction of lumbar lordosis;
- No reductions in the negative effects (e.g. lower glycosaminoglycan concentration), on quality and/or anterior wedging of vertebral bodies, or endplate irregularities.

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[2] http://www.nasa.gov/mission_pages/station/research/experiments/944.html and (http://www.nasa.gov/mission_pages/station/research/experiments/872.html).

3.8.4. Cartilage

Since the risk of cartilage degeneration as a result of prolonged immobilization and microgravity is not known, the potential for exercise to counteract the initiation of cartilage degeneration in a healthy joint can only be estimated at present. Furthermore, cartilage tissue has not been properly examined during postflight reconditioning, thus leading to the current scarcity of data. Inflight studies of human cartilage health are only now in progress (CARTILAGE[3]) so the postflight status of astronauts' articular cartilage health remains unknown and cartilage status is not considered in the current CM programme.

3.8.5. Aerobic Capacity

Following ISS flights, crewmembers exhibit elevated heart rate responses to submaximal exercise initially, with a return to pre-flight levels occurring 1 month after return to Earth (Moore et al. 2014; Moore, Lee 2010). With the current inflight CM exercise programme, VO2peak decreases on average to 82% of pre- flight levels by Flight Day 15, but partially recovers during the remainder of the mission (Moore, Downs 2014). As such, on return to Earth, VO2peak is typically only 15% below pre-flight levels immediately after flight and recovered by approximately 50% after 10 d and completely after 30 d back on Earth (Moore, Downs 2014; Moore, Lee 2010). This is comparable to previous investigations from short (8–14 d) duration flights (Levine, Lane 1996) and illustrates that how unlike bone loss in space, aerobic capacity does not continue to degrade (with adequate CM) and is probably related to subacute CV changes and possibly biomechanics, etc. Although those with a higher pre-flight VO2max appear more susceptible to inflight deconditioning (despite following the same CM programme), their postflight absolute level of aerobic capacity remains both acceptable and still greater than those who were less fit pre-flight. In addition, a closer examination of the individual crewmember data indicates that 50% actually maintain or even increase their aerobic capacity during their missions, and that those who attained higher exercise intensities during CM sessions were less susceptible to a loss of function (Moore, Downs 2014).

3.8.6. Functional Performance

To understand how physiological changes affect functional performance, a pre- and postflight testing regimen, the Functional Task Test (FTT), was developed. (Arzeno et al. 2013; Ryder et al. 2013; Spiering et al. 2011). It was found that for Shuttle, ISS and bed rest (control and exercise) subjects, functional tasks requiring a greater demand for dynamic control of postural equilibrium (i.e. fall recovery, seat egress/obstacle avoidance during walking etc.) showed the greatest decrement in performance after microgravity. Functional tests with reduced requirements for postural stability (i.e. hatch opening, ladder climb, manual manipulation of objects) showed little reduction in performance. These changes were paralleled by similar decrements in sensorimotor tests designed to specifically assess postural equilibrium and dynamic gait control. Bed rest subjects who performed an integrated high intensity interval-type resistance and aerobic training programme while in bed showed significantly improved lower body muscle performance compared to bed rest controls and spaceflight subjects. However, resistive and aerobic exercise alone was not sufficient to mitigate decrements in functional tasks that require dynamic postural stability

3 http://www.nasa.gov/mission_pages/station/research/experiments/872.html

and mobility, and point to the need for the addition of balance/sensorimotor adaptability training to current CM systems.

Bed rest subjects experienced similar deficits as spaceflight subjects, both in functional tests with balance challenges and in sensorimotor tests designed to evaluate postural and gait control, indicating that body support unloading and proprioceptive alterations plays a central role along with vestibular disturbances postflight. Additionally, ISS crewmembers who walked on the treadmill with higher pull-down loads had enhanced postflight performance on tests requiring mobility. Taken together, the spaceflight and bed rest data point to the importance of supplementing current inflight exercise CM with balance training that requires coordination and integration of proprioceptive feedback i.e. motor control training (exercises for performance of controlled, good quality movement), and body loading information. This suggests that other systems responsible for balance and postural control (proprioception, mechanical loading, muscle afferents, etc.) may be suitable targets for inflight CM development. Therefore, preflight sensorimotor adaptability training (as in injury prevention programmes in elite sport; see Section 7.4.2) can be supplemented with inflight balance and treadmill training to enhance overall adaptability of balance and gait control enabling rapid recovery of function postflight.

Crewmembers who exercised on the ARED on ISS have shown less decrement in postflight postural stability and agility scores compared to subjects using the Intermediate Resistance Exercise Device (iRED) (Wood et al. 2011), which offered less resistance than ARED. The Functional Fitness Tests (FFT; not part of the FTT) includes practical exercise tests such as push-ups, pull-ups, bench press, and leg press, and, for all but one measure, crewmembers with access to ARED fared better than their iRED counterparts, with either small postflight decrements or even improvements after spaceflight (Center 2008).The increased body loading during ARED exercises may have provided greater postural challenges during exercise improving postflight balance performance. Another key factor in performance training is motor control training and warrants attention in all phases of astronaut training (see Sections 4.2.2, and 7.2.2).

3.8.7. Orthostatic Intolerance

As mentioned in section 3.5.2, crewmembers undertaking long duration mission (LDM), such as 6 month ISS missions, have a significantly greater chance of experiencing postflight orthostatic Intolerance (OI) than those undertaking Short Duration Missions (SDM) (4-18 days), and their cardiovascular response to an orthostatic challenge recovers more slowly (Lee, Feiveson 2015). The true rate of landing day OI is likely higher still, as crewmembers who are very ill on landing are either not tested (and thus not included in calculations) or testing is delayed until they are sufficiently well to participate. Whilst LDM crewmembers appear highly susceptible to landing day OI, the most recent data suggest that the majority (89%) recover sufficiently to pass the 10 minute tilt test after two days of recovery, and all are recovered by day three (Meck et al , 2004) (Lee, Feiveson 2015). Although the exact magnitude of inflight CM programme effect on OI is unknown, anecdotally crew report a positive effect in particular as a result of the pre-landing fluid loading regimen (Appendix B) and the use of lower body anti-G garments (Buckey, 2006).

3.8.8 Sensorimotor Function

Despite the large body of sensory-motor and psychological research data obtained from space flight experiments over the years, there is little published information specifically concerning pre- to postflight changes with LDMs and advanced exercise CM. The time to complete a functional mobility test – walking at a self-selected pace through an obstacle course on a base of 10-cm-thick, medium-density foam – is increased by 48% and is estimated to take up to 15 d postflight to return to preflight levels (Mulavara et al. 2010). Likewise, performance of a sensory organization test – using sway-referenced support surface motion with eyes closed – is decreased after LDMs (Cohen et al. 2012). Disruptions in lower limb kinematics leading to reduced toe clearance have also been reported, but this decrement corrects by the 1st day postflight (Miller, Peters 2010). The most recent data from NASA utilising a computerised dynamic posturography protocol indicates the presence of postflight decrements, which vary considerably between individuals (Wood et al. 2011). However, these data also suggest improvements in some aspects of postural performance since the introduction of ARED, including sensory organisation and motor control.

Although studies of the magnitude and recovery of sensorimotor symptoms following return to Earth after LDMs are limited, Clément and colleagues (Clément et al. 2016) undertook a review of available data and concluded that recovery of function takes an average of 15 days to return to within 95% of preflight performance levels. It is noted that the subjects and populations from which this conclusion is drawn did have varying exercise countermeasure programmes and operational circumstances (Clément et al 2016).

3.9 Reconditioning following prolonged simulated microgravity

An intervention programme post bedrest (Bed Rest Study BBR-2), which incorporated motor control training and graduated weight bearing (with special attention to maintenance of spinal curves) has been shown to be effective in restoring the size of the spinal and abdominal muscles to their pre-bed rest size and relationship to each other (Hides et al. 2011). Postflight reconditioning programmes in current practice are outlined in Chapter 4, which have yet to be evaluated for their effectiveness.

3.10 Conclusions

This chapter has highlighted the physiological changes experienced by the human body during space missions which have a bearing on post mission reconditioning. The musculoskeletal, neurovestibular and neuromuscular control systems are especially affected and require substantial CM in an attempt to ameliorate the changes. Positive responses to CM used on ISS have been detailed to help provide an understanding of the status of astronauts as they start their reconditioning on return from space.

- *MUSCLE*: With access to the current exercise CM devices, and specifically ARED, in general, the magnitude of inflight atrophy of the major muscle groups has been reduced in comparison to the pre-ARED era. However, on an individual level, some crew members continue to lose muscle strength of clinical proportions. Recent evidence from a small number (<10) of crew members with access to ARED indicates that the deep spinal muscles are still subject to marked atrophy;

- *BONE*: Recent preliminary evidence suggests that, compared with the pre-ARED era, some crew members with access to ARED display little or no change in BMD during LDM, however, variability between crew indicates that the issue is not yet fully addressed;

- *OI*: Whilst LDM crewmembers appear highly susceptible to landing day OI, the majority recover sufficiently to pass the 10 minute tilt test after two days and indications are that all may recover by day three. However, due to use of other pre-landing CM (*i.e.* fluid loading) the exact magnitude of inflight CM programme effect on OI is unknown;

- *CARTILAGE*: There is insufficient knowledge of changes to human cartilage as a result of LDMs for adequate conclusions at present, although studies have begun;

- *SPINE*: Preliminary inflight data suggests that the effect of LDMs on the spine is variable (between crew and different spinal levels). IVD water content changes with no significant changes in disc height, but increased spine stiffness and straightening occur;

- *AEROBIC CAPACITY*: With access to the current exercise CM devices, it appears that as many crewmembers maintain or increase their aerobic capacity during their mission as those who experience losses. Those who attain higher exercise intensities during CM sessions appear less susceptible to a loss of aerobic function;

- *FUNCTIONAL PERFORMANCE*: In postflight functional tests, including postural stability and agility push-ups, pull-ups, bench press, and leg press, crewmembers with access to ARED showed less decrement in performance compared to those from the pre-ARED era;

- SENSORIMOTOR FUNCTION: Sensorimotor function, as measured using computerised dynamic posturography, indicates improvements in some aspects of postural performance since the introduction of ARED, although with considerable inter-individual differences in performance. A number of measures of sensorimotor function suggest that preflight performance is recovered by around 15 days postflight.

The following Chapter provides a small number of personal insights from astronauts and Medical Operations specialists on the topics covered in the present chapter and documents their proposed recommendations for future improvements in the field.

CHAPTER 4:
ASTRONAUT AND OPERATIONS EXPERT PERSPECTIVES ON EFFECTS OF MICROGRAVITY INFLUENCING POSTFLIGHT RECONDITIONING

4.1 Introduction

An Astronaut/Operations Experts Sup-group of the Post-Mission Exercise (Rehab) Topical Team (TT) was set up to enable their perspectives to be captured. Engaging these experts is analogous to PPI in terrestrial research (see Section 8.2.6). The purpose was to gain valuable insights into the challenges they face to help ensure the research priority areas for postflight reconditioning proposed by the TT were feasible. For example, are the right questions being asked to solve challenges for effective reconditioning? If a research project/programme was developed and funded, would it be workable on a practical level?

Aspects during preflight and inflight exercise that impact on postflight reconditioning have been considered, and the NASA and ESA postflight reconditioning programmes are outlined in Section 4.2. The experiences and challenges of astronauts and operations teams are reflected in this chapter, which are reported in full in Appendix C.

4.2 Postflight Reconditioning Practices

Despite rigorous inflight CM exercise programmes, postflight reconditioning after return to Earth is still required (Chapter 3) and implemented by space agency reconditioning specialists. Strategies differ between agencies, and common practice guidelines do not yet exist, and thus reconditioning practices vary between crew member and space agency.

4.2.1 NASA Postflight Reconditioning

In 2003, Chauvin et al (Chauvin et al. 2003) reported (in a conference abstract) that reconditioning of United States crewmembers to full functional preflight status following flights on the Russian Mir Space Station had required more than six months. Chauvin et al (2003) also reported findings of the postflight reconditioning for crew members returning from the ISS, which lasted 45 days (2 hours per working day). Phase 1 began on landing day and placed an emphasis on ambulation, flexibility, and muscle strengthening. Phase 2 added proprioceptive exercise and cardiovascular conditioning. Phase 3 (the longest phase) focussed on functional development. Programmes were tailored for each astronaut according to their test results (of functional fitness, agility, isokinetic strength, and submaximal cycle ergometer performance) and preferred recreational activities. Most crewmembers reached or exceeded their preflight test values 45 days postflight. Since 2003 the ARED device has been introduced to the ISS and reconditioning has emphasised functional fitness/agility and proprioception (Section 3.8.5 and 3.8.6). Wood et al (2011) describe an individualised sensorimotor reconditioning programme that challenges multisensory integration with an increasing level of difficulty.

4.2.2 The ESA Postflight Reconditioning Programme

Since 2006, the ESA reconditioning team has managed the CM programme of eight long duration (6-month ISS) crewmembers. One Physiotherapist and three Exercise Specialists are now responsible for developing and conducting the ESA reconditioning programme. The ESA Exercise Specialists are sports scientists who give CM support to ESA crewmembers by providing exercise prescriptions based on interfacing with flight surgeons and biomedical engineers. This programme also includes the preflight training and the inflight prescription and monitoring of exercise performance on the ISS, as these phases are related and cannot be managed in isolation. A brief overview of the programme follows. Operational challenges are also outlined (Sections 4.4 & 4.5).

The objective of the ESA reconditioning programme is to trigger and enable the complete recovery process, comparable with pre-flight status, using an individualised, efficient and functional reconditioning approach. The unique combination of physiotherapy and sport scientific methods leads to a comprehensive and efficient recovery programme over the first 21 days after return from space (Lambrecht et al 2016 & Petersen et al 2016 in Appendix D).

4.2.2.1 Principles of the ESA postflight reconditioning programme

a) *Reorganisation of postural control, muscle control and muscle balance* – the stabilizing muscular system, which enables an optimal upright posture, is first re-educated (soleus, vastus medialis, deep lumbopelvic muscles). Functional exercises, progressing from simple to complex movement patterns, are used to retrain postural control and to balance the activity between the stabilizing and mobilizing muscular systems. To retrain muscle balance, it is essential to avoid using the wrong muscles or compensation movements, and to integrate and consolidate the readjusted movement quality into functional exercise during the reconditioning phase.
b) *Use of motor learning principles* - motor control exercises, training of proprioception, balance and coordination are used to reorganize the astronaut's motor capabilities and functional fitness. Optimized motor skills are fundamental for pain and injury prevention.
c) *Respect the centre of gravity* – the Gravity Line is the optimal line of load transfer through the human body, which enables the body to use the positive effect of pressure to reduce stress on weight-bearing joints and optimize muscle function. The centre of gravity is at the 3rd lumbar vertebra (L3). Both the centre and line are lost after a period of microgravity exposure and have to be retrained to produce economic movement and to avoid long lasting additional stress on the musculoskeletal system. Exercises during the reconditioning period focus on paying close attention to movements respecting the gravity line and posture.
d) *Apply appropriate stimuli at the right time* - through a careful combination of physiotherapy interventions and physical exercise that is gradually intensified to respect individual adaptation capabilities, avoiding injury yet stimulating functional re-adaptation.
e) *Strength and endurance training following motor control training* – building on the basis of stable motor control, posture and movement patterns, physical exercises are determined and progressed to enable not only functional but also structural recovery processes, requiring higher intensities later in the reconditioning process.

4.2.2.2 Objectives of the ESA postflight reconditioning programme

a) Initiate and complete an efficient postflight reconditioning programme, beginning within 24h of landing, independent of location of crewmember on return
b) Prevent short and long-term pain (e.g. LBP) and mission-induced physical health problems

c) Return the astronaut to their preflight physical capabilities as assessed in preflight medical and physical assessment defined in Medical Operation Document (MED B[4]), Astronaut Functional Fitness Assessment (AFA[5]). The aim is to achieve full recovery without risking the development of pain or injuries associated with readaptation and to enable the resumption of loading (relevant to joint health and preventing osteoarthritis in longer-term; see sections 6.2.1.3 and 6.2.1.4).
d) Support physical recovery to allow crewmember flight recertification
e) Support resumption of unimpaired activities of daily life and preferred physical activity (such as sports)
f) Encourage astronaut self-management of exercise after postflight recovery
g) Minimise long-term effects of space flight on the musculoskeletal system (as far as possible)

4.2.3.3 Structure of the ESA reconditioning programme

The ESA postflight programme combines physiotherapy, sports science and exercise methods in sequential order. It uses good communication techniques to ensure that a highly coordinated programme can be operated by a small, well trained team in different locations within 21 days. This period can be extended up to 45 days if required. To be able to adapt to individual crew conditions, and short and long-term exposure to external conditions (such as mission duration or profile), an interdisciplinary and individualized programme tailored to each crewmember is implemented. The programme consists of three phases:

A. Back to gravity (first week)
B. Back to function (second week)
C. Back to work i.e. return to duty (third week)

Return to duty involves high performance flight, EVA training in Neutral Buoyancy Lab (NBL) and other activities that differentiate the astronaut job from the typical work place. Full return may take up to 45 days, depending on the individual's progress with recovery.

Programme conditions and considerations include:

a) Daily, supervised implementation of 2-hour reconditioning programme for 21 days, using facilities either at the host agency or at the European Astronaut Centre. Unsupervised reconditioning exercise sessions continue after completion of the initial reconditioning phase of 21 days.
b) Consideration of tight schedules and medical and experimental constraints associated with post-mission Baseline Data Collection (BDC), which impacts the reconditioning intervention programme (e.g. frequency or intensity).
c) Daily programme adjustment to crewmember's physical condition and rate of progress
d) Close interaction between astronaut and reconditioning team and within the team, between physiotherapist and Exercise Specialist, and with medical doctors, schedulers, and management.
e) Implementation of daily reconditioning programme in available gym facilities, applying training principles established by ESA exercise and reconditioning specialists.

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[4] Med B - Medical Evaluation Documents (Med) Volume B, preflight, inflight, and postflight medical evaluation requirements for long-duration ISS crewmembers, SP 50667.

[5] AFA – Astronaut Fitness Assessment used by the ESA Medical Operations office.

The programme involves progressive development of complexity and intensity, beginning with motion quality developed through motor control and postural control exercises, merging into an individualized functional fitness conditioning programme, which can be implemented without continuous supervision. Preliminary service evaluation (i.e. documenting effectiveness of the programme) indicates that the programme is effective (Petersen et al. 2016 in Appendix D).

4.2.2.4 Conclusions

The ESA programme was developed using evidence from extensive terrestrial studies and limited studies on postflight and post-bed rest reconditioning research, as well as experience in working with astronauts. Developing optimal postflight reconditioning programmes and evaluating their effectiveness in astronauts is a major research challenge within this relatively small field. Research designs and methods appropriate for space research need careful consideration (Chapter 8). Studies of reconditioning post-bed rest could contribute to the evidence base for reconditioning but are lacking (Section 6.3.3). The unknown challenges with longer missions are discussed from the medical and operations team perspectives below (Sections 4.4 & 4.5).

4.3 Astronaut Perspective Case Reports

Space flight experiences of two astronauts are outlined below and detailed in Appendix C.

4.3.1 Astronaut Case Report 1

Astronaut 1 flew three short duration space missions with the Shuttle Transportation System (STS). Personal trainer availability for consultation and treatment was appropriate, as was their skill and knowledge. The astronaut perceived trust in physiotherapists and trainers to be crucial to good working relationships and to feeling supported.

4.3.1.1 ***First Flight (9 days duration)***

Astronaut 1 suffered from mild low back pain (LBP) early inflight which resolved within a few days. His stature increased inflight by about 5cm placing pressure on his shoulders during EVA. Post-mission he felt mild orthostatic intolerance when upright during the first few hours on Earth and had balance and orientation difficulties for the first few days. He began running three days postflight and suffered from a large cervical disc extrusion which progressed in severity from the 2^{nd} week and it was treated successfully with surgery and recovered within 3 months of return. There had been no pre-existing neck pain or injury.

Key Messages in brief

- Close monitoring of postflight effects is important and may have prevented the post-mission injury suffered after this flight.
- Gradual re-loading during reconditioning is crucial to minimise the risk of injury.
- Appropriate levels of assessment are necessary to prevent medical complications
- Standardized assessments of relevant functional activities can enable the efficacy of pre, in and postflight programmes to be better assessed and monitored.

4.3.1.2 ***Second Flight (3 years later – 10 days)***

Astronaut 1’s postflight experience was an improvement over the first mission. Minimal orthostatic intolerance was felt, which lasted for only an hour or so on return. Ccoordination and orientation issues were much less severe and aspects of recovery that took days after the first flight only took one day after the second.

Key Messages

- The nature and enjoyment of inflight exercise is seen as important to maintain motivation.
- Group activities inflight were seen as more enjoyable and may enhance exercise compliance
- Increase post-mission weight-bearing exercise duration and intensity very gradually.

4.3.1.3 ***Third Flight*** **(*2 years later* – 12 days)**

Astronaut 1 had no conditioning or strength issues and felt that post-mission effects were less than in previous flights, for instance not needing any pressure in his anti-G suit during entry and experiencing normal feelings of orthostasis within an hour postflight. A pressure and friction wound was, however, suffered during his first EVA which extended to the bone of the 5th metacarpal. Although this injury did hurt a little during the second EVA, it did not interfere with overall performance and healed without complications.

Key Message

- Some adaptation to the effects of microgravity on orthostasis from undertaking repeated missions might be evident, or exercise CM programme of the 3rd mission may have been more effective (included bike, treadmill, iRED).

4.3.1.4 ***Recommendations from Astronaut 1***

1) Focus on functional tasks postflight as well as preflight. Understand the specific areas of strength and conditioning needed to accomplish the tasks and train with these in mind to make the routines shorter, less boring, and to increase compliance.
2) If possible, use techniques that use multiple aspects of function, e.g. strength, co-ordination etc, for exercise in flight. For example, create routines like flying exercises (described in Appendix C) to maintain the required combination of coordination, impact, strength, and conditioning needed. They are also much more enjoyable, and therefore contribute to the crew's mental well-being. *[However, the space available for current missions would not allow as much freedom to move around the space station and future long-duration missions are likely to have even more space restrictions.]*

4.3.2 Astronaut Case Report 2

Astronaut 2 undertook two missions, both using Soyuz to fly to the International Space Station. The first mission was an 11 day flight and the second was for 6.5 months.

4.3.2.1 ***Flight 1 (11 days)***

Astronaut 2 had three musculoskeletal issues during the preparation phase. The first involved pain over the patella and tendon of the right knee, which impacted his postflight reconditioning. Although the issue resolved sometime after the first mission it returned (on the left knee) during the Soyuz simulations in preparation for the 2nd flight. The second issue was acute LBP pre-mission, which local physiotherapy and electro-stimulation resolved. The third issue was Plantar Fasciitis on the left side, probably caused by running, which was painful when standing on the heel of the foot after sitting still or when getting up out of bed. It was treated successfully with special shoe soles in daily and running shoes. Neuromuscular coordination was adversely affected on return, requiring aid from medical staff during the first day but resolving by week 2 post-mission.

4.3.2.2 ***Flight 2 (6.5 months)***

Astronaut 2 noted an inflight increase in stature of 2–3 cm, but with no back pain. A mild back injury was, however, suffered with associated pain during an early ARED session, which affected physical performance for approximately one week thereafter.

Neuromuscular coordination was also adversely affected on return and required longer to return to pre-flight levels (Appendix C). Orthostatic intolerance was felt during the first few days post-mission. A near fainting (syncope) episode was experienced after a maximal exercise test. Aching muscles were noted for about 3 months on return.

Key Messages in brief

- Recreational videos can make exercise more enjoyable and help with motivation
- Real-time feedback from the ground support team when exercise is performed in space is important and may prevent crew injuries.
- The ergonomics of spacecraft design needs to be considered in more detail to prevent crew discomfort bordering on injury (e.g. prolonged sitting in cramped conditions, see below).

4.3.2.3 ***Recommendations from Astronaut 2***

1) Special attention to physiotherapy/flexibility etc. to deal with the prolonged sitting position in the Soyuz simulator (where space is restricted and the knees are bent for hours and cannot be stretched out), in order to prevent stress injuries (particularly in tall astronauts). The discomfort can be distracting during the simulation/flight, difficult to recover from and may persist.
2) Direct video AND voice contact is needed with fitness instructors during several ARED sessions, early, midway and later in the mission, for effective exercise and to prevent injuries due to incorrect body positions and movements.
3) It is useful to have access to video clips of each ARED exercise, easily accessible before the session, with warnings for wrong positioning.
4) DEXA monitoring sufficient to document return to preflight bone density.

4.4 Flight Surgeon Perspective

This section is a personal perspective from an experienced ESA Flight Surgeon.

One of the primary concerns for a Flight Surgeon (FS) is to protect the astronaut during the very busy post-mission phase. The first few weeks after a mission include an intensive schedule of postflight medical assessments, baseline data collection for scientific studies, Public Relations and media activities, space agency briefings and other calls upon the crewmember's time. The FS is the astronaut advocate and must try to enable post-mission reconditioning in the face of an aggressive postflight schedule.

The preflight exercise programme is very important too. The busy pre-mission schedule makes it difficult for crew to accurately follow their fitness programme, and yet we need them to be as fit/healthy as possible as they start their mission. Preconditioning needs to be as structured as inflight training (although this is very challenging).

The TT recommendations in this report might help the Medical Operations team to know:

- The R+1-21 period evolved as a compromise with competing demands on astronauts' time. What evidence exists to support postflight reconditioning programme in the first 21 days?
- What evidence supports the prescription used to bring crew back to an appropriate level of well-being?
- Are astronauts being pushed too hard? Is the rigidity of the postflight schedule dictating the nature of the reconditioning programme?

4.4.1 What are the most common problems observed by flight surgeons that impact on postflight reconditioning of astronauts?

- Astronauts are typically tired and dehydrated when they first return to Earth but ‘blossom’ by R+2.
- The physical impairment of crew returning is, at present, reasonable given the nature of 6 month ISS missions. What evidence exists to allow us to state what is ‘good enough’ for an astronaut to be released, for example, for a transatlantic flight?
- Upon returning from a six-month flight most astronauts face various medical conditions, some of which are acute but others require longer recovery times.
    - The major challenges the astronaut faces upon landing is re-adaptation to gravity. In particular fatigue and neurovestibular symptoms make unaided reambulation on landing day extremely difficult, fatiguing and provocative. Although it is reasonable to believe that orthostatic hypotension may play a role, in my personal experience this has not been the case as no fainting episodes have been observed in my presence. Dizziness and emesis were often linked to sudden head or body movements, thus assumed to be neurovestibular in nature. Currently, astronauts typically pre-medicate before landing to mitigate neurovestibular symptoms on landing. This improves their performance in the immediate post-landing period. Within 24 hours of landing, unaided ambulation is usual; however, an incomplete neurovestibular re-adaptation (turning corners, unstable balance in absence of visual cues, etc) persists for 10 to 15 days after landing.
    - In my experience, I have not witnessed significant evidence of orthostatic hypotension; however, some mild oedema of the ankles observed in some astronauts, in the early postflight period (days-weeks) is testimony that the interstitial tissues gradients are still re-adapting to the gravity-induced increase in hydrostatic pressure in the lower body areas.
    - Fatigue, both physical and mental, is a chronic symptom that persists for longer periods of time and beyond the current 21 days acute rehabilitation phase. Recovery from fatigue and the lingering muscloskeletal discomforts (weeks to months) is not supported by the intense pace of the postflight activities, making adherence to physical rehabilitation difficult beyond the first 21 days postflight. At this time, both physically and psychologically, the astronaut is nearly exhausted, after six months of enduring work and spaceflight-induced environmental and physical challenges. The astronaut realises that the months ahead will be possibly more intense and less structured than those on ISS with postflight testing, public relations, travelling and debriefings. This holds the potential to delay optimal physical and psychosocial rehabilitation and a proper re-integration into private life, until much later than desired, in the postflight phase.

4.4.2 Perceptions for exploration length missions

- Preliminary informal comments from the 1 year mission crew flown on ISS indicated that postflight effects are much more marked after 12 months than 6. When considering 2 year missions, although exercise countermeasures programmes for 6 & 12 month missions appear efficient, we probably need better ways of exercising so that crew do not need to exercise for 2 hrs every day for 2 years. This might come in the form of better equipment but also less conventional activities such as motor imagery, which is known to improve physical skill and muscle strength, possibly using video/computer games.

- With respect to space vehicles and engineering processes there is a need to not see human needs as constraints but as requirements around which engineering solutions are centred. Space habitats need to be developed with humans more fully in mind so that a 'human compatible environment' results. For example, more thought is needed behind where exercise equipment is placed and how it is designed, e.g. treadmill harness and loading devices.
- Space vehicle design needs to fit the needs of astronauts to keep them healthy inflight by more closely mimicking the Earth environment without imposing non-physiological effects e.g. avoiding high CO_2 content within the space environment.
- Future mission architects need to take into account postmission rehabilitation needs (as reflected by inflight CM efficacy) and build post-mission schedules with these needs in mind, rather than the reconditioning programme being 'shoe horned' into the schedule.
- Exercise countermeasures may never be able to totally prevent the effects of microgravity, so technological solutions are needed in the long-term (e.g. artificial gravity) to better create a human environment that is compatible with the need to maintain Earth physical standards.

4.5. Operations team (physio/exercise specialist) perspectives

4.5.1 Operational challenges in postflight reconditioning

Postflight reconditioning of astronauts is implemented within a very compact post-mission schedule, accompanied by medical checks, social and public relations (PR) commitments, debriefings and experimental baseline data collection. Daily reconditioning exercise needs to be individually tailored, requiring daily 2 hr sessions and appropriate and focused adjustment of the programme. Differences in available equipment and facilities will depend on the location of the returning astronauts, so these need to be considered and the programme tailored accordingly. Large intra-individual differences and diverse mission profiles do not allow simple implementation of a standard protocol, but reconditioning principles (section 4.2.2.1) can be interpreted for the individual and the surrounding conditions.

4.5.2 Future reconditioning challenges after longer missions

Discussion with the ISS CM Working Group (CMWG) indicates that operational experts generally agree on the nature of the problems typically seen after long duration space flight and that these need to be addressed and further understood, especially for mission durations longer than 6 months. The emphasis of intervention for reconditioning of astronauts after 1-year missions might be more focused on neuromuscular training than is currently carried out after six month ISS missions.

Greater understanding is needed to identify tailored and efficient intervention strategies for the individual. A scoping exercise, via survey or focus groups, may be a useful research activity to capture the views of operations experts. Specifically, it would be useful to hear what challenges might be anticipated after longer duration missions (> 12 months) based on those currently experienced after 6-month missions.

Inflight preconditioning during deep space cruise will be required to prepare for planetary exploration after a period in which physical deconditioning has occurred. There will also be a need for autonomous treatment effective enough to ensure mission operations can be undertaken quickly and safely. Furthermore it can be envisaged that future exploration missions will be followed by intensive media interest, so it will be important not to allow this to impact the post-mission reconditioning programme.

4.6. Conclusions

4.6.1 The astronauts and operations specialists consulted perceived that:

- Trust in reconditioning specialists is crucial to good working relationships;
- The nature and enjoyment of inflight exercise is important to maintain motivation to follow the programmes provided.
- Postflight reconditioning of astronauts is implemented within highly demanding post-mission schedule of 3 to 4 weeks, and must be co-ordinated with medical checks, social and public relations commitments, debriefings and postflight tests required for scientific experiments for which astronauts serve as volunteers;
- Large inter-individual differences and diverse mission profiles do not permit implementation of a standard reconditioning programme. As such, programmes provided by ESA specialists are individually-tailored during daily, two hour sessions, and can be influenced by differences in equipment and the facilities at the location to which the astronaut returns.
- A key feature of the success of the ESA Reconditioning Programme is the close collaboration between the physiotherapists and Exercise Specialists.

4.6.2 There will be a wide variability of crew experiences and operations expert views, so those reflected in this report only provide a small perspective and wider involvement is needed:

- Patient and public involvement (PPI) is fundamental to the feasibility and success of terrestrial research, so involvement of astronauts and operations experts needs to become integral to human space research.
- Such involvement includes participating in setting research and operational evaluation priorities, and conducting associated projects, as appropriate. These activities require the training of representatives in research processes and governance procedures.
- The astronaut case histories are of value (Appendix C) and have highlighted aspects of spaceflight and post-mission challenges that are important to them that may not be considered as important to those responsible for their health. Gaining astronauts' views provides insights into how their care might be improved, what might increase adherence to exercise and also aid decisions on research priorities. An effective system is needed to capture views from serving and retired astronauts but it must be anonymised so as not to compromise their trust (see Section 7.8.4). An example is the NASA Crew Comments Data Base, which logs all debriefs and is searchable on terms and topics in a non-attributable fashion.

Recommendations related to these conclusions are summarised in Chapter 10. The report thus far has discussed the effects of microgravity on the neuro-musculoskeletal system and the challenges faced on return to Earth, with the postflight reconditioning programmes from two agencies (ESA & NASA) outlined. The next chapter identifies what is unknown and requires research to develop optimal postflight reconditioning programmes for current and future longer duration missions.

CHAPTER 5: KNOWLEDGE GAPS

5.1. Introduction

As stated in Chapter 1 (Section 1.1), the goal of postflight reconditioning is to correct any physiological and functional deficits incurred during exposure to the space environment, thus returning crew to their pre-flight status. Knowledge gaps and research priorities are, therefore, related to the presence and magnitude of the deficits:

1. *Currently observed*, in medical tests and by re-conditioning specialists, and experienced by crew members, returning from nominal 6-month missions to ISS;
2. *Likely to be observed in, and experienced by*, crewmembers returning from future missions, including those of longer duration, those outside Low Earth Orbit (LEO) and those involving planetary surface excursions (Long Duration Exploration Missions – LDEM).

In the case of the LDEMs, the two most likely destinations for surface explorations will be Moon and Mars, both of which have partial gravity (> µG and < 1G) environments (moon: 0.16 G; Mars 0.38 G). As such, LDEMs will consist of time in µG (transit out), time in partial gravity (surface exploration) and further time in µG (transit back). Human adaptation to prolonged µG has been well-documented, but currently little is known about the adaptation that will occur in partial gravity. The extent of adaptation will depend on the forces acting on the body during surface locomotion and, although these have yet to be quantified, they are likely to be substantially less than those routinely experienced by the body in Earth's gravity. It is likely, therefore, that exercise CM, consisting of both novel exercise programmes and novel exercise devices, will also be required to support crew living and working in partial gravity environments as part of LDEMs.

5.2 Knowledge gaps for current six-month missions

The knowledge gaps in postflight reconditioning for current missions to the ISS are listed below in Table 5.1.

Table 5.1. Postflight re-conditioning Knowledge Gaps for crewmembers returning from nominal 6-month missions to ISS.

Parameter	Knowledge Gap(s)	Rationale	Report Section Reference
Musculoskeletal System			
Major Muscle Groups	How can the residual loss of muscle mass and strength on return to Earth be recovered as rapidly and effectively as possible by postflight reconditioning?	The response of the major muscles of the lower limbs to space flight is well documented in Chapter 3. Although inflight CM are more effective than ever, they do not completely prevent the loss of muscle volume/force production. Some crew continue to lose in excess of 20% muscle strength in some muscles.	Section 3.1.1 and 3.8.1
	What is the nature of changes at the neuromuscular junction?	Knowledge of these links is important for understanding afferent and efferent signal transmission, and subsequently the nature of muscle deconditioning/reconditioning.	Section 3.6
	Are alternative CM protocols helpful to support re-adaptation postflight ?	Recent findings show that short-term resistive vibration (RVE) mechanostimulation as a CM in bed rest is well tolerable, less time consuming than others (resistive exercise), highly effective in outcome, and acceptable to bed rest participants (works via neuroreflexive activation independent from motivation) and effectively support a close-to-normal muscle fiber microstructure, molecular composition and function in disused human skeletal muscle (soleus).	Section 3.1.1
	What are the adaptation mechanisms of the neurovestibular system affecting skeletal muscle structure and bone density, and how can postflight re-conditioning protocols make use of such novel findings ?	As suggested by animal studies, impaired vestibulosympathetic reflexes affect skeletal muscle structure (myofiber type pattern) as well as bone density with potential risk of injury in crew during spaceflight and thereafter. One pharmacological target could be administration of ß-adrenergic receptor agonists in microgravity to mimic sympathoadrenergic activation in spaceflight. More knowledge is needed to better understand such highly unique linking mechanisms (systems cross-talk) in the body	Section 3.6

Postural muscles	What is the condition of the postural muscles on return from LDMs?	Little is documented about the postural muscles postflight but preliminary evidence suggests the muscles that support the trunk are particularly vulnerable, similar to LBP patients. The postural hip and leg muscles (gluteus, adductors, soleus/gastroc, anterior tibialis) and others involved in gait control at 1G and not in use in µG (such as plantar foot short muscles) are also important to consider. Changes in these muscles on return to Earth are likely to influence many functional tasks, including those requiring spinal stability, which need addressing/accounting for during re-conditioning activities.	Section 3.1.2, 3.3 and 3.8.1.2
	What are the adaptation processes of the lumbopelvic muscles during inflight CM and postflight reconditioning?	Research on the adaptation processes of lumbopelvic muscles during microgravity and post-microgravity reconditioning has been limited to bed rest studies, but it is unknown how far these findings can be translated to astronauts. More crew-focused research is needed to help improve spine-specific inflight CM and postflight reconditioning strategies.	Section 3.1.2 and 3.8.1.2
Cartilage	What is the effect of LDM on human cartilage and what is the significance of these changes for the days/weeks after landing?	Little is known about the effects of LDM on human cartilage but ground-based analogue studies point to a loss of tissue thickness and possible sensitivity to re-loading, which could directly impact re-conditioning strategies.	Section 3.4 and 3.8.4
	What are the long-term effects on cartilage and implications for development of osteoarthritis (OA)?	CM in bed rest studies have not been able to compensate for the effects of immobilisation on cartilage metabolism. Effects of microgravity on cartilage could have implications for OA in later life in a similar way that overuse of joints in young athletes causes greater incidence and earlier onset of OA than in the general population. The occurrence of OA in astronauts is unknown.	

Bone Mineral Density	What is the short and long-term significance of postflight decreases in BMD that persist in some crew members despite the recent improvements in effectiveness of inflight CM?	The current inflight CM Programme results in some crew maintaining their BMD inflight, but some crewmembers continue to display decreases. Given the evidence of delayed recovery of BMD postflight, such changes may need specific management during re-conditioning activities for affected individuals. Long-term reduced BMD has implications for osteoporosis. Also see neurovestibular effects on BMD (Section 3.6)	Section 3.2 and 3.8.2
Spine	What is the condition of the spinal structures, including its shape, BMD and the intervertebral discs on return from LDMs?	Spinal elongation and changes to the IVDs occur during bed rest, and crewmembers' spines elongate during space-flight, potentially increasing risk of postflight IVD herniation. Little is known about inflight changes to the IVDs, particularly with the chronic use of ARED, and thus the condition of the spine at the onset of re-conditioning activities, although variable (between crewmembers and between spinal levels) water content changes have been observed with no change in disc height.	Section 3.3 and 3.8.3
Injury	Is µG exposure a factor in inflight exercise-related musculoskeletal injuries and are the residual effects of these injuries still evident on landing/during reconditioning?	Inflight exercise-related injuries are relatively rare, but they are the most frequent source of injuries in astronauts living aboard the ISS. Treadmill and/or resistive exercise equipment accounts for 85% (12 of 14) of reported musculoskeletal injuries.	Section 4.3.2.2

Orthostatic Intolerance	Do orthostatic symptoms continue to affect crewmembers in the days/weeks after landing, and what, if any, is the functional impact?	Although highly susceptible to orthostatic intolerance (OI) on landing day, most LDM crew recover sufficiently to pass the 10 minute tilt test after only one day of recovery, which suggests that OI symptoms are not an issue for the re-conditioning activities. However, qualitative research with astronauts and crew surgeons is needed to confirm this.	Section 3.5.1, 3.5.2 and 3.8.7
Sensorimotor Function	Do sensorimotor symptoms continue to affect crewmembers in the days after landing and what, if any, is the functional impact?	Recovery of function appears to take an average of 15 days to return to within 95% of preflight performance levels. A collaborative experiment between NASA and Russia is currently conducting sensorimotor Field Tests on astronauts and cosmonauts returning from ISS http://www.nasa.gov /mission_pages/station/research/experiments/1768.html Recovery in relation to activities of daily living beyond the early postflight period has yet to be determined and comments from astronauts suggest that qualitative studies would be useful in documenting challenges experienced in everyday activities.	Section 3.6 and 3.8.8
Functional Performance	What exercises are effective for restoring dynamic control of movement?	Reduction in Functional Task Test (FTT) performance is greater for tasks requiring high dynamic postural control than those requiring less postural stability	Section 3.8.6
	To what degree and for how long does a LDM affect crewmembers' ability to perform functional tasks in the days/weeks after landing?	Functional tasks requiring a greater demand for dynamic control of postural equilibrium (i.e. fall recovery, seat egress/obstacle avoidance during walking) show the greatest decrement in performance. Functional tests with reduced requirements for postural stability (i.e. hatch opening, manual manipulation of objects and tool use) show little reduction in performance.	Section 3.8.6 and 7.8

Aerobic Capacity	What is the functional impact of postflight decreases in aerobic capacity that persist in some crewmembers, particularly those who have low/moderate pre-flight values?	The present inflight CM programme results in some crew maintaining, or even increasing, their aerobic capacity inflight, but some crewmembers continue to display decreases. Such decrements are of little significance in those who display high values, but might have a functional impact on return to Earth that needs addressing/accounting for during re-conditioning activities.	Section 3.5 and 3.8.5
Psychological Status	How motivated are astronauts to continue with self-guided reconditioning once the supervised element is complete, and what effect does this have on adherence and efficacy?	Whilst for most astronauts the nominal 3-4 week supervised element of postflight reconditioning programme is sufficient to completely correct many of the residual effects of spaceflight, several partially remain (including reduced muscle volume/force production capacity, BMD and VO_{2max}). Such parameters are known to change more slowly, even with active reconditioning, so complete restoration of pre-flight status requires longer and self-guided reconditioning, and against a backdrop of competing demands from other postflight requirements, many of which require international travel.	

5.3 Knowledge gaps for future missions

The knowledge gaps for future missions fall into two categories:

5.3.1 Those that directly affect the delivery and effectiveness of post-mission reconditioning on Earth by re-conditioning specialists following longer missions in LEO (*e.g.* the recently initiated One Year missions) and LDEMs;

5.3.2 Those that are related to preparation for, and execution of, surface activities during LDEMs that include planetary surface (low gravity) excursions.

In the case of the latter:

a) Crewmembers may be required to undertake a reconditioning/preparation (preconditioning) programme prior to performing excursions, either in flight and/or on the surface. The gravity environment will be novel, e.g. 1/3 G on Mars, and the normal CM and reconditioning programmes are already oriented toward planetary surface excursions, e.g. on Earth, but the support from reconditioning specialists that occurs after return to Earth will be absent. It is highly likely that reconditioning specialists will be called upon to advise on the design and implementation of these preparatory programmes to ensure they are safe to conduct (*i.e.* minimise injury risk) and task specific, to both ensure safety and maximise productivity during subsequent excursions;

b) LDEM vehicles will be far smaller than ISS and likely contain only a single exercise CM device. As such, it might not be possible to maintain the current efficacy of the ISS inflight exercise CM programme during these missions;

c) In an attempt to conserve resources (*e.g.* oxygen, food) and minimize undesirable effects that could compromise the mission (*e.g.* production of moisture, heat and carbon dioxide, and excessive wear and tear to exercise devices), it is possible that mission planning will require crew to partially abstain (*e.g.* during the early stages) from exercise during transit, which would further impact on the efficacy of the CM programme. Given the known negative effects of microgravity on the body and the fact that current CM do not mitigate these entirely, such reduction in exercise would need to be introduced with caution after calculating the risks. For instance, sound evidence would be needed to indicate that negative effects of reduced exercise could be reversed through preconditioning CM in space, prior to vital tasks during planetary surface excursions, and would not cause irreversible impairment in the longer-term. These suggestions are speculative but nonetheless necessary to consider;

d) The effectiveness of an inflight exercise countermeasure programme is heavily reliant on an individual's compliance with its prescription, which itself, is strongly influenced by personal motivation. In a NASA report from 1986, astronauts indicated that exercise counteracted stressful aspects of the inflight period by maintaining morale and providing a source of enjoyment (Stuster 1986). The mental health benefits of exercise are well documented and, given the general level of crew satisfaction with inflight training programmes, adherence is likely to remain high during the ISS mission phase. There is only limited evidence from LDEM mission analogue studies on the effects of prolonged confinement/isolation on voluntary physical activity and motivational state (Belavý et al. 2013), but the high level of compliance with inflight exercise CM currently observed on ISS cannot be assumed during longer and more isolated missions, particularly where contact for support from ground will be less available. Monotony is a potential problem and staying motivated over a two year period with limited variety could be a challenge. The stress and different priorities of planetary exploration could also make adherence more tenuous. It is only possible to speculate on these issues at this stage, but evidence from terrestrial analogues suggests that adherence might suffer in these situations, and prevention strategies will be needed.

It is expected that the challenges to the human body and effects of microgravity will be greater after longer duration missions but the magnitude, duration and emphasis of effects on the different systems and specific parameters are difficult to anticipate.

Research questions aimed at addressing these gaps in knowledge about longer missions in LEO will need to be developed and tested. In particular, the effects on crewmembers during the days after landing and the functional impact of these effects will be important to know. Table 5.2 focuses on knowledge gaps specific to future missions that relate to factors other than greater mission duration, such as challenges from missions beyond LEO and those involving planetary surface excursions.

Table 5.2. Postflight re-conditioning Knowledge Gaps for crewmembers participating in future long-duration missions, primarily those outside Low Earth Orbit and those involving planetary surface excursions.

Parameter	Knowledge Gap(s)	Report Section Reference
Musculoskeletal System		
Major Muscle Groups	Will losses in muscle volume/force production during transit impair planetary surface excursions? What magnitude of effect can be considered acceptable, in terms of impacting on functional performance of tasks and safety?	Section 3.1 and 3.8.1
	Will the postflight decreases in muscle volume/force production that persist in some crewmembers following LDM be exacerbated (*i.e.* suffered by all crewmembers and/or suffered more profoundly by some), if the inflight exercise CM programme is less effective?*	Section 3.7 and App B
Functional Performance	To what degree and for how long will crew members' ability to perform functional tasks in the days/weeks after return to Earth be affected if the inflight exercise CM programme is less effective?*	Section 3.8.6 and 3.7
	How will crewmembers' ability to perform functional tasks during planetary surface exploration be affected?	Section 3.8.6
Postural muscles	Will potential decrements in postural muscle volume/function impair planetary surface excursions?	Section 3.1.2 and 3.8.1.2
Cartilage	What will be the magnitude of changes in human cartilage with µG exposure during the reloading that will occur during preconditioning for planetary surface excursions, and with re-loading during excursions themselves?	Section 3.4 and 3.8.4
		Section 3.1.2, 3.3 and 3.8.3

Spine	What will the condition of the spinal structures be on return to Earth following LDEMs?	
	What will be the significance of the condition of the spinal structures during the reloading that will occur during preconditioning for planetary surface excursions, and with re-loading during excursions themselves?	
Injury	Will there be an increased risk of musculoskeletal injury on return to Earth if the inflight exercise CM programme is less effective?*	Section 4.3.1.1
	Will prolonged microgravity during LDEM transit increase the risk of musculoskeletal injury during preconditioning for planetary surface excursions, and with re-loading during excursions themselves?	
Preparation for planetary surface excursions	What inflight preconditioning exercise programmes will be effective for preparing astronauts to perform functional tasks safely and efficiently during surface excursions?	Section 6.3.2 and 4.3.1.4
	Quantification required of the physical demands of planetary surface excursions.	
Contingency exercise programmes for equipment failure	What exercise programmes / low specification technologies could be used in the event of equipment failure	Section 6.3 and 4.3.1.4, Table 6.1
Orthostatic Intolerance	How much worse will OI symptoms be on return to Earth if the inflight exercise countermeasure programme is less effective?*	Section 3.8.7 and 3.5.2
	Will OI symptoms be significant when conducting planetary surface excursions?	
Sensorimotor Function	To what extent will sensorimotor symptoms affect crew members in the days after landing on Earth if the inflight exercise countermeasure programme is less effective*, and what, if any, will be the functional impact?	Section 3.6 and 3.8.8
	Will sensorimotor symptoms associated with µG exposure impair planetary surface excursions?	
Aerobic Capacity	How much worse will losses in aerobic capacity be on return to Earth if the inflight exercise CM programme is less effective?*	Section 3.5 and 3.8.5

	Will losses in aerobic capacity associated with µG exposure impair planetary surface excursions?	
Bone Mineral Density	Will the postflight decreases in BMD that persist in some crewmembers following LDM be exacerbated (*i.e.* suffered by all crewmembers and/or suffered more profoundly by some) if the inflight exercise CM programme is less effective?*	Section 3.2 and 3.8.2
	Will losses in BMD associated with µG exposure be operationally significant during preconditioning for planetary surface excursions, and with re-loading during excursions themselves?	
Psychological Factors	How will prolonged confinement and isolation affect inflight mood state, motivation to exercise and adherence to inflight exercise countermeasures and preconditioning for planetary surface excursions?	Section 4.3.1.2

* if inflight exercise CM programme is less effective due to (in isolation or in combination) a planned reduction in exercise volume, a reduction in device effectiveness, hardware failure, reduced exercise adherence.

5.4 Summary

Several questions have been posed in this chapter to address unknown factors that could influence the outcome of postflight reconditioning and preconditioning during LDEMs prior to planetary surface excursions.

The following two chapters propose ways of filling these knowledge gaps identified. The first (Chapter 6) concerns research opportunities for astronauts and microgravity analogues. Chapter 7 then proposes how parallels with terrestrial situations, including clinical conditions and challenging environments, could be exploited by implementing strategies from current evidence based exercise programmes and adopting similar designs used in relevant terrestrial rehabilitation research.

CHAPTER 6:
FILLING THE KNOWLEDGE GAPS – RECONDITIONING RESEARCH IN ASTRONAUTS AND MICROGRAVITY ANALOGUES

6.1 Introduction

This chapter proposes solutions for filling the knowledge gaps identified in the previous chapter, focussing on reversing neuro-musculoskeletal deficits and improving performance using physical and psychological strategies. The chapter also covers factors that may impact on the effectiveness of reconditioning, and therefore must be considered for future research, as well as practical and operational situations. Specifically, it is important to consider that inflight CM on long duration missions may be less effective due to possible planned reduction in exercise volume, reduced effectiveness or failure of exercise equipment (compared with that currently available on ISS), and reduced exercise adherence (Chapter 5, Table 5.2), and these factors may impact postflight reconditioning.

6.2. Research to address knowledge gaps

6.2.1. Musculoskeletal system

6.2.1.1. Major muscle groups

Studies of optimal exercise protocols (Section 6.3.1) for increasing muscle strength and endurance would determine the most efficient methods for regaining muscle function as soon as possible postflight. In relation to preparation for surface planetary exploration, we need to understand the dose-response to inflight exercise CM to inform preconditioning programmes, e.g. what is the threshold (minimum effort) required to stimulate muscle development (not just maintain it) in microgravity?

A novel non-invasive digital palpation device (MyotonPRO), for the measurement of biomechanical properties (stiffness, tension, elasticity) in disused human skeletal muscle, (MYOTON in ESA´s RSL Study at DLR: envihab, 2015-2016, PI Blottner) has been successfully used in parabolic flight (Schneider et al. 2015) and, more recently, in LDBR to monitor the overall muscle status and training efficacy in several major muscle groups (including postural muscles) following reactive jumping as a CM (Blottner D et al., manuscript in preparation). Myometric measurements on human subjects with MyotonPRO are planned to be performed on ISS (D. Blottner, PI Myotones, ILSRA-2014-0015). In addition to existing inflight monitoring systems (i.e., cardiovascular, sympathetic, neuromotor behaviour), the outcome of individual myometric monitoring of the muscle status during all mission phases will potentially be very helpful to assess the overall neuromuscular status; it may be even more important to monitor during re-loading within 24 h post-landing.

6.2.1.2 Postural muscles

The postural muscles of the trunk that protect the lumbar spine appear to be particularly vulnerable and further research is needed to confirm preliminary evidence (Hides et al. 2016a). Studies of strategies used in terrestrial rehabilitation of LBP patients could be conducted on astronauts, e.g. use of rehabilitative ultrasound imaging to provide feedback of optimal muscle contraction to treat muscle imbalance (Section 7.3), screening of movement control (Section 7.8) and motor control exercises (Section 7.3.2). The ESA reconditioning programme already incorporates ultrasound imaging and motor control retraining (Section 4.2.2), but the effectiveness needs to be evaluated. Ultrasound imaging has only been used to monitor the effects of the programme on trunk muscles in one astronaut (Hides et al. 2016a). An example of novel, innovative apparatus that may augment reconditioning is the Functional Readaptive Exercise Device (FRED), which targets the lumbopelvic muscles (Caplan et al. 2015; Winnard et al. 2016 in Appendix D).

6.2.1.3 Postflight reloading for health of cartilage and bone

Studies are needed to determine safety guidelines to minimise risk of injury to cartilage and bones, whilst ensuring adequate loading to stimulate tissue recovery.

a) Re-loading protocols for minimizing damage to cartilage
Since the effect of microgravity on articular cartilage is unknown (Section 3.8.4) postflight reconditioning might best be guided by what is known about excessive loading and cartilage damage, and risk of osteoarthritis (Maly 2008). A priority for postflight research is to investigate the status of cartilage, to address the problem if it exists.

b) Re-loading protocols for bones
It is currently unknown which factors predispose astronauts to incomplete recovery of bone loss (Section 3.2). Lack of mechanical loading or endocrine alterations may play a role. Establishing such factors would fill an important research gap. Research is needed to systematically monitor the time course of recovery of bone loss and to understand the inter-individual variability of loss during unloading and gain during reloading. For the time being,astronauts and participants from bed rest studies are probably well-advised to attempt resumption of the original habitual loading patterns as fast as reasonably possible, until evidence is provided to guide a more specific reloading strategy. Notably, the cervical spine disc prolapse described by the astronaut in Chapter 4 (Case history 1) appears to have been caused by a premature return to running (3 days postflight), so caution is needed. Studies using the anti-gravity treadmill[6] may help establish guidelines for safe return to more strenuous load-bearing activities during postflight reconditioning.

6.2.1.4 Longer-term effects of spaceflight on bone and joint health

a) Osteoporosis
Bone losses incurred during spaceflight and bed rest (Section 3.2) generally appear to recover after return to Earth and after re-ambulation, respectively (Lang, Leblanc 2006; Rittweger & Felsenberg 2009). However, recovery may not be complete in all individuals (personal communications by D Felsenberg and by L Vico to Jörn Rittweger). The long-term effects of spaceflight on bone in astronauts is unknown and warrants studies to monitor bone mineral density, both to map the time course of recovery in the first few months postflight, as well as periodically throughout the life of the astronaut, although the latter may be contentious, as DEXA involves radiation.

b) Osteoarthritis (OA)
The incidence of OA in astronauts is unknown but NASA's Lifetime Surveillance of Astronaut Health (LSAH) database provides the opportunity to compare astronauts of different ages with matched groups in the general population.

6.2.1.5 The spine

The condition of spinal structures was recently reported on by the ESA Intervertebral Disc Herniations in Astronauts Topical Team (Belavy et al. 2016). Their report was based on bed rest studies and an increased risk of postflight IVD injury, so the priority is to learn more about the effects of LDMs on spinal structures to enable their impact on postflight reconditioning to be understood.

6 Treadmill with air-tight positive pressure system surrounding the lower body, decreasing foot impact on running/walking.

6.2.1.6 Musculoskeletal injury

Accurate reporting of exercise-related injuries during spaceflight and their persistence postflight is needed to determine the prevalence of such events and any association with mission duration and activities. This would help to develop strategies to manage injuries during postflight reconditioning. Safe exercise is vital to minimise injury risk, as relatively minor injuries could cause life threatening situations postflight and during planetary surface excursions. Exercise concepts that involve potential risk of injury, such as those with high loads and/or high loading rates, need to be evaluated carefully before being implemented as inflight CM for astronauts. The problem of confidentiality could be overcome by anonymised reporting (Table 6.1).

6.2.2 Orthostatic intolerance

Studies of efficient and accurate ways of monitoring orthostatic intolerance (OI), both inflight to prepare for planetary surface excursions, and during the postflight period will help determine the effect of OI on the effectiveness and risks of preconditioning and reconditioning, to inform exercise programmesInflight testing requires the development of technologies for sensors that would provide feedback to crew and ground medical operations staff, to tailor the exercise programme. An interactive system would be needed for use without direct input from reconditioning specialists on the ground. . Knowledge is also needed concerning the likelihood of OI in lunar and Martian gravity following a prolonged period in microgravity, although operationally OI is likely to have minimal impact and not warrant high priority for research.

6.2.3 Sensorimotor function

As with OI, studies to monitor sensorimotor function during the postflight period will help inform reconditioning. Knowledge of sensorimotor function in lunar and Martian gravity is also needed. Tests suitable for inflight monitoring need to be developed to inform exercise programmes for preconditioning to prepare astronauts for planetary surface excursions. Tests could also be developed for planetary post-landing assessment of performance prior to an EVA, e.g. simple tests of postural stability could be performed after landing in a gravitational environment to provide a go/no decision for EVA.

6.2.4 Functional performance

The Functional Task Test (FTT) battery being developed for astronauts described in Chapter 3 (Section 3.8.6) requires further development to include activities of daily living relevant to the postflight period. This, together with the more aerobic Functional Fitness Test (FFT), would help determine the extent and duration of effects of spaceflight on ability to perform functional tasks and thereby inform the design of reconditioning programmes relevant to the astronaut’s life on Earth. The FTT will enable assessment of performance risks and inform the design of CM for exploration class missions. Other forms of movement screening and exercise programmes to improve quality of movement (control) used in terrestrial populations (Section 7.4) may also be useful to incorporate into the preparation (preconditioning) and reconditioning of astronauts.

6.2.5 Aerobic capacity

The exact exercise prescription for the maintenance or improvement of aerobic fitness in weightlessness is still under investigation. Work is underway to ascertain the correct elements of such a programme and a systematic and statistically appropriate programme of work is required to elucidate the nature of the issue. Some analysis of the field is being pursued by the International Association for the Advancement Study Group of Space Safety (IAASS) Multilateral Exercise Countermeasures Working Group (personal communication J Scott, Wyle GmbH). The findings of this work will inform and aid the development of postflight reconditioning programmes. Based on recent ISS data, aerobic capacity is maintained well in crewmembers and is not a high priority for reconditioning research.

6.2.6 Psychological Factors

Adherence and motivation strategies to help astronauts maintain physical activity levels beyond the supervised phase of postflight reconditioning need to be investigated. Psychological factors will become more important for long-duration missions, both for mitigating the effects of long periods in microgravity and for inflight preparation (preconditioning) for planetary surface excursions (Table 5.2). Recommendations have been made by Kanas et al (2009) for preparing to deal with psychological factors during long periods of isolation in future missions but these do not make specific reference to inflight or postflight exercise. It is unknown whether the benefits of exercise reported for reducing stress and maintaining morale during pre-ISS missions (Stuster, 1986) will translate to long duration missions of 1-2 years. Psychological research in the astronaut population has not focussed on health behaviours, which is necessary to achieve good adherence and self-motivation but extensive terrestrial research provides a basis for developing these aspects of space research and promoting good practice (Section 7.8).

6.3 Considerations for research unique to postflight reconditioning

When reviewing the knowledge gaps and identifying strategies to address them (and subsequently producing recommendations), it is important to consider factors that are unique to postflight reconditioning and how these may influence the effectiveness of reconditioning. Several key factors are outlined below in Table 6.1, with some areas explored in further detail in subsequent sections.

Table 6.1. Considerations for research into postflight exercise re-conditioning

Consideration	Rationale
Programme Focus	Unlike terrestrial rehabilitation which may focus on one or a small number of systems (*e.g.* aerobic capacity) or specific parts of that system (*e.g.* the knee after injury), postflight exercise re-conditioning must aim to correct changes in many different systems simultaneously and thus must be designed accordingly.
Accurate reporting of symptoms and injuries	Problems can only be addressed effectively if the medical operations team are alerted to them. As in elite sport, where athletes may withhold the presence of injuries and symptoms so as not to threaten their selection for the next competitive event, openness in reporting by astronauts is inhibited by the concern of not being deemed medically certified for the next flight (Harrison 2005). Anonymised reporting of postflight conditions using mixed methods research in active astronauts would provide a more complete picture of postflight problems. Effective management of individuals pre- and postflight requires the astronaut to be open with medical operations, so research to enhance the therapeutic alliance and operations procedures would be beneficial. Accurate reporting impacts on all the knowledge gaps identified in Tables 5.1 and 5.2, to establish the presence and effects of various factors on postflight status of musculoskeletal structures and function, and planetary surface task performance.
Research Questions	Research questions driven by astronauts and operations teams (physiotherapists/Exercise Specialists/Flight Surgeons) are important (Section 4.1). Their involvement at all stages of research is equivalent to PPI in terrestrial research (section 8.2.6) and needs to begin when developing research questions, to ensure research is relevant to the needs of astronauts and that the studies are feasible.

Programme Design

Postflight constraints

Supervised postflight exercise reconditioning must take place within a relatively narrow timeframe (approximately 21-28 days; Section 4.2) and crewmembers typically have other commitments during this early postflight period including: standard operational postflight medical testing, testing for human physiology science experiments, and media commitments for both their Space Agency and home nation, as well as vacations. The optimal reconditioning period is unknown and research would reveal whether this should be extended.

Optimal programmes

Optimal postflight reconditioning programmes are needed to maximise function in the most efficient and effective way (Section 6.3.1).

Links between phases of astronaut cycle

Effective postflight reconditioning cannot be achieved in isolation. Preflight preparation and inflight CM will impact its success. As well as preflight strength and conditioning status affecting subsequent phases, movement quality preflight may affect inflight and postflight functional performance and injury risk, as poor movement patterns can involve abnormal loading on joints and cause damage (repeated microtrauma, possibly leading to osteoarthritis), as in sports (Section 7.4). Close links between the three phases not only applies to research but also to management of the astronaut. Preferably, the same team would follow individual astronauts throughout the cycle, as in the ESA Programme (Section 4.2.2).

Surface activities during Long Duration Exploration Missions

Human surface exploration is not new, with experience gained from the Apollo programme. What will be new with LDEMs is the need to undertake activities following prolonged periods in microgravity in novel (e.g. Martian) low gravity environments. Preparation for such activities will be vital (see Section 6.3.2).

Contingency exercises for equipment failure

In the event of failure of exercise equipment, backup exercise programmes are required to preserve cardiovascular and musculoskeletal function. Programmes using simple, low mass and volume devices are needed, e.g. use of high resistance therabands as a replacement for a resistance training device. Motor imagery to improve strength and motor skills (Section 6.3.1) could potentially play a role in the absence of equipment. Electrical stimulation of muscles is another option but the efficacy of use in astronauts would need to be investigated (Sections 7.5 and 7.6.4).

Research Opportunities

Existing evidence across Agencies

Multi-agency collaboration to map current reconditioning practices would enable the best available evidence to be implemented and inform research to improve practice. Delphi studies of medical operations specialists would capture practices and future study designs could involve experts in different areas of terrestrial rehabilitation (musculoskeletal, sports, neurorehabilitation etc.). A Delphi study involves asking specific questions to panels of experts to reach consensus statements or recommendations (Section 8.2.6).

With astronauts

Opportunities for postflight exercise re-conditioning research are limited by the small number of astronauts and the low frequency with which they return from missions (due to standard LDMs being of 6-months duration). This issue may, in part, be addressed by collaborative investigations with the other ISS Partners, which would require overcoming specific challenges relating to between-Agency coordination to deliver standardised protocols.

With microgravity analogues

Long-duration best rest (LDBR) is currently considered the ‘Gold Standard’ ground-based analogue for prolonged exposure to microgravity for musculoskeletal issues. As such, it offers an opportunity to conduct exercise reconditioning research (Section 6.3.3); however, to date, this is an opportunity that has not been exploited fully.

6.3.1 Optimal reconditioning programmes

The effectiveness of exercise programmes to restore muscle and functional performance is multifactorial. The ISS Countermeasure Working Group (CMWG) is an international group of ISS partners, which forms part of the Multilateral Medical Operations Panel (MMOP). It' constituent specialists discuss pre-, in- and postflight exercise matters. It will be important to engage this group in considering future research about optimal reconditioning programmes. Addressing all factors for all scenarios in a single research project would require too complex a design to be feasible. The desired effects of exercise vary, e.g. strength, power, local muscular endurance, cardiovascular fitness, motor control for quality of movement, vestibular function, performance of specific tasks etc., so will require different approaches. Development of optimal reconditioning programmes requires studies to determine the various components:

- Dose (frequency and intensity or load)
- Duration (within sessions and length of reconditioning period)
- Recovery - rest periods within and between sessions to minimise muscle damage and fatigue
- Timing of intervention – prior to planetary excursions and during postflight period
- Tailored to account for inter-individual variability

Strategies to maximise effectiveness and minimise exercise time warrant investigation, for both inflight and postflight programmes. For example, motor imagery of muscle contractions and functional tasks can, without the person moving, improve strength (Ranganathan et al. 2004) and motor skills (Nyberg et al. 2006), and can select the type of contraction (Guillot et al. 2007).

6.3.2 Surface activities during Long Duration Exploration Missions (LDEMs)

6.3.2.1 Preparation for surface activities in microgravity: on-board 'preconditioning'

The requirement to undertake surface exploration activities following prolonged periods in microgravity means that the performance effects on crew must be taken into account in the planning phase. Recent data from ISS suggests that with current knowledge and access to a range of complex exercise CM devices, some crewmembers are able to largely resist the characteristic changes to musculoskeletal and cardiovascular systems. However, in relation to surface exploration activities during LDEMs, several important factors must be considered:

a) The individual response to microgravity and inflight exercise CM is highly variable, and despite progress, some crewmembers still experience marked losses in muscle volume/strength, BMD and VO_{2max} (Chapter 3). Even larger changes can be expected following long transits in microgravity;
b) The effectiveness of the ISS exercise CM programme relies on a range of large, highly complex devices that must be used on a regular basis to achieve CM efficacy (see Section 3.7). However, the vehicles for LDEMs will be much smaller than ISS and likely contain only a single, far simpler (for more reliability and lower maintenance needs) exercise CM device. Although further advancements in CM technologies – exercise and otherwise – will be made prior to the commencement of LDEMs, it is possible that, within the constraints of a LDEM vehicle, the current efficacy cannot be maintained or improved;
c) Due to the constrains of an LDEM vehicle, attempts to conserve resources (*e.g.* oxygen, food) and minimize undesirable effects that could compromise the mission (*e.g.* production of moisture, heat and carbon dioxide, and excessive wear and tear to exercise devices), mission planning may require crew to abstain, either partially or completely, from exercise during the early part of a transit, increasing the volume only shortly before surface exploration and landing on Earth. This scenario is only hypothetical but needs to be considered.

Alone or in combination, these factors may result in some or even all crew experiencing marked physiological deconditioning when arriving in orbit around the body to be explored. Crew may therefore be required to undertake a reconditioning (or preconditioning) programme prior to landing and commencing planetary surface excursions. This preparation is analogous to the prehabilitation programmes used in sport to optimise performance and minimise injury risk (see Section 7.4.2) and research will be needed to develop appropriate programmes for astronauts. As ESA's current postflight reconditioning programme is instructor-led, requires a number of intensive face-to-face sessions, and is conducted in Earth's gravity, the need for on-board preconditioning presents a range of novel challenges that must be resolved. It is likely that current reconditioning specialists will be called upon to advise on the design and implementation of these programmes to ensure crew safety on return to Earth, and both ensure safety and maximise productivity during surface activities.

6.3.2.2 Performance in low (Lunar and Martian) gravity environments

Surface explorations during the Apollo programme demonstrated that humans can operate effectively in Lunar (0.16 G) gravity, with no crew reporting disorientation or vestibular illusions (Homick 1975). Based on these reports, it was concluded that lunar gravity is sufficient for the otolith organs to sense gravity and to distinguish up from down. This conclusion is supported by data from a recent centrifuge study, which found that 0.15 G is the critical acceleration threshold where perceived upright and the 'real' upright coincide (Harris et al. 2014). Future LDEMs that visit Moon or Mars (0.38 G), will likely require greater duration surface explorations than the Apollo programme (three days during Apollo 17), and will thus impose novel physiological and biomechanical demands.

Virtually nothing is known about the physiological effects of prolonged exposure to reduced (< 1G) gravity. Terrestrial models of reduced gravity includes parabolic flights, supine centrifugation, vertical body weight support systems (e.g. lower-body positive pressure 'anti-gravity' treadmills), tilt tables, supine suspension systems with sagittal loading and exoskeleton devices. Whilst all these models are sufficient to reduce the gravitational force acting on the centre of mass, none are capable of, or practical in, mimicking the physiological effects of prolonged reduced gravity exposure. However, short-term studies using these models suggest that Lunar and Martian gravity will significantly alter gait kinematics, muscle activation and muscle coordination patterns during locomotion (Ivanenko et al. 2002). These are likely to translate to changes (reductions) in loading on bones and muscles which, as suggested by animal studies, might be insufficient to maintain BMD and muscle mass (Swift et al. 2013). This prognosis is reinforced by a theoretical model assuming that bone follows a similar adaptation pattern to < G as it does to increased loading, and predicts a weekly bone loss of 0.39% in lunar gravity (Keller 1988).

As demonstrated by studies of astronauts and bed rest subjects, complete gravitational unloading eliminates the demands on the cardiovascular system to support and transport the weight of the body, and results in a marked decrease in aerobic capacity (Section 3.5). In contrast to microgravity, however, crew will experience bodyweight and ground reaction forces during surface explorations, and the latter will likely increase as a result of the EVA suits and portable life support systems necessary to conduct activities. In addition, the cardiovascular system will adapt favourably to long periods of relatively low intensity aerobic exercise. However, whether the loading and associated cardiorespiratory demand during surface activities will be sufficient to maintain aerobic capacity within acceptable limits is unknown. Studies with anti-gravity treadmills suggest that cardiorespiratory demand decreases with reductions in effective body weight, although this decrease is non-linear, with the change in oxygen consumption becoming significantly smaller as bodyweight support increases from 0 to 40% (McNeill et al. 2015). Whilst this might suggest that locomotion in low (0.38 or 0.16 G) gravity could still demand reasonable respiratory effect, particularly with EVA suits and portable life support systems, this assumes the maintenance of normal terrestrial locomotion. As demonstrated during the Apollo programme, however, where astronauts adopted a two-footed skipping technique to optimise O2 use/CO2 production (Kuehnegger et al. 1966), normal locomotion might not be the preferred method of surface movement in reduced gravity (Minetti 1998).

Should future investigations suggest that the forces acting on the human body during normal locomotion in partial gravity will most likely be insufficient to maintain musculoskeletal and cardiovascular function within acceptable limits, exercise CM will also be required during prolonged periods of surface activity. When and how intensively such CM need to be undertaken will depend on a number of factors, including the extent of adaption during transit out, the length of stay on the surface and the nature of operations whilst there.

6.3.3 Reconditioning after bed rest studies

Best rest studies are an under-exploited opportunity to develop effective reconditioning programmes after deconditioning. The focus of LDBR is on the effects of bed rest itself and only very infrequently (*e.g.* Hides et al., 2011) have they been used to study reconditioning after bed rest. An advantage of bed rest studies is that they typically contain a Control Group that does not participate in any intervention and thus experiences marked deconditioning. However, control-only groups in bed rest studies have already generated a knowledge base and the ethical justification for control groups in future studies needs to be considered. Active control groups to compare interventions would be justified.

There are important considerations for exploiting the reconditioning research opportunity post-LDBR:

a) *The ethical requirement to perform post-bed rest reconditioning* – this is not universal across different nations:

b) *Participant numbers* – typically not large to start with (less than 20) and will reduce further if the control group is divided into two for comparative studies. Alternatively, if all subjects are used, the intervention group and control group will likely differ markedly in their physical condition at the end of bed rest;

c) *Participant availability* – after spending a long period of time at a bed rest facility, if not required for ethical reasons, participants may not be willing to prolong their stay to take part in supervised re-conditioning research. If unsupervised re-conditioning research is planned, participants may disperse widely throughout a country (or even several countries) following bed rest, which creates its own specific challenges for experimental teams.

d) *The study investigating the reconditioning process should not interfere with the research question of the bed rest study.*

e) *A bed rest study design that allows post-bed rest reconditioning research to be conducted would be optimal*

A strategy could be implemented across Space Agencies to enter participants into large multinational randomised controlled trial (RCTs) of reconditioning, using standardised protocols, once the bed rest component of the study is completed. This approach would be an efficient use of resources already being invested in the bed rest phase. Exclusions to entering a reconditioning trial immediately post-bed rest would be studies that aim to monitor lasting effects of interventions administered during bed rest but reconditioning research could still be built into such studies at a later stage of recovery.

6.4 Conclusions

Ways to fill knowledge gaps through astronaut and analogue studies have been proposed in relation to each of the areas identified in Chapter 5 and recommendations are listed in Chapter 10. Considerations specific to postflight reconditioning research have also been outlined and the design of such studies are considered further in Chapter 8. Parallels drawn with terrestrial research, where these may be beneficial for postflight reconditioning research and practice, are expanded upon in the next chapter.

CHAPTER 7
FILLING THE KNOWLEDGE GAPS – LESSONS FROM PARALLELS WITH TERRESTRIAL REHABILITATION AND CHALLENGING ENVIRONMENTS

7.1 Introduction and Relevance

This chapter considers how the identified knowledge gaps in post-mission reconditioning (Chapter 5) could be partially filled using evidence from terrestrial research. Translation of practices from terrestrial rehabilitation, which are not possible to investigate in astronauts, may provide valuable lessons for postflight reconditioning (Section 4.2). Similarly, drawing on knowledge from research where the reconditioning needs are similar to those of astronauts could inform the designing of robust studies.

Whilst microgravity induces well-documented changes in the neuromuscular system (Chapter 3), interesting parallels can be seen with various populations on Earth. Examples include responses to exposure in elite sports (increased activity and muscle imbalances), prolonged bed rest (decreased activity) and clinical conditions involving deconditioning, such as muscle atrophy following immobilisation or low back pain (LBP) and neurological disorders. Other aspects associated with sport that could inform postflight reconditioning include preconditioning exercise programmes to prevent musculoskeletal injury and promote for example, neuromuscular responsiveness (motor unit recruitment) and joint health, and psychological strategies to enhance motivation and adherence.

Some terrestrial environments pose specific challenges to conducting research, e.g. on the sports field and in intensive care units, where the conditions are difficult to control and numbers of participants are relatively small. Parallels between changes seen in astronauts and terrestrial populations also allow researchers to pose questions and conduct experiments involving astronauts which can inform and underpin applications that can benefit all of these populations. The benefits of exchanging knowledge and expertise between the two environments are therefore reciprocal. Key aspects of terrestrial scenarios are discussed briefly (Hides et al 2016b in Appendix D).

7.2 Parallels with low back pain (LBP)

7.2.1 Trunk muscle function and impairments in people with LBP

As mentioned in Section 3.1.2, the pattern of atrophy of the lumbopelvic muscles in astronauts is similar to that in patients with LBP and therefore these patients represent an appropriate population to learn lessons from. In addition to testing changes in muscles, such as atrophy using imaging techniques (ultrasound or MRI), control of muscles can be examined using neurophysiological techniques, such as electromyography to record electrical activity and transcranial magnetic stimulation to test cortical representation of spinal muscles in the brain. Low back pain (LBP) is known to have wide-ranging effects on the neuromuscular system. In acute LBP, muscles such as the lumbar multifidus can decrease rapidly in size (Hides et al. 1994). In contrast, other trunk muscles may increase their activity (Geisser et al. 2005; Radebold et al. 2000) , which may represent a strategy of the neural control system to stiffen the spine. Interestingly, the cortical representation of spinal muscles like the multifidus muscle is discretely organised (Tsao et al. 2011). This, as well as the muscle's segmental innervation, may explain the ability of the multifidus muscle to provide precise control of the segmental spinal segments, which allows control of the position of the lumbar lordosis. The representation on the cortex has been shown to be altered in people with chronic LBP, where the cortex is "smudged" (Tsao et al. 2011). It is possible that exposure to microgravity could also influence sensory feedback from the muscle system to the brain and result in changes in the neuromuscular system which parallels those seen in people with LBP. It is important to understand these changes, as these factors are modifiable and could inform the development of interventions. Future research could investigate whether cortical representation is altered following exposure to microgravity. Strategies to improve processing of sensory information (such as training two point discrimination of the trunk) in people with chronic LBP could be trialled and assessed on astronauts postflight. Transcranial magnetic stimulation could be used to see if "smudging" of the cortex occurs in astronauts, and if it does, if "de-smudging" is possible in this population through reconditioning.

7.2.2 Motor control retraining in rehabilitation of people with LBP

Despite high levels of fitness, elite athletes are not immune to LBP. For example, elite cricketers with LBP showed alterations of trunk muscle size and function when compared with asymptomatic cricketers (Hides et al. 2008). Motor control training (MCT) is a broad term which can include consideration of all sensory and motor aspects of spinal motor function. A MCT programme demonstrated effectiveness at decreasing LBP and restoring trunk muscle size and function after prolonged bed rest (Hides et al. 2012). As outlined in Section 3.3, and in an ESA TT report on inflight CM for LBP (Snijders & Richardson 2005), LBP is an important consideration in the reconditioning of astronauts postflight and MCT is a vital part of early ESA postflight reconditioning (Section 4.4.2) but research is needed to provide evidence of the effectiveness of MCT in astronauts.

7.3 Muscle imbalances in elite athletes

Muscle imbalance is not just about symmetry between the two sides of the body but about imbalances between muscles within the same movement segment of the body, e.g. agonists and antagonists, flexors and extensors etc. Also, undertaking apparently symmetrical exercises using ARED does not guarantee symmetrical muscle activation or movement patterns. In certain sports, the principles of training and skills required to perform the sports can lead to development of muscle imbalances. For example in sports which are flexor dominant in nature, the size of extensor muscles can decrease (Hides & Stanton 2012). Within a group of muscles, such as the anterolateral abdominal muscles, the effects may vary between muscles that have different roles and are controlled independently by the neural system. A major torque producing muscle, such as the internal oblique muscle, may increase over a football playing season, whereas the deep transversus abdominis muscle may decrease in size over the same period of time (Hides, Stanton 2012). In line with different activities, muscles may change function between sides of the body in response to functional demand. In summary, muscle imbalances can occur between muscle groups, within muscle groups and between sides of the body. It is important to consider rehabilitation strategies for muscle imbalances, as they can be related to injuries. Such imbalances need to be examined in astronauts and managed with exercise programmes.

Rehabilitation of muscle imbalances using a motor control training programme has been shown to decrease injury rates in footballers, and was associated with increases in the size of lumbopelvic muscles and improved ability to draw in the abdominal wall (Hides et al. 2012; Mendis & Hides 2016). Because stability and protection of the lumbopelvic region involves dynamic trunk control to allow production, transfer, and control of forces and motion to the distal segments of the kinetic chain (Kibler et al. 2006), good control of the lumbopelvic area is likely to be required to meet the high demands imposed on the body in sports such as football.

7.4. Movement control strategies for functional performance and joint health

Controlled movement is not only important for optimal performance of functional tasks but also for healthy loading on joints (e.g. good alignment and distribution of load (within and between joints in the kinetic chain). The specific effects of microgravity on functional performance were highlighted in Section 3.8.6, with tasks requiring more dynamic postural control being more negatively affected than those requiring less postural stability. Ways of assessing movement control and functional performance, as well as exercise strategies for improving them, are gaining attention in terrestrial and space research, but optimal tools and exercise programmes have yet to be established.

It is recognised that despite high levels of athletic performance, poor movement patterns may increase the risk of injury (Teyhen et al. 2014), e.g. control of the response of the trunk muscles to trunk perturbation is predictive of lower limb injuries in athletes (Zazulak et al. 2007). Assessment of injury risk using movement screening tools is translating from elite sport to amateur sport and occupational groups, including military personnel (Teyhen et al. 2014), fire fighters (McGill et al. 2013) and astronauts (Bloomberg et al. 2015a). Injury does not just refer to acute trauma but also to repeated microtrauma, e.g. abnormal loading of joints through poor alignment can lead to osteoarthritis and can be reduced by motor control exercises to correct movement patterns (Bennell et al. 2012). Exercise programmes using motor control exercises to improve movement quality are used in sport to optimise performance and prevent injury (prehabilitaiton or preactivation) but research is in the early stages (see below).

7.4.1 Movement quality (control) and functional performance screening

Movement screening comprises two types of tests: physical performance tests, which assess function, e.g. Triple Single Leg Hop, Star Excursion Balance Test (Hegedus et al. 2014; Hegedus et al. 2015), and movement control tests, which assess quality of movement. Movement quality tests involve identifying and rating functional compensations, asymmetries, impairments or efficiency of movement control through transitional (e.g. single knee bend, squat, lunge) or dynamic (hopping, walking, landing) movements tasks. Several movement control screening tools exist, e.g. the functional movement screen or FMS (Frohm et al. 2012; Kiesel et al. 2007) and the Performance Matrix (Mottram & Comerford 2008). However, consensus is needed to harmonise terminology and definitions used for both types of tools (Hegedus, McDonough 2014; Hegedus, McDonough 2015; Teyhen, Bergeron 2014). Evidence of the robustness of tools (reliability, validity) is emerging but further research is needed to determine which tool is most appropriate for a given situation. An International Movement Screening Group led by the Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis is co-ordinating efforts by movement screening researchers across the globe to reach consensus and share protocols to advance the field in research and clinical practice (http://tinyurl.com/IntMovScrGrp). The ESA Physiotherapist (Lambrecht) recently joined the group.

An example of how a simple observational screening test of movement quality can be used to correct poor movement control is the small single knee bend test (Botha et al. 2014). Poor alignment of the knee is illustrated (left picture in Figure 7.1), which causes higher loading and microtrauma on the medial (inside) aspect of the knee and there is evidence that this results in greater loss of articular cartilage in the medial compartment of the knee joint (Bennell et al. 2011). The findings of this test would then be used to inform the exercises needed to retrain the muscles and improve movement control and alignment of joints (motor control retraining), as in the right hand picture. It is not just about ability to perform a task but the quality with which the task is carried out as well.

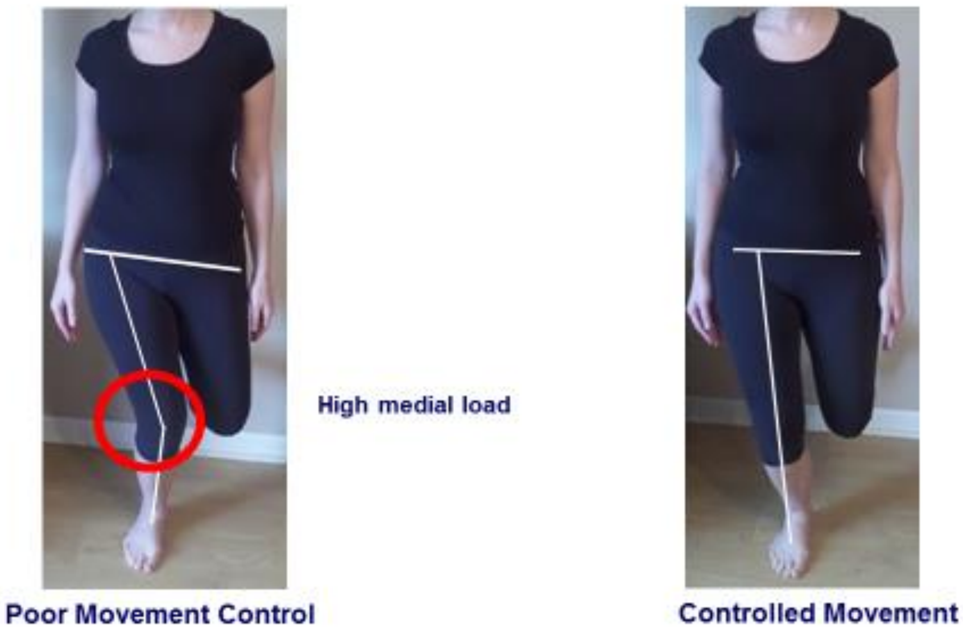

Figure 7.1. The small knee bend test– used to assess quality of movement during a simple semi-squat and inform motor control exercises needed to improve joint alignment (reproduced from Botha et al 2014, with permission from Nadine Booysen)

As outlined in Sections 3.8.6 and 6.2.4, a movement screen of functional performance introduced by NASA, the Functional Task Test (FTT), could be complemented with other tests of movement control. Movement control testing in the immediate post-landing period, when motor control changes rapidly, may help to inform intervention.

7.4.2 Prehabilitation in sport

Bed rest and spaceflight studies (Section 3.8) highlight the importance of supplementing current inflight exercise countermeasures with balance training that requires coordination and integration of proprioceptive feedback and body loading information. This suggests that other systems responsible for balance and postural control (proprioception, mechanical loading, muscle afferents, etc.) may be suitable targets for inflight and postflight countermeasure development. The FIFA 11+ used as a warm-up by football (soccer) players is perhaps the most widely implemented neuromuscular exercise injury prevention programme (Soligard et al. 2010). More targeted preventive training programmes aimed at correcting specific movement impairments identified by screening tools are now being developed for specific sports and occupations (Padua et al. 2014). Astronaut preconditioning (Bloomberg et al. 2015b) and reconditioning may also benefit from this approach, as suggested in relation to the performance tests mentioned above (Bloomberg et al 2015a).

The relatively new concept of using exercises to protect joints from overuse injury and abnormal loading warrants consideration across pre-to-postflight phases, to protect long-term joint health in astronauts at all times (Figure 1.2). Consultation with elite athletes and coaches reveals that the motivation for prehabilitation exercises is to optimise sport performance rather than prevent injury, which they see as a secondary benefit (personal communication, Maria Stokes). Optimising performance may be an appropriate way to view preconditioning for astronauts, as injuries are relatively few, although prevention of microtrauma and long-term effects, such as osteoarthritis are important to consider.

7.5 Parallels with rehabilitation in intensive care

Survivors of critical illness experience significant deconditioning which can have detrimental effects on quality of life for years after recovery (Herridge et al. 2011). The well-known consequences of bedrest are compounded in critically ill patients by systemic inflammation associated with sepsis resulting in up to 12% muscle loss within the first week of illness (Puthucheary et al. 2013). Further heavy sedation and use of neuromuscular blocking drugs can induce complete ‘mechanical silence’ of the muscles. It is now recognised that rehabilitation physiotherapy in critically ill patients needs to start early to prevent deconditioning. Evidence-based choice of therapy depends primarily on the patient’s level of consciousness as to whether they are able to follow instructions. If so the patients engage in increasingly demanding active interventions and if not the patients receive passive interventions, often delivered by therapist or new technology (Gosselink et al. 2008; Sommers et al. 2015) in an effort to maintain joint range of movement and prevent muscle loss.

The recent application of very early rehabilitation (within 2-5 days of critical illness) in an attempt to attenuate this rapid deconditioning has focused on non-volitional mobility therapy. Studies applying unilateral continuous passive movement (daily for 9-10 hours over 7-10 days) in sedated critically ill patients can preserve muscle architecture, reduce protein loss (Griffiths et al. 1994) and help preserve force generation capacity of muscle (Llano-Diez et al. 2012). The introduction of cycle ergometry into Intensive Care Units (ICU) means that both passive and active cycling can be implemented from the very early stages of illness ((Pires-Neto et al. 2013) with improved functional outcomes (Burtin et al. 2009).

Neuromuscular electrical stimulation (NEMS) creates passive contraction of skeletal muscle using low voltage electrical impulses delivered through electrodes attached to the skin. Its use increases muscular blood flow, oxidative capabilities and maximal force generation capacity (Bax et al. 2005). Similar effects are seen in the critically ill with preserved muscle mass (Gerovasili et al. 2009), improved function and improved microcirculation (Gerovasili et al. 2009) which interestingly has been shown to have both local and systemic effects (Routsi et al. 2010). In chronically ventilated patients mobility therapy with NEMS results in significantly improved muscle strength compared to those who receive standard mobility therapy alone (Zanotti et al. 2003), although these effects have not yet been reproduced in the critically ill (Kho et al. 2015). A potential alternative to NEMS is functional electrical stimulation (FES) which differs from NEMS in that it stimulates muscles in functional patterns in an effort to mimic 'normal' contraction under volitional control. FES in conjunction with cycle ergometry may be potentially beneficial to patients who are not able to partake in volitional exercise (Parry et al. 2014). Investigations as to whether this is beneficial alone or in conjunction with applied resistance are in development. Notably, much work in the critically ill is confounded by the heterogeneity of the population, absence of baseline assessment of function of patients prior to their illness and lack of consensus on outcome measures.

Deconditioning after six months on the ISS is not severe due to successful countermeasures. However, effects of longer duration missions are unknown but may present with more severe changes in neuromuscular tissues that are more difficult to reverse, which would resonate more with the challenges in managing deconditioning in intensive care patients. Lessons from the latest evidence in such patients may therefore be useful to draw on when the effects of longer duration missions become apparent. Moreover, similar intervention strategies may be appealing in these situations, given that non-volitional training (particularly in conjunction with resistance) may improve compliance and be considered time efficient, if 2-3 hours of training per day are required. There is also the possibility to train while doing other tasks.

7.6 Lessons from Rehabilitation of Muscle Wasting Diseases (Neuromuscular Diseases)

A number of the changes in the musculoskeletal and vestibular systems seen after spaceflight or bed rest (Chapter 3) are similar to the secondary deconditioning effects seen in people with neurological disorders. Strategies used in neurological rehabilitation, particularly for people with neuromuscular diseases (NMDs), may have relevance to space reconditioning and some of the key aspects are considered here.

7.6.1 Muscle atrophy

There has been a recent upsurge in MRI studies exploring ***primary and secondary muscle atrophy*** in NMDs that has enabled greater understanding of the mechanism of weakness and muscle function in this group. In primary muscle atrophy, due to muscle fibre necrosis or long term denervation, there is replacement with fat tissue (Morrow et al. 2016). Similar fatty infiltration also occurs with aging (Hogrel et al. 2015). People with NMDs tend to be sedentary and volume loss is observed in muscles not affected by the primary disease, with associated reduced muscle strength (Morrow, Sinclair 2016). This is thought to be secondary disuse atrophy and is a key focus of rehabilitation programmes in conditions where there is no reversal or treatment of the disease process (Ramdharry 2010). Secondary atrophy tends to be chronic and long term, so may be a good model for comparison with microgravity induced deconditioning in astronauts.

7.6.2 Sensory impairment

People with polyneuropathies commonly experience sensory impairment, particularly of proprioception (van der Linden et al. 2010). Transcranial magnetic stimulation suggests that NMDs with sensory impairment may have reduced central activation, implying central changes to the sensory pathways where there has been limited feedback (Schillings et al. 2007). This has implications for astronauts who may experience similar central changes due to altered sensory feedback during space flight (see Section 3.6). Sensory impairment has been found to impact gait and balance performance. Altered proprioceptive feedback can impact joint moments and power generation during gait, and altered postural stability is observed in people with NMDs, often with increased visual dependency (Mazzaro et al. 2005; van der Linden, van der Linden 2010).

7.6.3 Fatigue and fatigability

Fatigue and fatigability have specific definitions according to the different experiences and structures affected. Types of fatigue are commonly described using the following categories: physiological (peripheral) and central fatigue (Taylor & Gandevia 2008) though experienced fatigue has also been described in relation to people with NMDs and refers to the overwhelming feeling of tiredness that is unrelated to the number of muscle contractions and amount of work done, and tends to be pathological (Schillings, Kalkman 2007). Fatigue in NMDs and other neurological conditions is known to be multi-factorial (Kalkman et al. 2007; Schillings, Kalkman 2007) and may be of more concern for astronauts in long duration missions than current ISS missions.

7.6.4 Reconditioning strategies: methods and timescales

NMDs that are "single incident" and undergo full or partial recovery provide some parallels with deconditioning in astronauts, e.g. Guillain Barre syndrome (GBS), critical illness polyneuropathy (CIP) and critical illness myopathy (CIM). Recovery from these conditions, however, also relies on recovery from a pathological process that can take several months, so direct application to astronauts may be limited. However, parallels with space reconditioning may become more relevant for longer missions, as recovery may take longer.

A more relevant comparison will be rehabilitation of chronic secondary disuse and deconditioning in the less affected muscles groups/ sensory systems of people with lifelong NMDs. A number of studies have investigated both strength and cardiovascular training protocols for a spectrum of nerve and muscle diseases. For strength training, significant effects were observed with 16 to 24 week programmes using standard protocols recommended by the American College of Sports Medicine (Lindeman et al. 1995; Ramdharry et al. 2014). It is worth considering that the effect sizes to achieve functional improvement in these chronic, long term conditions may be a lot smaller than those required by astronauts to get back to pre-flight levels. The optimal time scale for full recovery may be longer than that required by some muscle groups not so well maintained by inflight CM. An additional inflight CM that could be considered for such muscle groups is electrical stimulation. It has been explored in critical illness polyneuropathy and critical illness myopathy (Section 7.5), and is available in the Russian space programme, however its efficacy is yet to be fully established (Hermans et al. 2014).

Rehabilitation strategies to challenge the sensorimotor control systems have also been explored in polyneuropathies. Approaches that may be most applicable to astronauts are ways of challenging stability to improve the coordination of balance responses. Small exploratory studies of moving and vibrating platforms show some potential in patients with neuropathy (Yoosefinejad et al. 2015) and vestibular dysfunction (Nardone et al. 2010). Vibrating insoles have also shown improvements in balance parameters in people with diabetic peripheral neuropathy (Ites et al. 2011).

Functional and exercise training have also shown benefits in patients with neuropathy, including Tai Chi showing improvements in balance (Ahn & Song 2012), proprioceptive balance training as part of mixed programmes that include lower limb strengthening (Ites, Anderson 2011) and improvements in laboratory based balance measures after multi-sensory balance training (Missaoui & Thoumie 2013).

When considering the timescales, it would appear that functional training requires several weeks to demonstrate change, but some of the higher tech approaches may give faster results. The studies are small, however, and we must still consider the differences in effect size required for people with NMDs to show functional improvement, and the effect size required for astronauts to return to preflight function.

7.7 Rehabilitation in Musculoskeletal Ageing

The most extensively explored parallel between microgravity and terrestrial musculoskeletal health is in ageing, so this is not covered in depth in the present report. Simulated microgravity in bed rest studies has been used widely in research as a model for ageing (Gianni et al. 2003). An ESA Topical Team report made reference to ageing in effects on muscle physiology (Wilson & Elmann-Larsen 2005). It may be that greater effects from longer duration missions result in changes that resemble ageing more closely in terms of ability to reverse physiological changes and declines in function.

7.8 Psychological aspects of postflight reconditioning

7.8.1. Introduction

Compliance with the reconditioning programme and adherence beyond the supervised phase are affected by personal and environmental characteristics, as well as previous cognitions and behaviours. Therefore, pre-flight, inflight, and postflight factors must all be considered together. Preconditioning programmes undertaken during mission preparation and inflight will provide the basis for postflight reconditioning by setting goals, outcome expectations, relationships with the medical team, motivational climates, barrier mitigation strategies, and behavioural routines.

7.8.2. Compliance and Adherence

There is limited understanding of postflight barriers/resources affecting reconditioning. In terrestrial populations, poor understanding of medical conditions or prescribed rehabilitation is a key factor in treatment non-compliance (Marshall et al. 2012), , whereas achieving recovery milestones and realising anticipated outcomes are positive determinants of ongoing adherence (Bauman et al. 2002). Similar to elite athletes, astronauts may adopt aggressive reconditioning regimens to promote rapid recovery (Brewer et al. 2000), but the consequences of over-adherence include risk of injury and decreased motivation over time (Frey 2008).

Compliance with clinic-based treatment, with supervision and feedback, is generally better than home-based programmes in patient populations (Granquist et al. 2014) and the ESA reconditioning programme follows this evidence-based practice. Other facilitators include individualized programmes (also used by ESA), reference materials (e.g., videos) (Marshall, Donovan-Hall 2012), treatment diaries or activity monitors, (Levy et al. 2006), accurate outcome expectancies, social support, exercise enjoyment (Bauman et al. 2012;) and self-selection of exercise types and intensities (Williams 2008). Similar strategies may be applied with astronauts. On extended missions or between missions, these strategies may become crucial, as barriers and resources are likely to be situational and could change rapidly, necessitating both self- and external monitoring to maintain behaviour. Access to resources in such cases would be essential, and environmental factors (e.g. temperature, clothing requirements, absence of feedback) will likely present novel barriers during extended missions.

7.8.3. Motivation

During supervised early postflight reconditioning, astronaut motivation and compliance are typically high. Based on operational experience, self-motivation is likely to be most challenging preflight and following supervised postflight reconditioning. Two primary motives for astronauts to comply with reconditioning are the recovery/maintenance of functional health and the desire to return to preflight status (and thus qualify for future missions). These powerful drivers do not exist in isolation. Astronauts are likely motivated more globally by extrinsic (e.g. policy or performance requirements) and intrinsic (e.g. enjoyment of exercise, challenge, professional and personal identity) factors. Extrinsic motivation has consistently been implicated in poor adherence to rehabilitation and exercise programmes (Ng et al. 2012), whereas intrinsic (self-determined) motivation predicts adherence (Brewer, Van Raalte 2000).

Self-reliance and self-efficacy (perceived competence) are essential factors for behavioural maintenance (Wilson et al. 2008), and practitioner support for patient autonomy and competence is directly related to treatment outcomes in rehabilitation settings (McGrane, Galvin 2015). Therefore, during preflight and inflight phases, supporting these needs will be crucial in promoting intrinsic motives for programme compliance. The importance of such support was stressed in the astronaut case histories in Section 4.3. During postflight reconditioning, the balance between autonomy and medically necessitated interventions will change along with the transition from acute reconditioning to health maintenance, but should be considered in the design of long-term exercise plans.

7.8.4. Therapeutic Alliance and Trust

The therapeutic alliance (the relationship between patient and therapist) is positively associated with treatment compliance, treatment satisfaction, physical function, and depressive symptoms (Hall et al. 2015). Provision of emotional support and allowing patient involvement in decision making are key in both athlete (Clement et al. 2013) and clinical populations (Pinto et al. 2012). It is important for therapists to understand patient preferences and priorities in order to tailor reconditioning programmes that will be acceptable and feasible on a case-by-case basis (Dean et al. 2005).

Similar to elite athletes, astronauts are often reluctant to report medical symptoms or health problems for fear it will result in disqualification (Flynn 2005). Developing trust in medical staff is therefore a critical component of pre-flight and inflight care that will translate to postflight reconditioning. Trust was highlighted as a key factor in the astronaut case history in Section 4.3.1. A positive relationship with the therapist will lead to better decision-making and will likely provide a foundation for more realistic outcome expectations, more meaningful feedback, and better astronaut buy-in to long-term exercise programming.

7.8.5. Recommendations for practice

For astronaut care, there is a need to routinely monitor psychosocial factors that may influence reconditioning compliance and treatment outcomes (Foster & Delitto 2011). Considering common postflight medical concerns, symptoms are likely the largest barrier to compliance in the acute reconditioning phase, but personal motivations and social/physical environment factors will play a larger role with adherence over time. Addressing these issues will assist therapists in making appropriate decisions and tailoring programmes to fit individual needs, ultimately enhancing treatment results (Seefeldt et al. 2002). Creating autonomy-supportive climates will be challenging within the constraints of existing training procedures and mission requirements, but building astronaut self-efficacy and providing detailed information to allow for realistic outcome expectations is feasible. Additionally, given the norms of confidentiality within the astronaut corps (Harrison 2005), developing strong therapeutic alliances can help to mitigate concerns related to health care and provide necessary social support (Slade et al. 2009).

7.8.6. Future research on psychological aspects

Most behavioural health research within the space exploration domain has focused on psychiatric problems rather than social psychology, and there has been no investigation of health behaviours either inflight or post-mission (Brady 2005). Therefore, recommended areas of research include examination of astronaut experiences to inform the design of multifactorial barrier mitigation and motivation enhancement strategies, and investigation of the links between pre-flight, inflight, and postflight behaviours. Understanding the nature of the therapeutic alliance would allow maximization of existing personnel resources and enhance reconditioning outcomes, and could lead to better uptake of evidence-based recommendations (Palinkas et al. 2005). Finally, with a view to longer duration and exploration missions, investigating potential barriers to ongoing health behaviours will become important in designing mission specifications and generating policies (Pascoe et al. 1994).

7.9 Spin-offs for terrestrial rehabilitation from space research and vice versa

The reciprocal benefits of terrestrial and space research to aid recovery from deconditioning have been alluded to throughout this chapter. Back pain and risk of back injury are very relevant to astronauts, so research in this area may be applied directly. Training in elite sports is also directly applicable, as astronauts are healthy, but, due to microgravity derived deconditioning could exist at the opposite end of the activity spectrum at the culmination of a LDM. Rehabilitation research into deconditioning associated with clinical conditions, such as neurological disorders, intensive care for critical illness and ageing, can provide useful lessons for astronaut reconditioning. Psychological approaches to motivation and adherence to exercise may be particularly effective in astronaut reconditioning.

The advantage of translating research on astronauts to terrestrial rehabilitation is that changes to the neuromuscular system which may take a long time to develop on Earth develop at an accelerated rate in microgravity. Also, the adaptations in response to microgravity occur without the complications of specific pathologies which may be associated with clinical conditions on Earth; e.g. a clearer picture of deconditioning is seen. Some of the spin-offs may be technological advances, an example from space research being the anti-gravity treadmill, now used in terrestrial sports training and rehabilitation.

7.10 Conclusions on lessons from terrestrial rehabilitation

There are several parallels between the deconditioning effects of microgravity on astronauts and those on Earth, associated with different environments, activities and clinical conditions. Understanding the effects on the neuromuscular system is important, as this system is plastic and interventions can therefore be planned based on observed modifiable changes identified. For example, if specific muscles are atrophied, exercises can be planned to target the group/muscle, leading to potential development of better and more effective interventions for astronauts and the wider community. Recommendations proposed from these terrestrial parallels to fill knowledge gaps in postflight reconditioning are listed later in Chapter 10. Specific challenges faced in astronaut and microgravity analogue studies are now addressed in Chapter 8, which suggests ways of applying different research designs to provide non-conventional yet robust solutions.

CHAPTER 8

RESEARCH METHODOLOGY

Research methodology for space medicine can, for the most part, draw from established designs and practices (as described in standard literature), yet there are unique aspects to space science which demand special consideration. The challenge is to identify which aspects of terrestrial methodology remain robust for space science, identify which aspects are inappropriate and then present solutions.

8.1 Study design challenges in existing literature/knowledge

The methodological considerations unique to space travel and reconditioning are described in brief. The overall objective is to create or enhance the body of space travel related knowledge, particularly with regard to efficacy of reconditioning treatment. Whilst evidence on treatment efficacy is preferably generated from randomised controlled trials (RCTs) and meta-analyses of such studies, the space science environment with its extremely small population restricts the relevance and applicability of such a design. Randomised N = 1 trials may have a limited role to play in this area although they cannot address final rehabilitative outcomes. Alternative and hybrid methods or modifications are required to generate a body of knowledge (see Fig 8.1), including;

1. Assimilation, extraction and summation from existing studies (specifically on space reconditioning). However, there will be very few to reference.
2. Translation from existing observational studies from the realms of physiology and psychology.
3. Evidence from directly related terrestrial studies of similar problems in relation to deconditioning/pathology.
4. Indirect evidence from corollary studies of hostile environments (these may have similar limitations to space travel science)
5. New tailored and specifically designed interventional studies (accepting the small study sizes and the restrictions inherent in the environment).

Designing new studies will be the most challenging and the majority of the chapter is given over to this topic (Beard & Cook, 2016 in Appendix D). Little detail is provided in terms of reconditioning content, as this has been covered in Chapters 4, 6 & 7).

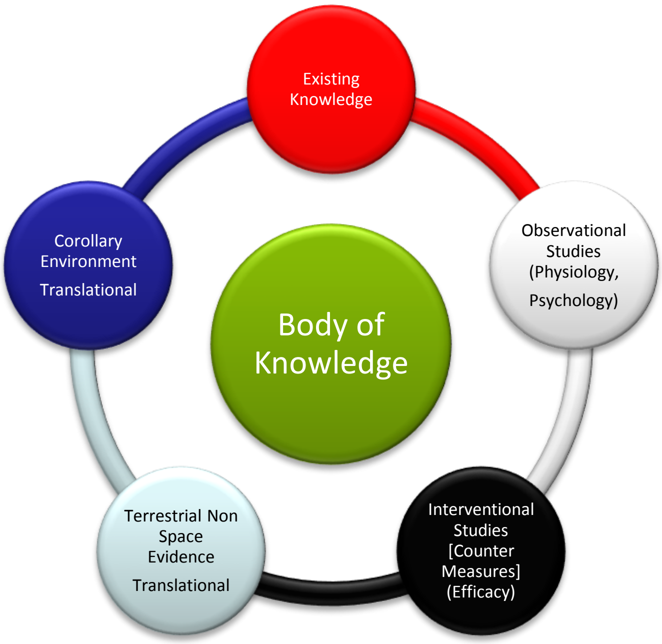

Figure 8.1: Schema of information source for reconditioning science and efficacy

8.1.1 First in human characteristics of interventions

Interventions for space medicine, including reconditioning, share similar characteristics with "first in [hu]man studies"[7i], particularly with the surgical specialities. These studies are the first time the device or drugs have been used in/for human subjects and are usually tested in very small controlled sample sizes. The very low ceiling on available participants (of astronauts) with the associated reduction in statistical precision to detect differences is of particular note and suggests that formal statistical analyses are not likely to be appropriate, except in very restricted and modified (accepted a much lower level of certainty than is commonly used) sense.

With this in mind it is recommended that an ordered and systematic approach to prospective data collection is pursued, similar to that of IDEAL (Idea, Development, Exploration, Assessment, Long-term follow-up) recommendations for surgical sciences (McCulloch et al. 2009; McCulloch et al. 2013). The IDEAL is a systematic approach to the introduction of surgical innovation which consists of the five phases and the first two (idea and development), in particular, may lend themselves to postflight reconditioning. The first part of the IDEAL approach does not involve inferential statistics.

Realistically, the majority of studies will have low numbers of participants and may span several years and multiple missions (Genc et al. 2010). This poses a challenge to robust statistical analysis. Statistical precision to show meaningful effects will be negligible without very strong assumptions external to the study. Rather than pretending that sufficient precision can be achieved, authority of subsequent studies will depend on the transparency and quality of data capture, choice of measurement variables/instruments and the ability to amass/assimilate compatible data, perhaps from wide ranging sources. A coordinated approach to data capture systems will help. Data analysis will therefore be informal and with each individual participant assessed on their own.

8.1.2 Control of bias

A major issue will be control of bias in such an evaluation. The previous lack of authoritative data and studies may have unintentionally introduced preference behaviour for specific interventions for space travel. For example, the inflight CM exercise programmes differ between agencies, which may introduce bias to the results. Minimising this bias, including assessor bias, will be critical and interpretation will need to be cautious. The reader is reminded to beware of anecdotes, which are common in space medicine literature, and tend to be propagated.

8.1.3 Account of unique and variable population

The study population is undoubtedly unique. This has implications for generalisability to other populations of new work outside any particular study, but perhaps more importantly, for related or external studies being used to support a specific hypothesis. Each astronaut is unique, and it is suspected, quite distinct from an "average" individual (reflecting a high physical and cognitive performance level). This introduces a challenge and some consideration is needed to assess whether the variation between individual astronauts (intra-group) is considered with regard to more typical extreme individuals (normal population).

Space medicine methodology is not all compromise and bleak. The rarefied nature of the population does offer some advantages over a typical medical research environment in that the entire population could feasibly be recruited. Given the culture of furthering scientific understanding, along with complete data return, the "captive" nature of the population lends itself to good data sets, even in the early post-mission phase when they are closely monitored for a sustained period. Human space research also offers the unique opportunity to study deconditioning without the complications of pathologies seen in clinical cohorts, offering potential

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7 "First in man" studies are those where initial testing, usually of drugs and devices, have been carried out using simulations, bench testing and in animal models. These studies are the first time the device or drugs have been used in/for human subjects and usually tested in in very small controlled sample sizes

solutions for terrestrial rehabilitation. Other reciprocal spin-offs from research between the two environments are discussed in Section 7.9.

8.1.4 Account of unique reconditioning goals

The content of reconditioning for space travel is a challenge to any study assessing efficacy of rehabilitation. The problems encountered and the goals of the intervention will be distinctive, so this limit of direct experience could be problematic. The small sample sizes and limited knowledge of normal variation in astronauts make it difficult to recognise outliers in the data. There is often no previous data with which to compare, be it incomplete or non-published. An open mind will be required, yet organised “sense checking” by the researchers will be paramount.

8.1.5 Timing of measurements and diffusion

Space travel research may not afford the flexibility of follow up assessment timing found in comparable terrestrial studies. The reasons for this include mission-related safety and operational duties, and the limited postflight contact with the astronaut beyond the period of supervised postflight reconditioning. All efforts should be made to achieve optimised follow up with the importance of data being a high priority for the medical ops team. Essential data sets should be established.

In addition, astronauts may be involved in many simultaneous medical experiments. There is unlikely to be contamination between effects of interventions because attempts are made to prevent astronauts being involved in multiple interventions. However, there is potential for effects from multiple measurement to contaminate the results. A solution is not obvious. An awareness that this problem exists and could confound findings may be all that is possible. Any obvious experimental redundancy can be omitted in an attempt to mitigate although it is unlikely on space missions that any such redundancy exists on space missions. All experiments are likely considered imperative. Moreover, with small sample sizes diffusion of treatment effect or contamination of intervention is a real concern.

8.1.6 Transferable designs – translation capability

A sensible approach is to take advantage of the more substantial body of terrestrial rehabilitation research, particularly where similar problems exist such as in rare diseases, elite sports or neurological conditions (see Chapter 7). When designing studies it is recommended that (providing sufficient quality exists) the terrestrial equivalent of the study is used as an initial basis. The use of standardised outcome measures and universally agreed time-points for measurement would help in this goal.

8.2 Optimum study designs for future space life science studies accounting for known limitations in existing literature/knowledge

There is no perfect study design solution for space related medical research and authoritative efficacy studies will be difficult to achieve. The optimal approach involves any design or method that limits bias and provides the greatest level of external validity.

8.2.1 Use of systematic review and summary methods

The limited number of studies in space reconditioning lends itself to an amalgamation model to generate evidence. A systematic review approach should be considered with a broad inclusion of study designs. This has been demonstrated well in the recent literature review of Winnard et al (under review for *Manual Therapy*). The use of systematic review and amalgamated data may result in loss of detail for some experiments, but this disadvantage is outweighed by achieving greater experimental numbers.

8.2.2 Use of case studies

The rarity of events and small sample size promotes single case studies as a way to increase knowledge. In this design the subject acts as their own control (appropriate for astronauts because of their rarity). Although single case studies are low on the evidence pyramid (RCT’s and systematic reviews being the highest), they can still be used to establish facts (Paynter

2009). Single case studies have the advantage of being sensitive to individual organism differences, are flexible and are easily managed. They can, however, suffer from carry over effects and issues with ordering/sequencing in the intervention. They are best used when multiple episodes of the same intervention can be applied (i.e. a ABABAB design, involving an intervention period inflight [A], then a wash out period postflight [B], then another intervention period flight [A] etc.). Identical (as far as possible) repeated missions for an individual would allow the potential for single case designs. The single case design will also be affected by the multiple space medical experiment issue reported earlier.

8.2.3 Use of case control studies

Case control studies are a somewhat more robust method of forming evidence than single case studies. The higher sample size provides greater certainty. However, the retrospective nature of case control studies, e.g. looking at the difference between individuals who have and who have not been exposed to the intervention or incident stimulus is a distinct disadvantage. Similarly to single case studies, case control studies in astronauts could be compromised by the multiple investigation model on a single mission. A limitation of this design for space research is low participant numbers.

8.2.4 Other approaches to optimise

In view of the above limitations the following strategies are recommended. The empowerment of descriptive studies, use of internal controls (Cavanagh et al. 2009) where possible (including the single case design outlined above), for example animal work (Martin 1988), observation of patterns (to gauge safety), modelling techniques (such as those that have been used in joint force understanding and implant manufacture (Feikes et al. 2003; Kumar et al. 2012), and appropriate adaptive designs where immediate outcomes can be used to inform design modifications (Wassmer 2004). A pressing requirement might be to standardise data collection protocols across space agencies to enable pooling and sharing of data. This will substantially increase the usefulness of individual studies.

8.2.5 Mixed methodology and qualitative work

Consideration should be given to mixed methods research (which combines quantitative and qualitative methods), and particularly qualitative studies to delineate or focus any specific research questions. Interviews with astronauts will be especially important to direct future investigations. The perspectives of astronauts involved in the present Topical Team have already provided great insight into specific aspects relating to musculoskeletal problems that the direction of the Team's remit required (see Chapter 4).

8.2.6 Involvement of astronauts and medical operations experts

Involvement of users, e.g. patients and public, in setting research agendas has increased substantially. As mentioned earlier in this report, PPI has become mandatory in some areas of terrestrial research in the UK and a number of other countries, and it is becoming more widely recognised on an international stage. A space medicine equivalent is appropriate and required. Astronauts who have experienced space travel and the subsequent and related health problems are best positioned on how to advise the Medical Operations team and their research programmes. They have direct knowledge and insight into the unique issues experienced during and after spaceflight. Medical Operations experts are also key in informing research at all stages. Focus groups, directed feedback and Delphi type processes should be considered to achieve these goals, involving both astronauts and Medical Operations. The Delphi study process generates an agreed set of guidelines and/or recommendations on a specific problem generated by input from individuals with the necessary knowledge from all relevant areas of expertise (Yousuf 2007). Time, distance, cost and other factors make it unlikely for a full panel of worldwide experts to meet face to face. The Delphi technique is efficient in terms of low cost and high participation by facilitating consensus through a series of surveys from one contact person, often via email, until agreement of the panel is reached.

The limited amount of PPI performed at the ESA as part of this Topical Team's activities has shown that this approach is beginning to be understood and is welcomed by the astronaut fraternity and Medical Operations team. Involvement of user groups can range from consultation on views to actual involvement in designing and conducting research, and varies according to the needs of each project. The James Lind Alliance is an organisation that is dedicated to these aims and their model may be useful to follow (http://www.jla.nihr.ac.uk/).

8.3 Outcome measures

8.3.1 Overview

An overriding principle should be, wherever possible, to use existing well established and well validated outcome measurement tools. Guidelines have been produced for standardising for bed rest study protocols (Sundblad & Orlov 2015). Where space specific tools have been developed these should be assessed comprehensively for face, construct, content and criterion validity before application in any reconditioning related space study (Mokkink et al. 2010; Scholtes et al. 2011). Content validity is important in that it demonstrates that any measure is comprehensive and covers all aspects under investigation. Specifically, whether the content of a measurement instrument provides an adequate reflection of the construct measured. If overall function is to be evaluated it is important that the content of the scores or system reflects function. Reliability should also be considered and demonstrated, as reliability or repeatability in the spaceflight environment cannot be assumed to be similar to terrestrial data (Mokkink, Terwee 2010; Scholtes, Terwee 2011).

The outcome measures used should also fit with the World Health Organisation (WHO) international classification of diseases and measurement. The relatively more recent International Classification of Functioning, Disability and Health (ICF), is a classification of the health components of functioning and disability(Ustun et al. 2003). The system allows evaluation of various domains including impairment, disability and participation. For example a torn back ligament (impairment) may produce an inability to extend an astronaut's back (disability), and also a restriction in being able to move about the spacecraft or spacewalk (participation limitation). In the postflight reconditioning period, the Physiotherapist would first treat the ligament impairment using techniques to reduce pain and swelling and help heal the injury (reduce impairment), to improve range of movement and enable exercising to improve function (reduce disability), and enable the astronaut to resume work and leisure activities (participation) as soon as possible. Any chosen outcome measures for space reconditioning must fit with this system, particularly if a standardised approach across agencies is sought.

Examples of outcome measures to consider for space related reconditioning studies include: general health questionnaires (Chen et al. 2016); screening tools for assessing movement quality and functional tasks (Section 7.4); gait analysis variables, including moments and forces (Genc et al. 2010) and EMG profiling (Layne et al. 1997).

8.3.2 Physical/clinical assessment tools

These should not necessarily differ from terrestrial instruments, providing they can be applied in space and by appropriate personnel (if assessment is required in space). These tests may include specific range of movement, strength and/or function tests, directed at a (WHO) impairment level (Ustun, Chatterji 2003), such as joint stiffness, muscle weakness or inability to perform a particular task. Teaching of testing protocols may be required for astronauts.

8.3.3 Outcomes specific to space travel reconditioning

Some tests have been developed specifically for space related evaluation, both during and post mission. These include a variety of functional, balance and postural tests (Bloomberg et al. 2003; Bloomberg et al. 2015a,c; Bloomberg et al. 1997; Brady et al. 2009; Mulavara et al. 2010; Newman et al. 1997; Reschke et al. 1998). These evaluation techniques include the postural stability tests described by Bloomberg et al (1997) and NASA's Functional Task Test (Arzeno, Stenger 2013) (also see Sections 3.8.6 and 7.4.1). Technologies being used in a current ESA bed rest study (Blottner et al., RSL Study 2015-2016, Cologne, Germany) may be suitable for use in monitoring muscle status inflight and postflight to assess the effects of exercise programmes. For example, rehabilitative ultrasound imaging (RUSI) of muscle and related structures is used increasingly in terrestrial rehabilitation research (Whittaker et al. 2007) and is already being used by the ESA physiotherapist (Lambrecht et al 2016 in Appendix D) in clinical practice to monitor recovery from muscle atrophy. An ultrasound scanner is already used on the ISS for other purposes.

A relatively new portable device (MyotonPRO) for non-invasive measurement of muscle mechanical properties (e.g. tone, stiffness and elasticity), also being used in the bed rest study, has been tested in terrestrial cohorts (healthy and clinical) and found to be valid (Ditroilo et al. 2011), reliable (Chuang et al. 2012) and sensitive to the effects of ageing (Agyapong-Badu et al. 2016), pathologies such as Parkinson's disease (Marusiak et al. 2012) and stroke (Chuang, Wu 2012). The device was found to be robust for testing astronauts on parabolic flights (Schneider et al. 2015) and is currently being reviewed by ESA for monitoring inflight muscle status (ILSRA-2014-0015, Myotones, PI Blottner et al.). As mentioned, the non-invasive MyotonPRO technology has been successfully tested on 22 different measurement points of the body in n=20 LDBR participants (60 days RSL Study 2015-2016, DLR: envihab, Cologne) with and without exercise CM, including global and postural muscles. Preliminary results show very promising outcome with respect to monitoring of functional muscle status in disuse vs. trained skeletal muscle (Blottner et al., manuscript in preparation; see Section 6.2.) This technology therefore has the potential to measure the effect of spaceflight on the mechanical properties of muscle (e.g. muscle tone and stiffness), which indicate individual muscle status in crew, for example in relation to strength and EMG activity that are not possible to monitor inflight (during preconditioning) or routinely postflight.

8.3.4 Patient reported outcome measures (PROMS)

Patient reported outcomes have enjoyed much recent popularity in medical research (Ashford et al. 2015; Kearney et al. 2012; Lee et al. 2013; Worth et al. 2012). Such measurement instruments report the self-perceived status of the health problem or disability. Self-reported outcome measures are easy to administer and provides the best impression of how a patient or participant feels their condition is impacting on them. Several "off the shelf" instruments may be of value for assessing reconditioning effectiveness after spaceflight, including activity scores and self-report functional scores (Briggs et al. 2009; Kocher et al. 2004).

Whilst the use of existing tools is advised, some consideration should be given to the extended remit of these instruments. As in the case of NHS PROMS (UK) the use of patient reported outcome measures have sometimes outstretched their original design purpose without revalidation (Harris et al. 2013). PROMS are self-reported outcome measurement tools (questionnaires) that have usually been designed for a particular purpose and their measurement characteristics usually only hold when used for the intended purpose. Using outside the remit gives potential for bogus or uninterpretable results. As an example the Oxford Knee and Hip scores were designed for clinical trials assessing efficacy of arthroplasty. Their validity does not extend to, for example, setting thresholds for surgery or other intervention. Inappropriately extended remit should be avoided.

If appropriate, there may be the opportunity to develop new PROMS for space related research, directed by strong astronaut and medical operations involvement. All PROMS should be assessed for construct and criterion validity before use. It will be particularly important to ensure the tools are valid for measuring response over time. Hence, the tools should also have good sensitivity to change, allow calculated Minimal Important Change (MIC) / Minimal Important Difference (MID) values, and demonstrate repeatability. Many established measures do not yet have this level of measurement property evidence in the terrestrial environment, never mind for spaceflight. The MIC or MID is the minimally important change or difference between groups in a variable that is deemed clinically important or relevant. Given the low number of astronauts, these measures of precision may need to be established in terrestrial studies that inform space R&D. Without these values it is difficult to ascertain what magnitudes of change in health status are measurable or are important (Beard et al. 2015).

8.4 Conclusions

8.4.1 Research to support evidence-based practice in postflight reconditioning can draw from established designs and practices, but must also recognise the unique aspects of the operational environment, which demand special consideration. The challenge is to identify which aspects of terrestrial methodology remain robust and which do not.

8.4.2 When designing research protocols, involvement of Medical Operations experts, including Flight Surgeons and reconditioning specialists, and astronauts themselves is essential for ensuring their feasibility.

8.4.3 Creative/hybrid research methodologies will likely be required to account for the unique aspects of the operational environment in which research will be performed.

8.4.4 Although clearly challenging, multi-agency collaborative studies and/or concordance in postflight protocols will counter the issue of the relatively low number of subjects (i.e. astronauts) who will be the subject of these studies.

8.5 Recommendations

8.5.1 Use standardised outcome measures and universally agreed time-points for measurement.

8.5.2 Use population-reported outcome measures, such as quality of life, activity scores and measures of return to normal functional activity measures.

8.5.3 Establish clinically meaningful changes in outcome measures, possibly in terrestrial cohorts.

8.5.4 Use efficient research designs to reduce waste without adversely impacting on the validity and reliability of research, e.g. in line with NIHR Carbon Reduction Guidelines[8], using strategies such as:

- a) Analysing existing data sets fully.
- b) Fostering multi-space agency collaboration to develop standardised data collection protocols, promoting pooling and sharing of data from small groups of astronauts and bed rest participants to enable substantial advances in human space research.
- c) Drawing knowledge and information from elsewhere whenever possible, e.g. clinical disorders in terrestrial populations involving deconditioning.
- d) Answering several questions in one study (factorial design).
- e) Using sensible trial monitoring methods and timing of data collection, given limited astronaut availability postflight.

8.5.5 Involving methodologists when designing studies.

8.5.6 Using creative/hybrid methodology if required with cautious interpretation

8.5.7 Strategies recommended for study design, in view of the limitations of medical space research, include:

- a) Continued use of microgravity analogues, e.g. bed rest studies.
- b) The empowerment of descriptive studies.
- c) Use of internal controls where possible (including the single case design).
- d) Observation of patterns (to gauge safety)
- e) Animal work
- f) Modelling techniques (such as those used to understand joint biomechanics and implant manufacture).
- g) Pilot studies with astronauts in bed rest to collect disuse/exercise data sets from the same participant that will fly to space and return thereafter (increases data quality if terrestrial vs. spaceflown vs. reconditioning data will be compared in a subject-matched design

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[8] (http://www.nihr.ac.uk/policy-and-standards/nihr-carbon-reduction-guidelines.htm

CHAPTER 9

CONCLUSIONS

These conclusions relate to current ISS missions and also look to future postflight reconditioning in readiness for longer duration excursion missions. The Topical Team's work has covered gaps in knowledge on effects of microgravity, inflight CM and postflight reconditioning on musculoskeletal structure and function, and proposes how lessons can be learned from terrestrial R&D and practices to fill these knowledge gaps. Conclusions are related to the original Objectives set in Chapter 2 and relevant chapters are indicated.

9.1 Effects of spaceflight on neuro-musculoskeletal function *(Objective 1 - Chapters 3,4,5)*

Neuro-musculoskeletal problems experienced by astronauts as a result of space missions of different durations persist despite inflight CM (Chapters 3, 4). There are many knowledge gaps that remain (Chapter 5). Problems identified include:

- *MUSCLE*: With access to the current exercise countermeasure devices, and specifically ARED, in general, the magnitude of inflight atrophy of the major muscle groups has generally been reduced in comparison to the pre-ARED era. However, on an individual level, some crewmembers continue to experience muscle strength losses of clinical proportions. Recent evidence from a small number (<10) of crewmembers with access to ARED indicates that the deep spinal muscles are still subject to marked atrophy. Inflight and postflight data on structural, molecular and functional changes at the human neuromuscular junction (motor endplate) are completely lacking, but important for postflight reconditioning protocol design. Transmission of neural signals from motor nerve to muscle is likely still impaired during recovery in the first weeks postflight

- *BONE*: Recent preliminary evidence suggests that, compared with the pre-ARED era, some crewmembers with access to ARED display little or no change in BMD during LDM, however, variability between crew indicates that the issue is not yet fully addressed;

- *OI*: Whilst LDM crewmembers appear highly susceptible to landing day OI, the majority recover sufficiently to pass the 10 minute tilt test after two days of recovery and indications are that all may recover by day three. However, due to use of other pre-landing CM (*i.e.* fluid loading) the exact magnitude of inflight CM programme effect on OI is unknown);

- *CARTILAGE*: There is insufficient knowledge regarding changes to human cartilage as a result of LDMs for adequate conclusions at present, although studies have begun.

- *SPINE*: There is only preliminary inflight data on a small number of astronauts regarding the effect of LDMs on the spine. This data suggests variable (between crew and different spinal levels) IVD water content changes with no significant changes in disc height, but increased spine stiffness and straightening;

- *AEROBIC CAPACITY*: With access to the current exercise CM devices, it appears that as many crewmembers maintain or increase their aerobic capacity during their mission as those who experience losses. Those who attain higher exercise intensities during CM sessions appear less susceptible to a loss of function;

- *FUNCTIONAL PERFORMANCE*: In postflight functional tests, including postural stability and agility push-ups, pull-ups, bench press, and leg press, crewmembers with access to ARED have shown less decrement in performance compared to those from the pre-ARED era;

- SENSORIMOTOR FUNCTION: Sensorimotor function, as measured using computerised dynamic posturography, indicates improvements in some aspects of postural performance since the introduction of ARED, although with considerable inter-individual differences. Several measures of sensorimotor function suggest that preflight performance is recovered by around 15 days postflight.

9.2 Risk factors affecting successful reconditioning following spaceflight *(Objective 2; Chapters 3, 4 & 5)*

- Loss of muscle mass and strength
- Impaired neuromuscular transmission (less signals from nerve to muscle) and increased oxidative stress (fatigue and stiffness factors)
- Risk of bone fractures and spinal injuries due to bone loss and changes in spinal structures
- Inappropriate motivation for compliance with postflight exercise regimes
- Poor access to continued reconditioning facilities and support
- Age
- Pre-existing conditions
- Competing commitments on the astronaut's time for reconditioning

9.3 Existing reconditioning strategies *(Objective 3; Chapters 3 & 4)*

- The ESA postflight reconditioning programme is based on principles from the best available evidence for terrestrial rehabilitation (Chapter 4) and although it has yet to be investigated for effectiveness the limited operational and research findings available indicate that specific motor control training intervention is effective in restoring the size of the spinal and abdominal muscles to their pre-bed rest size.
- Large inter-individual differences and diverse mission profiles do not permit implementation of a standard reconditioning program. As such, programs provided by ESA specialists are individually-tailored during daily, two hour sessions, and can be influenced by differences in equipment and the facilities at the location to which the astronaut returns.
- The astronauts consulted perceived that:
  - trust in reconditioning specialists is crucial to good working relationships;
  - the nature and enjoyment of inflight exercise are important to maintain motivation to follow the programmes provided
- Postflight reconditioning of astronauts is implemented within highly demanding post-mission schedule of 3 to 4 weeks, and must be coordinated with medical checks, social and public relations commitments, debriefings and postflight tests required for scientific experiments for which astronauts serve as volunteers
- *Systematic Review Conclusions on CM studied during bed rest*
  With respect to exercise CM for lumbopelvic muscles studied *during* bed rest, the report concludes that:
  - Consistency in outcome measures is needed to enable meaningful comparisons between studies and between countermeasure interventions.
  - No CM intervention has been successful in limiting or preventing all musculoskeletal changes seen in the lumbopelvic region, including spinal morphology, muscle physiology and function.
  - More research is required into the different mechanisms of interventions to inform their further development studies of their effectiveness
  - Future research should use standardised outcome measures, including population-reported outcomes and functional measures relevant to astronauts.

9.4 Anticipated challenges to reconditioning after longer (exploration) missions *(Objective 4; Chapter 5)*

Knowledge gaps in relation to longer missions can be categorised as those related to the delivery and effectiveness of post-mission reconditioning on Earth, and those related to the preparation for (preconditioning), and execution of, activities during LDEMs that include planetary surface (low gravity) excursions.

Research is needed to determine:

- The extent of the negative effects of prolonged microgravity on the neuro-muscular, cardiovascular and skeletal systems, and what magnitude can be considered acceptable, both prior to planetary surface excursions and on return to Earth
- Whether inflight CM will be less effective than during current ISS missions and whether any resulting loss of functional performance will impair planetary surface excursions
- The requirements for inflight preconditioning programmes to prepare for safe and effective planetary surface excursions
- The psychological effects of prolonged confinement and isolation on inflight mood state, motivation to exercise and compliance with inflight exercise CM and preconditioning for planetary surface excursions
- Preliminary evidence after 12 month missions indicates that the effects of spaceflight are more severe than after 6 month ISS missions and recovery takes longer. It is unknown whether all effects of prolonged microgravity will be fully reversible between flights and what the longer-term effects will be on the health of the astronaut, e.g. osteoporosis, osteoarthritis.

9.5 Reconditioning strategies after long duration missions *(Objective 5; Chapters 6, 7 & 8)*

The short and long-term effects of LDEMs need to be understood in terms of factors that will influence the astronaut's ability to perform postflight reconditioning programmes effectively, as well as chronic conditions (e.g. as osteoporosis and osteoarthritis) that would need measures to prevent premature onset.

- Optimal reconditioning exercise programmes are needed that consider:
  - Safe reloading protocols that provide sufficient stimulus for recovery whilst preventing/minimising damage to soft tissues, cartilage and bones
  - Dose, duration, rest periods, timing
  - Recovery of functional performance of everyday activities
  - Psychological factors to enhance motivation, compliance (with exercise during the supervised reconditioning period) and adherence (to an active lifestyle post-reconditioning)
  - The potential for local muscle training with functional movements in an upright spinal posture may be a potentially useful adjunct to specific motor control training in astronauts following return to Earth, to rehabilitate the lumbopelvic muscles.
- Lessons for postflight reconditioning can be learned from parallels with terrestrial reconditioning strategies, including those used for LBP, sports (physical and psychological), neuromuscular conditions and intensive care.
- Research to support evidence-based practice in postflight reconditioning can draw from established designs and practices, but must also recognise the unique aspects of the operational environment, which demand special consideration. The challenge is to identify which aspects of terrestrial methodology remain robust and which do not
- Patient and public involvement (PPI) is fundamental to the feasibility and success of terrestrial research, so astronauts and Medical Operations specialists' involvement (AMOSI), including Flight Surgeons and reconditioning specialists, needs to become integral to human space research. Involvement can range from consultation on views to actual involvement in designing and conducting research, and may vary according to the needs of each project. AMOSI will be essential to ensuring relevance of research questions, feasibility of studies and implementation of findings to achieve optimal impact on postflight reconditioning
- Creative/hybrid research methodologies will likely be required to account for the unique aspects of the operational environment in which research will be performed
- Although clearly challenging, multi-agency collaborative studies and/or concordance in postflight protocols will counter the issue of the relatively low number of participants (i.e. astronauts) in these studies by harmonising research protocols and pooling data.

CHAPTER 10

RECOMMENDATIONS

The recommendations below in relation to the Objectives (Chapter 2) are based on information synthesised from evidence in the literature about negative effects of microgravity (Chapter 3), experiences of astronauts and Medical Operations specialists (Chapter 4) and the identified knowledge gaps (Chapter 5). Possible solutions for research to fill knowledge gaps were presented in Chapter 6 (space and analogue studies), Chapter 7 (parallels with terrestrial research) and Chapter 8 (research methodologies).

Research priorities will need to be determined by an initial Delphi study involving relevant space and terrestrial communities of scientific experts (basic and reconditioning sciences) and users (astronauts and Medical specialists).

Reconditioning after longer missions refers both to the space destination, to prepare for planetary surface excursions (preconditioning), as well as postflight recovery after return to Earth.

10.1 Effects of spaceflight on neuro-musculoskeletal function *(Objective 1)*

Recommendations to increase knowledge of negative effects of microgravity after spaceflight.

1. Conduct more crew focused research on adaptation processes of muscles to further knowledge and improve inflight CM and postflight reconditioning strategies, and place particular focus on trunk muscles (and their neuromuscular junctions) relevant to spine-specific reconditioning.
2. Investigate the occurrence of osteoarthritis and osteoporosis in retired astronauts and compare with general population norms.

10.2 Postflight effects *(Objective 1)* and risk factors affecting successful reconditioning *(Objective 2)*

Recommendations to further document postflight effects and risk factors that may impact on reconditioning

1. Implement effective system(s) to capture data on musculoskeletal symptoms and injuries from current astronauts more fully, using anonymised methods, so as not to compromise trust.
2. In addition to existing clinical tools, use population-specific personalised outcome measures, including astronaut-specific and everyday functional measures, for reporting postflight symptoms and injuries to fully document challenges to effective reconditioning.
3. Use novel technologies to assess muscle status inflight to help improve inflight CM to reduce postflight deficits in musculoskeletal health and function.

10.3 Existing reconditioning strategies *(Objective 3)*

Recommendations to improve existing postflight reconditioning after ISS missions

1. Conduct multi-agency studies (quantitative and qualitative, including Delphi) to capture current reconditioning practices to produce international consensus guidance on practice guidelines and priorities for future research.
2. Obtain views of astronauts about how their reconditioning programmes might be improved, using qualitative (e.g. interviews) and quantitative (e.g. surveys) methods.
3. Synthesise and build on the existing evidence base from research in relevant terrestrial clinical reconditioning specialties to integrate into current postflight practice with multiagency consensus to address immediate needs for improving post-ISS reconditioning, for which research would take too long to conduct and implement.
4. Evaluate the effectiveness of current and new post-ISS programmes.

Recommendations to minimise injury and ensure safe exercise for postflight reconditioning programmes

1. Establish re-loading protocols that minimise damage to joint cartilage and bone.
2. Determine the most appropriate movement screening tools to assess quality of movement (control) pre- in- and postflight.
3. Develop tailored exercise programmes for re-educating movement control to protect joints from abnormal or excessive loading during exercise, to prevent asymptomatic damage that could lead to osteoarthritis.

Recommendations to improve functional performance evaluation in postflight reconditioning

Complement NASA's Functional Task Test (FTT) with functional tests of activities of daily living.

Recommendations to identify motivation strategies for complying with and adhering to postflight reconditioning after ISS missions

1. Investigate the links between pre-flight, inflight, and postflight behaviours.
2. Document astronaut experiences using qualitative and quantitative methods to inform the design of multifactorial barrier mitigation and motivation enhancement strategies.
3. Conduct studies to increase understanding of the nature of the therapeutic alliance to maximise existing personnel resources and enhance reconditioning outcomes.
4. Draw from motivation and adherence strategies used in elite sports.

10.4 Anticipated challenges to reconditioning after longer (exploration) missions *(Objective 4)* and reconditioning strategies *(Objective 5)*

Recommendations to identify challenges for Long Duration Exploration Missions and for the development of appropriate reconditioning strategies

1. Identify inflight exercise CM that are functional, enjoyable and which target multiple physiological systems at once, such as resistive vibration exercise, RVE).
2. Implement systems for involving astronauts and operations experts in setting research priorities and conducting projects, giving them equal status to scientists.

Recommendations to establish inflight monitoring procedures for exploration duration missions to inform preconditioning programmes and readiness for planetary surface excursions.

1. Develop technologies for inflight monitoring of Orthostatic Intolerance using sensors/monitoring that provide feedback to astronauts.
2. Develop tests suitable for inflight and immediate postflight monitoring of sensorimotor function.
3. Establish a battery of tests to assess functional performance for safe and effective planetary surface excursions

10.5 Reconditioning strategies after long duration missions *(Objective 5)*

Recommendations for the development of preconditioning and reconditioning strategies for longer duration missions

1. Identify the elements and format of optimal postflight reconditioning exercise programmes.
2. Design and conduct bed rest studies (including astronauts as bed rest participants) to develop inflight preconditioning exercise programmes to rehabilitate crew after long flights to deep space destinations, to prepare astronauts for planetary surface excursions.
3. Determine the equipment/hardware needed for inflight preconditioning programmes.
4. Develop non-technology based preconditioning exercise programmes e.g. motor imagery, simple space-efficient equipment.
5. Investigate potential barriers to ongoing health behaviours for designing mission specifications and generating policies

Appendix A

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Appendix B
The ESA International Space Station Exercise Countermeasures Programme

A detailed account of ESA's International Space Station exercise countermeasures (CM) programme has been described elsewhere (Petersen et al., 2016 – Journal of Extreme Physiology and Medicine, In Press). This report gives a short summary of ESA's international space station exercise CM programme.

B.1. On-board Exercise Equipment

The current inflight exercise CM programme followed by ESA crewmembers is delivered using three exercise devices available in the US Orbital Segment (USOS): a cycle ergometer, a treadmill and a resistance training machine. The cycle ergometer with vibration isolation and stabilisation (CEVIS) provides workloads from 25 to 300 watts, accommodates cadences of 30 to 120 revolutions per minute, and is provided for non-weight bearing aerobic conditioning.

In combination with adjustable bungee cords and a body harness system, the Combined Operational Load Bearing External Resistance Treadmill (known as COLBERT or T2) allows for weight-bearing aerobic conditioning, with running speeds of between 5 and 20 $km \cdot h^{-1}$ in Powered Active mode (belt driven by an electric motor) and can also be used in Powered Passive mode (user moves belt and motor provides resistance) and Unpowered mode (user moves belt against only the rolling resistance of the system). The body harness, which is anchored at the shoulders and hips, connects to the adjustably bungee cords and pulls the user down on the belt. The bungee cords can create loads equivalent of up to 100% of bodyweight for even the largest crewmembers. However, due to the prolonged external pressure created by the harness, typical loads during T2 exercise do not exceed 80% of body weight.

The Advanced Resistive Exercise Device (ARED) is provided for resistance training and supports loads of up to 600 lb (272 kg). Similar to a standard 'multi-gym' device, ARED allows crewmembers to perform 33 different exercises that target specific muscle groups in the lower and upper body, including squats, dead-lifts and the bench press. ARED was installed in 2009 to replace the Interim Exercise Device (iRED), which provided a maximum load of only approximately 300 lb (136 kg). ARED also utilizes vacuum cylinders and inertial flywheels to simulate constant mass and inertia of free weight exercise.

B.2. The Exercise Countermeasure Programme

The ESA programme is divided into three phases:

- An initial 14–30d Adaptation phase;
- A 120d Main phase and;
- The Preparation for Return phase in the 14–30 d immediately before un-docking and re-entry.

The Adaptation phase provides crew with the opportunity to familiarise themselves with the on-board exercise equipment and, during this time, the ESA Exercise CM Specialist assigned to the mission gradually increases the intensity of exercise sessions towards that required for the Main phase of the mission. This process is necessary not only for safety reasons, but also because exercise capacity on the ground does not always translate directly to ISS. This is likely due to both physiological changes due to microgravity and physiological and biomechanical issues resulting from the design of three on-board devices to allow them to operate in this unique environment.

The goal of the Main phase is to provide a regular and appropriate physiological stimulus sufficient to maintain:

- aerobic capacity (VO_{2max}) at ≥75% of pre-flight levels (or a minimum of 32.9 $ml \cdot kg^{-1} \cdot min^{-1}$);
- muscle strength at ≥80% of pre-flight levels;
- bone mass (measured by Dual Energy X-ray Absorptiometry, DEXA) T-score at not less than -2.0 SD below the mean for a healthy young adult (NASA-STD-3001, 2007).

With the exception of VO_{2max}, which can be measured during CEVIS exercise, these values cannot be measured inflight with currently available technology and thus can only be confirmed immediately postflight. To achieve these goals, individualised exercise regimes are designed for each crewmember utilising all three devices. Common features of these regimes are described in Table Ap B.1.

Table Ap B.1. Common features of individual exercise regimes followed by ESA crewmembers on ISS using the three exercise devices in the USOS segment.

Device	Session Frequency	Target Duration	Target Intensity	Details
CEVIS	0 to 4 / wk	30 min	Average of 80% HR_{max}	Range of different protocols, including steady-state, interval and ramp.
T2	3 to 7 / wk	30 min	80% of BW and average of 80% HR_{max}	Range of different protocols, including steady-state, interval and ramp.
ARED	6 to 7 / wk	45 min	1–5 sets of 6–15 repetitions	>20 different exercises for upper and lower body; upper and lower body exercises in alternate sessions.

1RM, one-repetition maximum; ARED, Advanced Resistive Exercise Device; BW, 1G body weight; CEVIS, cycle ergometer with vibration isolation and stabilisation; HR_{max}, maximum HR derived from pre-flight maximal exercise test; T2, Combined Operational Load Bearing External Resistance Treadmill.

Throughout the 120d of the Main phase, ESA's Exercise CM Specialists constantly review the performance of the crewmember (by heart rate during CEVIS and T2 sessions, and total sets and repetitions for ARED) and adjust subsequent protocols to maintain appropriate intensities.

The goal of the Preparation for Return phase is to ensure the crewmember is in the best possible condition to withstand the stresses of the re-entry procedure, to react to off-nominal situations on landing, and to return to normal locomotion in Earth's gravity. This phase is characterised by:

- An increase in the number and frequency of T2 and ARED sessions, and a decrease in the number and frequency of CEVIS sessions;
- An increase in the intensity of T2 and ARED sessions.

B.3. Fluid Loading Countermeasure

To attenuate alterations in cardiovascular function due to redistribution and loss of body fluid, and to protect against postflight orthostatic intolerance, crew returning from ISS are required to ingest a "fluid load", consisting of either a high salt broth or salt tablets and water. In the case of the latter, crew take 2-3 tablets with 200-300 ml of water (depending on body size) with each meal starting from around 24 hours before departure from ISS, followed by two further doses on Soyuz between undock and re-entry. The efficacy of this CM has been evaluated by measuring heart rate and blood pressure during a passive stand test before and after spaceflight (Bungo et al., 1985). Compared to control flights (no fluid load), both variables were significantly improved, but not totally restored. However, plasma volume was not measured during this study and subsequent studies suggest that, even with fluid loading, postflight plasma volume deficits still range from 5 to 19% (NASA Evidence Book, Risk of Orthostatic Intolerance During Re-exposure to Gravity, March 2008).

Appendix C

Astronaut Perspective Case Reports

C.1 Astronaut Case Report 1: Space flight reconditioning

Three flights are reported here from a retired astronaut. Exercise support was generally very good for crew, both before and with flight assignments. Personal trainers were available for consultation and treatment. They were skilled, knowledgeable, personable, and worked hard to help crewmembers get into shape.

Trust is a critical component in the reconditioning process (Section 7.8.4). Good medical teams establish trust through long-term relationships with crewmembers, demonstrating a willingness to listen, understanding of medical concerns, expertise in diagnosis and treatment, and a commitment to keep the crew qualified to fly. One important component is beginning strength and fitness training early with trainers that work with the crew throughout the pre-flight and postflight timeframes. The trainers learn how to motivate their crewmembers on an individual level. They develop a keen understanding of the crewmembers exercise patterns, allowing them to intervene early when they see patterns change that suggest pain or injury. In turn, the crew learn to trust the trainers. This translates into higher compliance with exercise regimens and also a willingness to discuss symptoms when they first occur. Without a trusting relationship, crewmembers are tempted to hide injuries and symptoms, hoping that they heal without treatment, from concerns about losing flight status. This can lead to minor problems becoming worse, to the point where they are more difficult to address.

C.1.1 First Flight
The first flight was nine days and the process for physically preparing for EVA was straightforward; mostly hand strengthening and endurance exercises, along with general conditioning. The general conditioning was primarily running with some basketball.

In flight, I used the exercise bike for about 30 minutes on non-EVA days. The first morning after sleep I had some mild low back pain. Subsequent nights I used a loose strap to help keep my knees and hips flexed and sometimes used a strap to keep my head on the pillow. I did not have any other back pain after that and in general slept very well in flight. In EVA prep, donning the Extra-Vehicular Mobility Unit (EMU) was difficult, as my crotch-to-shoulder height increased more than anticipated. My flight EMU was longer than my training EMU by about 1 inch. However, my height increased by about 2 inches (5 cm). There was considerable pressure on my shoulders in donning the suit and I had bruises post-EVA across both clavicles. However, I did not experience any neck or back pain during or after the EVA. I used a standard fluid pre-load before entry, with salt pills and water (Appendix B).

Postflight I had mild orthostasis which resolved over a few hours. I had reduced balance, used a wide-based gait, and had a decreased sense of orientation that persisted for a few days. My daughter did her science fair project on my recovery. Over the course of my first week postflight, she measured my ability to point my arm straight up in the air while seated in a rotating chair with my eyes closed *[proprioception]* and measured the deviation from a straight line while walking forward with my eyes closed, among other measurements.

Key Messages

- Close monitoring of postflight effects is important and may have prevented the post-mission injury suffered after this flight.
- Gradual re-loading during reconditioning is crucial to minimise the risk of injury.
- Thorough assessment is necessary to prevent medical complications
- Standardized assessments of relevant functional activities can enable the efficacy of pre, in and postflight programmes to be better assessed and monitored.

It did not occur to me to avoid impact training immediately postflight, so I returned to running on the third day. Around day seven I started having left shoulder pain that was evaluated and determined to be a muscular strain. Over the course of 6 weeks the pain extended to my elbow and increased to the point that I was unable to lift my arm above my head. Local X-rays were negative. Finally I was in a meeting one morning and felt a couple fingertips go numb in my left hand and realized, "this is a *[nerve]* root injury!" I had a neck MRI that day and the radiologist's report included this statement: "the largest cervical disc extrusion I have ever seen." Two days later I had a posterior foraminotomy. The surgeon's report stated that the nerve root was compressed to a thin ribbon by the disc.

The pain resolved immediately. The numbness and weakness persisted for about a month but eventually resolved and I had a complete recovery. I was greatly concerned that the diagnosis was missed by the flight clinic and the orthopedic consultant for so long and that, had I not been a physician and self-diagnosed, would likely have not been made for some time, perhaps resulting in permanent damage. I felt that the flight clinic personnel responded well to this feedback and were both supportive during my recovery and interested in finding ways to prevent a similar occurrence with other crewmembers in the future. Postflight clinical assessment did not capture what functional activities relevant to astronauts might be compromised and this would have aided reconditioning (see Section 3.8.6.

C.1.2 Second Flight

In preparation for my second flight (*3 years later – 10 days)*, I followed a very similar routine as the first. Hand strengthening and general conditioning with running. I increased the crotch-to-shoulder differential from training to flight EMU to two inches and that worked very well.

This was one of the early flights to dock with the ISS and there were no crew living on the ISS, so we had great freedom to fly throughout the cabin. Our mission was primarily to prepare the station for crew, so we spent a lot of time flying from the shuttle to the station with supplies to stow. I discovered an excellent form of exercise that provided, aerobic conditioning, and coordination. We would push off from one bulkhead and fly very fast to the opposing bulkhead about 10 meters away, push off that with hands or feet, and fly back and forth, sometimes tumbling in flight. This was exhilarating exercise, could be done without any equipment, was fun to do in groups, could be low or high intensity, and provided a wide array of conditioning (impact, aerobic, strengthening, coordination, with forces directed at the heels, hips, and along the spine). We did get one call from the ground that the accelerometers on the station were picking up the activity, but that was with four people flying simultaneously at very high speed and impact. We also played games such as tag, king-of-the-hill, and a modified version of Quidditch, as we had an empty module for our red rubber ball snitch. We also spun each other up for midair somersaults at very high rotation rates. We practiced three dimensional dancing, using music with beat and counterbeat, following each in a different physical plane. Turns out that you can follow music in three dimensions easily and the ability to "throw and be thrown" while dancing in microgravity is wonderful fun. Think of flying toward one another at high speed, locking arms and/or legs, spinning around, then releasing at just the right angle to fly off where you want to go.

I used the same fluid loading as on my first flight for entry and felt good. My postflight experience was much improved. I had minimal orthostasis that lasted for just an hour or so. The coordination and orientation issues were much less and what took days after my first flight only took only a day after my second. My daughter's experiments verified that. Again I wondered why *the agency* was not doing similar experiments. I delayed returning to running for a few weeks and also returned with a very gradual increase in distance and speed.

Key Messages

- Exercises employing multiple physiological systems but without the need for significant apparatus should be considered for inflight use.
- The nature and enjoyment of inflight exercise is seen as important to maintain motivation.
- Group activities were seen as more enjoyable and may enhance compliance
- Post-mission weight-bearing exercise duration and intensity should be increased only very gradually.

C.1.3 Third Flight

For my third flight (*2 years later* – 12 days I prepared in a similar fashion.
The exercise bike was available on the ISS, so I tried that. Even at the highest tension, the belt did not provide much force for your feet on the treadmill, yet it pulled hard on the pelvis, irritating the skin. Nevertheless, the treadmill was a coordination exercise, as you had to balance to stay on board, and was somewhat aerobic. I thought it did not provide any effective strength or impact loading, certainly not even close to that from pushing off bulkheads. The ARED was not available, but we did have weights attached to a spring-loaded device (iRED) that provided measured loads. It was tedious to setup, boring to use, and took up a lot of volume in the cabin.

We did two EVAs on this flight. During the first one I had a wrinkle in the pressure bladder that was adjacent to ulnar side of my right hand. This happened even though I did actively try to stretch and pull during suit press to eliminate wrinkles. It was mildly noticeable at first, became painful, and then subsided by the end. When I took off my glove, there was a lot of blood and I found that the pressure and friction created a wound that extended to the bone (5th metacarpal). I was surprised by the extent of the injury, as it did not feel that bad during the EVA, perhaps due to the mental focus you have while outside. Aware that wounds often become infected in flight, I cleaned with antiseptic and bandaged it. It hurt some during the second EVA, but did not interfere with overall performance. It healed without any complications. If this happened again, I would depress my suit, pull out the wrinkle, and repress, but I did not have the awareness or experience to do that. It was somewhat surprising, since I had so much training experience with pressured suits underwater. Discussing this postfight, apparently the frequent use that training suits get cause the pressure bladder to be softer, so that wrinkles are much more easily pulled out as the suit pressurizes. Overall, I had no issues with conditioning or strength during either EVA. I used the same fluid loading I used previously and did not even have a need for any pressure in the G suit during entry (previously I used two clicks[9]). I had no sensation of orthostasis and felt very good within an hour or so postflight. I did not alter what I had done previously, so this seems to be an automatic or spontaneous adaptation to returning to earth. We had an extra day on arrival before returning to the space station and I spent a lot of time at the beach and in the water. I felt completely comfortable even jumping around in the waves.

Key Message

• Some adaptation to the effects of microgravity on orthostasis from undertaking repeated missions might be evident, or exercise CM programme of the 3rd mission may have been more effective.

C.1.4 Recommendations

3) Focus on functional tasks postflight as well as preflight. Understand the specific areas of strength and conditioning needed to accomplish those tasks and train with those in mind. This makes the routines shorter, less boring, and will increase compliance.
4) Use techniques that use multiple physiological systems for exercise in flight. For example, create routines like the flying exercises described above to maintain the combination of coordination, impact, strength, and conditioning needed. Those sorts of exercises can be more effective than simple strength or conditioning exercises alone. They are also much more enjoyable, so they contribute to the crew's mental well-being and the crew are more likely to comply with the exercise regimes over very long durations.
5) Be creative in using the zero-g environment to enhance the exercise routines rather than fighting the zero-g environment with all sorts of harnesses.

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9 Increments of pressure increase

C.2 Astronaut Case Report 2 : Musculoskeletal aspects of two space flights

Introduction

The two missions include both Soyuz flights to the International Space Station. The first mission was an 11 day flight and the second mission was a 6.5 month expedition.

C.2.1 First Flight

Pre-flight issues

I had three musculoskeletal issues during my preparation phase, the first of which impacted on my postflight rebab and the other two did not and were managed successfully. The first problem happened before my first mission. The sitting position in the Soyuz forces tall astronauts on the left and right seats to sit for hours with bent knees without the opportunity to stretch or move them more than a centimeter. The very first time I got ready for a Soyuz simulation with the whole crew, I noticed that my colleague took pain killers before. I asked him why and he answered: “You'll find out”. I did. I got stress pain over the patella and tendon connection. After a while this pain stayed after the training and was sometimes annoying and distracting during the simulations. Massage and painkillers helped. This was on the right knee. After my 11 day flight it disappeared, but the same problem occurred during the Soyuz simulations in preparation for the 2nd flight. This time on the left knee. Again it was controllable with painkillers, taken preventively, and massage, and did not lead to degradation or abort of sessions.
A second issue was an attack of acute back pain in Star City. I do not recall the cause. Local physiotherapy and electro-stimulation relieved the pain, which disappeared, never to come back.
The third issue was Plantar Fasciitis on the left side. Probably caused by running. It was very painful standing on my heel after sitting still for a while or getting up out of bed. It was solved with special soles in my daily and running shoes. These soles were sent to the ISS as well and used on the treadmill. I had no further complaints.

Inflight countermeasures

On my first 11 day mission there was no time planned for any physical exercise. On the second mission (apart from Sundays), the daily work out consisted of exercises on the ARED, treadmill and bike.
The bike was the most unpleasant, due to the heavy workload and profound sweating, while cooling was minimal. Running on the treadmill was better. The shoes caused no problems and the pre-flight Plantar Fasciitis complaints did not re-occur.
While running it was possible to watch a movie or documentary instead of watching a wall all the time. This made it easier to go running. I looked forward to watching a movie and it therefore motivated me more to go running. I also saw recreational videos while on the bike but this was less useful, since you can look around the whole US lab as a distraction and the higher effort of cycling reduced the ability to concentrate on the video.
It was very important to have correct positioning of the body during the ARED exercises. I therefore valued the live video and audio connection with my ESA Medical Operations sports instructors and physiotherapist during a complete set of exercises on the ARED. This happened on several occasion. Twice I had direct voice contact, so I communicated live with my instructors during my exercise to learn if my position and movements were safe or what I had to correct.
Due to regulations I was not allowed to use the private phone line for work related contacts any longer during the video connections. Therefore the training effect was reduced to almost zero, since I got the feedback on the video images much later and could not relate to what I did wrong while exercising on the ARED.
In preparation for the ARED exercises, especially at the beginning, the pictures in the instructions were helpful. Good video clips of each exercise, with warnings against certain wrong, potentially harmful positions, are of great importance. They should be easily accessible.

Key Messages

- Recreational videos can make exercise more enjoyable and help motivation
- Real-time feedback from the ground support team when exercise is performed in space is important and may prevent crew injuries.

C.2.2 Second Flight

Inflight issues

On my first flight I measured my height increase, which was 2-3 cm. Both on my first and second mission I had no back pains. Once I injured my back on the ARED. I put too much force in while my body position was wrong. Due to this I could not do certain exercises, like dead-lifts and squats, anymore for a week.

Re-Entry

Despite my increased height I had no trouble getting into my suit and seatliner. The position in the seat, after 6.5 months ~~193 days~~, was again uncomfortable. My feet were jammed and there was no way to move or even slightly stretch my knees.

Key Message

- The ergonomics of spacecraft design needs to be considered in more detail to prevent crew discomfort bordering on injury.

After a while, pain started in my right leg. Paresthesia occurred in the right foot and then lower leg. After the 4.7G reentry the pain in the upper leg increased and I lost complete feeling in the lower leg and foot. Once the commander was taken out of the central seat after landing, I could lift myself from my seat and slide a bit to the commander's seat to relieve the right leg. This quickly solved the problem and soon I had feeling and control back.

Postflight effects

Muscle coordination was reduced and took about a week to recover. After the 11 day mission I would have stumbled into the helicopter if not supported by the crew surgeon. In the helicopter I dropped a bottle of water after drinking, assuming it would float. Also at arrival I almost stumbled on the stairs. I noticed that I took corners facing the wall for a while.
After the 6.5 month mission the coordination problems took longer to resolve. I was Earth sick, nauseated as soon as I turned my head.
I could take a shower on the airfield but due to the orthostatic intolerance and muscle coordination problems, there was a risk of slipping in the shower cabin, so support of the crew surgeon was helpful. The hot water caused vaso-dilatation and I felt sick quickly. So a hot shower directly after return is not a good idea.
After the maximum exercise test one day after the mission, I felt a blood pressure drop and had to lie down. I got a saline infusion to aid blood pressure.
In the plane to the space centre, I did not feel well and the chocolate, coca cola and pizza that were brought onboard during the refueling stop were provoking nausea. One day after the mission I had to vomit after a vestibular test.

Postflight recovery

The recovery was good. Every day there were sessions with good instructions. Coordination, force, physical condition, all aspects were addressed by the instructors. The exercises in the pool were pleasant and I would have liked more of that in the beginning. For about three months I had muscle aches and felt stiff after getting out of the car or bed. I noticed pain in my ankles, probably due to the fact I did not use the balance muscles inflight.

C.2.3 Long term issues

The Baseline Data Collection measurement with the DEXA scan were only done once. I understand that I lost 3-8% of bone mass in the weight bearing bones at that moment. For both scientific and med-ops reasons, as well as for my own peace of mind, more DEXA scans would have been welcome to gain knowledge on my bone mass recovery.
Due to the fact that there was no longer a training schedule with three planned exercise sessions scheduled per week, the amount of exercise became less and my weight increased by 5-8 kilograms.
The pain in the left patella/tendon has remained. It is not incapacitating but sometimes present in variable intensity and treated with physiotherapy when it becomes annoying. This is the same pain in a resting, bent, position as occurred for the first time in the simulator pre-flight.

C.2.4 Recommendations

5) Special attention on physiotherapy/flexibility/etc. to deal with the prolonged sitting position in the Soyuz simulator for tall astronauts, in order to prevent stress injuries which can be distracting during the simulation/flight and are difficult to recover from and may persist.
6) Direct video AND voice contact with sports instructors during several ARED sessions, early, mid and later in the mission, for effective exercise and to prevent injuries due to incorrect body positions and movements.
7) Video clips of each ARED exercise, easily accessible before the session, with warnings for wrong positioning.
8) More DEXA scans after flight to determine bone density recovery.

Appendix D

Papers in Special Issue of *Manual Therapy* journal 2016

Topics:

1. Editorial – Stokes M, Evetts S, Hides J

2. Systematic Review of countermeasures to minimise physiological changes and risk of injury to the lumbopelvic area following long-term microgravity.
   Winnard A, Nasser M, Debuse D, Stokes M, Evetts S, Wilkinson M, Hides J, Caplan N

3. The role of Physiotherapy in the European Space Agency strategy for preparation and reconditioning of astronauts
   Lambrecht G, Petersen N, Weerts G, Evetts S, Stokes M, Hides J

4. Service Evaluation of the European Space Agency Reconditioning Programme
   Petersen N, Lambrecht G, Weerts G, Hirsch N, Evetts S, Stokes M, Hides J

5. Lessons for postflight reconditioning from terrestrial rehabilitation and *vice versa*
   Hides J, Ramdharry G, Cusack R, McKay C, Stokes M (2016b)

6. Psychological aspects of postflight reconditioning for astronauts
   McKay C & Standridge M

7. Methodology for astronaut reconditioning research
   Beard D & Cook J

8. The influence of exercise using the Functional Re-adaptive Exercise Device on lumbopelvic kinematics in healthy and low back pain populations
   Winnard A, Debuse D, Wilkinson M, Bayat R, Caplan N

APPENDIX E

List of Abbreviations

AFA	Astronaut Functional Fitness Assessment
AMOSI	Astronauts and Medical Operations specialists involvement
ARED	Advanced Resistive Exercise Device
BDC	Baseline Data Collection
BMD	Bone Mineral Density
BW	Body Weight
CEVIS	Cycle Ergometer with Vibration Isolation and Stabilisation
CIM	Critical Illness Myopathy
CIP	Critical Illness Polyneuropathy
CM	Countermeasure
CMWG	Countermeasure Working Group
CO2	Carbon dioxide
COLBERT/T2	Combined Operational Load Bearing External Resistance Treadmill
COMP	Serum Oligomeric Matrix Protein
DEXA	Dual Energy X-ray Absorptiometry
EMG	Electromyography
ESA	European Space Agency
EVA	Extravehicular Activity
EVMU	Extra-Vehicular Mobility Unit
FES	Functional Electrical Stimulation
FFT	Functional Fitness Test
FIFA	Federation Internationale de Football Association
FMS	Functional Movement Screen
FRED	Functional Readaptive Exercise Device
FTT	Functional Task Test
GBS	Guillain Barre Syndrome
HR	Heart Rate
IAASS	International Association for Advancement of Space Safety
ICF	International Classification of Functioning, Disability and Health
ICM	Inflight Countermeasures
ICU	Intensive Care Unit
IDEAL	Idea, Development, Exploration, Assessment, Long-term Follow-up (in research)
iRED	Interim Exercise Device
ISS	International Space Station
IVD	Intervertebral Disc
L3	3rd Lumbar Vertebra
LSAH	Lifetime Surveillance of Astronaut Health
LBP	Low Back Pain
LDBR	Long Duration Bed Rest
LDEM	Long Duration Exploration Missions
LEO	Low Earth Orbit
MIC	Minimal Important Change
MID	Minimal Important Difference
MMP-	Matrix-metalloprotease-
MRI	Magnetic Resonance Imaging
n	Sample Size
NASA	National Aeronautics and Space Administration
NEMS	Neuromuscular Electrical Stimulation
NHS	National Health Service
NIHR	National Institute for Health Research
NMD	Neuromuscular Disease
NMSK	Neuro-musculoskeletal

O2	Oxygen
OA	Osteoarthritis
OI	Orthostatic Intolerance
PC	Preconditioning
PPI	Patient and Public Involvement
PR	Public Relations
PROMS	Patient Reported Outcome Measures
R&D	Research and Development
R+13	13 days following re-entry
R+19	19 days following re-entry
RCT	Randomised Controlled Trials
RM	Repetition Maximum
RUSI	Rehabilitative Ultrasound Imaging
SDM	Short Duration Mission
SPE	Surface Planetary Excursion
STS	Shuttle Transportation System
TEVIS	Treadmill with Vibration Isolation and Stabilisation
TT	Topical Team
UK	United Kingdom
US	United States of America
USOS	United States Orbital Segment
VO2max	Maximal Oxygen Consumption
WHO	World Health Organisation
µG	Microgravity

Measurement Units

cm	centimetres
d	day(s)
G	gravitational constant
Gz	vertical gravity (acceleration load)
hr	hour(s)
kg	kilogram
m	metre
min	minute(s)
ml	millilitres
mmHg	millimetres of mercury

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