Risks and Countermeasures for the Musculoskeletal systems in the Extreme Environment of Aviators and Astronauts

Rujman Khan¹, Daphne Ryan², Ryan Keller¹, Reece Rosenthal¹, Radina Khalid³, Jeffrey Jones

¹Baylor College of Medicine, Center for Space Medicine, Houston, TX, USA
²Naval Health Clinic Oak Harbor, Washington, USA
³Rice University, Chemical and Biomolecular Engineering, Houston, TX, USA

Correspondence should be addressed to Jeffrey Jones; Jeffrey.Jones9@va.gov

Received date: April 20, 2021, Accepted date: June 04, 2021

Abstract

There are many bodily risks associated with the high-performance environment of military aviation and spaceflight. With the advent of faster jet aircraft and rocket engines, the risk for injury to aircrew from hypoxia, g-loading, vibration and poor posture for extended periods of time has increased. As a result of the microgravity environment of space, there are significant orthopedic changes in humans. Specifically, the excessive osteoclast activity producing bone demineralization, and muscle atrophy in load-bearing regions of the body, are of greatest concern.

Lumbar back pain and skeletal muscle wasting can be decreased, but not completely prevented, with resistive exercise. Cervical pain after flight can be substantially diminished with a specific program of physical therapy. Musculoskeletal pain in the cervical region can be mitigated in aviators and astronauts with specific stretching and resistive exercise that targets the neck and shoulder muscles. Bone loss can be decreased with pharmaceutical and nutritional interventions, as a compliment to resistive exercise. However, neither exercise, nor specific nutrient consumption alone, are sufficient to completely prevent the negative impacts that these extreme environments can bring; but they can work synergistically and thus decrease the amount of loss.

Introduction

Resistive Exercise in Astronauts on Prolonged Spaceflights provides partial Protection against Spaceflight-induced Bone Loss showed very promising data on measures that can be employed to preserve the bone and muscular health of astronauts. The value of the information from these measures of bone and muscular health is how they demonstrate the effectiveness of treatments for the damage that aviation and spaceflight can induce in the musculoskeletal system [1].

Risks and Effects

Flying in Jets

Military aviation, especially when conducted in high performance jet aircraft (HPJA), produces defined unique stressors on structural elements of the human body. In addition, because many astronaut pilots and commanders are prior military HPJA aircrew, it becomes even more important to consider the physiologic implications of jet flight. Pilots are exposed to a large amount of both physical and mental stress during training and duty, and because of this selection pressure, pilots are typically young and fit compared to the general population [2]. New generations of fighter aircraft have pushed both planes and aviators to the limits of their capabilities, such that even young and fit pilots are prone to injuries that occur as a result of flight.

The high G-force maneuvers and rapid forces that act upon pilots are detrimental to the spinal cord and neck. The large magnitude of forces that a pilot experiences compounded with the small cockpit dimensions and
suboptimal seating posture of HPJAs place an above-average amount of stress on the musculoskeletal system [3]. Figure 1 illustrates the suboptimal seating posture that pilots must take in HPJAs. Compared with figure 2, it becomes apparent why many hours of flight in this position can create injuries. Neck and low back pain is experienced by 45-89% of aircrew [4-7]. For example, F/A-18 aircrew endure landings at 600 feet per minute, with a quick acceleration of the head-on-neck to the left increasing compressive loading into combined planes and the Z-axis [8]. Pilots of F/A-18 are unable to remove Joint Helmet Mounted Cueing Systems (JHMCS) during flight, which further obstructs full biomechanics of the cervico-thoracic spine in flight [9]. The check-six pilot position as seen in figure 3 puts cervical nerves and joints at risk during times of head compression when loading the jet. Cervical and lumbar spinal injuries are common amongst aviators, with estimates suggesting that up to 50% of pilots experience in-flight or post-flight spinal pain [10]. In centrifuge training alone, 2.3% of pilots experienced spinal injury, with a clear correlation between the occurrence of injury and the magnitude of forces endured [11].

Forward Head Posture (FHP) is also known as slump sitting. It is the standard position of aircrew and desk workers. Nachemson studied the relative pressure changes of the L3 vertebral disc in relative positions [12]. Forward head sitting and slumped sitting is associated with 185-275% more load to the disc, as shown in figure 4. The Nachemson chart has become well known in spine pain

Figure 1: Photograph of pilot’s Forward Head Posture maintained during flight. Provided by Dr. Daphne Ryan.

Figure 2: Comparison of Forward Head (slumped) Posture and Ideal Neutral Posture [72].

Figure 3: Check-six pilot position with canopy raised, used to spot tailing aircraft. Provided by Dr. Daphne Ryan.

Figure 4: Comparison of Disc Pressure and Posture [73].
circles, and speaks to neck and back pain issues associated with aircraft operation. Reclining sitting reduces pressure by 50-80%, as in the F-35, while forward slumped sitting increases pressure by over 100%, and forward leaning with rotation increases intra-discal pressure by 400% [13]. This is why the unloading position is used by Escamilla et al., and why we used them on the flight line [14]. These loads to the spine require specific interventions to treat the spine muscles that fatigue. We need to address the concept of tensegrity in spine rehabilitation in addition to focusing on pain. Tensegrity is a concept of tension plus integrity, a term originally used by Buckminster Fuller. Aviation interventions for spine pain need to understand that strengthening, not necessarily stretching, can mitigate the severity and intensity of injuries, and allow for more efficient recovery of tensegrity and reduction in pain.

Pain inhibits muscle activation because the motorneurons of a painful muscle are inhibited centrally [15,16]. Pain has been shown to lead to central sensitization, an overexcitability of nociceptor, causing prolonged symptoms. Fatigue limits the ability of a muscle to relax neurologically.

**Flying in space vehicles**

The human body did not evolve compensatory mechanisms to the microgravity environment of space. Our musculoskeletal system evolved as a countermeasure to gravity on Earth. The absence of gravity naturally leads to atrophy and dysfunction of those countermeasures. For example, the microgravity environment leads to a drop in bone mineral density (BMD) in astronauts, with the degree and type of which varying based upon the bone. Weight-bearing sections, including the pelvis, femur, and spine suffer the greatest loss of bone mass [17]. The mechanism of bone loss is thought to be increased bone resorption through changes in Wnt/B-catenin and RANKL:OPG mechanisms, along with changing levels of cytokines and morphogenic proteins [18]. From available data from previous astronauts, it is predicted that 62% of opposition class astronauts (400-600 day mission) and 100% of conjunction class astronauts (1000-1200) day missions will suffer from osteopenia while 33% will also be at risk for osteoporosis [19]. Considering the duration of a mission to Mars will be at least in the opposition class, this raises significant concerns for the health of those crewmembers and the viability of the mission.

Whole Body vibration is a risk to be taken into consideration for astronauts but does not pose as much of a continuous threat compared to Rotor Wing Aircraft (RWA) and High-Powered Jet Aircraft crew (HPJA). The only times astronauts will be exposed to this would mainly be during takeoff and landing or other instances when thrusters are ignited. Intense vibrations can affect crew through fatigue, microtrauma, nerve impingement, ligamentous injury, and degenerative changes [20,21]. Though no significant injuries have been specifically linked to this it could be more of a threat after BMD and muscle mass loss on long term missions that have their own return launches and landings.

When it comes to muscle atrophy, microgravity, similar to strict bedrest, eliminates the need for a hypertrophied muscular system since there is significantly less force needed to complete the same actions in space as opposed to gravitational influence. This phenomenon tends to precede BMD loss [22] and symptoms including fatigue, weakness, and loss of coordination are apparent after as little as a 1–2-week mission [23]. In a study of trunk skeletal muscle size measured by CT, it was reported that in missions spanning 4–6 weeks, astronauts experienced 5% muscle wasting on average, which is equivalent to about 10 years of aging on Earth [24]. Muscle groups that are primarily affected are postural muscles and ambulation muscles. When comparing atrophy in lower leg muscle groups, plantarflexors (medial gastrocnemius and soleus) exhibited a higher rate of atrophy than the dorsiflexors (specifically tibialis anterior), theorized to be due to the antigravitational purpose of the plantarflexors [25]. Changes to the posture and ambulation muscle groups should be further studied as astronauts will need their support when landing on another planetary body.

**Symptoms**

Lumbar and cervical spinal injury typically manifests as neck and back pain, sometimes associated with stiffness, in the peri- and post-flight periods [10,11]. Repeated injury often leads to impairment and decreased mobility, leading some to have difficulty performing activities of daily living. Chronic impairment can also affect an aviator’s ability to perform job-related tasks, which in severe cases may disqualify an individual for duty.

With regard to space travel, severe symptoms from BMD loss (fractures) have yet to be definitively linked to microgravity, although there have been 2 major fractures postflight in long duration crewmembers [26]. Herniated nucleus pulposus (cervical and lumbar) is common after spaceflight [27]. Symptoms from muscular atrophy have been common in astronauts with back pain (termed space-adaptation back pain {SABP}) being one of the most common with an incidence of 52-68% [26]. Ramachandran et al. has put together a detailed paper listing reports and statistics of detailed injuries experienced at all stages of spaceflight. In addition to back problems, a large portion of the injuries listed during flight included those of the fingers and upper extremities with many of them resulting from EVAs. Post flight injuries were also gathered in that same paper with spinal destabilization, muscle weakness,
ligamentous, cartilage, soft tissue, and fracture injuries all present in the astronaut population [26].

**Countermeasures – Prophylaxis/Prevention Results**

**Exercise**

Preservation of lumbar spine muscles may be a preventative measure towards lower back pain (LBP) related to spaceflight. Use of an advanced restrictive exercise device (ARED) significantly increased postflight bone densitometry [28]. When paired with bisphosphate alendronate, it was shown to be even more effective [1]. A recent study analyzed the preflight, postflight, mid-reconditioning, and post reconditioning of the lumbar multifidus (LM) cross-sectional area. This study reported that individualized exercise regimens to strengthen LM muscles did not mitigate, but reduced LM wasting [29]. Spring-loaded horizontal jumping as a form of exercise is being investigated as a possible way to mitigate lumbopelvic wasting, and may be comparable to vertical jumping on Earth [30]. Unfortunately, simple exercise may not be sufficient prophylaxis.

McNamara et al. in 2019 studied whether International Space Station (ISS) astronauts developed changes to their cervical muscle following long exposure to microgravity [31]. Sibonga et al. in 2016 reported that bed rest studies showed that there was no significant wasting in neck muscles, and this study supports this [1]. This study also reported a novel finding that there was an increase in cross-sectional areas in the trapezius, semispinalis capitis, rhomboid minor, and sternocleidomastoid, which may be due to the daily use of those muscles in microgravity [31]. Lower back pain is of greater concern in astronauts, whereas neck pain, is of greater concern for aviators. Regular exercise of the neck for strength and endurance was studied in a helicopter crew and was found to be beneficial [32]. Rausch et al. reported on a 12-week whole body training program, consisting of emphasis on neck, shoulder, and abdominal muscles that could be performed anywhere with minimal equipment. This regimen was studied in HPJA personnel to determine whether neck muscles could be built with minimal equipment for aviator needs. At the end of the study, a significant increase in muscle volume and strength was noted [33]. In another randomized control trial, normal exercise training regimens for military pilots were compared to a regimen that contained the same normal training plus training that emphasized neck muscle. There was a decrease in apparent neck pain and increased functionality of neck and shoulder muscles [34]. NECK X®, depicted in figure 5, is a patented portable cervical exercise device (PCED) device based on our previous research to strengthen neck muscles for military pilots [21]. Usage of this device in the prescribed physical therapy has been effective in reducing strain for pilots [21]. Literature review shows clearly that exercising the neck and shoulders can help mitigate neck pain that can ultimately make pilots unable to fly any more.

**Pharmacologic**

We previously reported that taking bisphosphate supplements, specifically bisphosphate alendronate (Fosamax®), may be beneficial in preventing bone loss in space flight when paired with advanced restrictive exercise [1,35]. Due to medical requirements, it is not possible to test whether the benefit of bisphosphate supplementation works synergistically or in additive fashion with advanced restrictive exercise in space flight. Recent studies on land imply that alendronate may inhibit bone formation [36], though this may only be at higher or toxic dosages, and the benefits are still present in lower concentrations [37]. While alendronate is currently used to treat osteoporosis, much research is devoted to alternative treatments that would inhibit Receptor Activator of Nuclear Factor Kappa-B ligand (RANKL), which, when functioning normally, can induce osteoclast differentiation. In terms of bisphosphates, a recent study shows that fructose 1,6-bisphosphate (FBP) can inhibit RANKL [38] and should be further explored for astronauts and aviators.

---

**Figure 5:** Portable cervical exercise device (PCED) used for physical therapy of HPJA aviators to strengthen neck muscles.
There are additional bisphosphonates which can have a role in our patient population studies. A yearly 5 mg infusion of Zoledronic Acid (Reclast®) has been shown to increase BMD in women with osteoporosis by 6.71% in the lumbar spine, 6.02% in the hip, and 5.06% in the femoral neck all compared to the placebo after a 3-year trial [39]. The effective annual dose in this study would be great for a long-term mission with limited space for medications. As with most bisphosphonates, there is a warning for renal impairment, atrial fibrillation, and osteonecrosis, but those occurrences were primarily in groups with predisposing risk factors including chronic kidney disease, for which astronauts are already screened. In a 52-week study comparing Alendronate (ALN) to Ibandronate (IBN), it was concluded that monthly intravenous IBN showed a statistically significant increase in BMD but there was also a significant increase in adverse effects (pyrexia, myalgia, nausea) [40]. While a monthly dosage is useful and higher BMD is the goal for countermeasures in flight, a higher incidence of adverse effects should indicate a risk analysis for viability of IBN as an acceptable option. For Pamidronate (PMD), a records analysis of 70 women in Brazil who were treated with PMD for osteoporosis showed a significant gain in BMD in the spinal column, but there was no concurrent gain in BMD of the femur [41]. It was also noted that there was elevated PTH levels in some of the patients which was correlated with lower femoral BMD [41]. Another study showed that in a retrospective cohort of 74 postmenopausal women, a placebo group showed elevated spine, hip, and femur BMD compared to a group treated with PMD [42]. These studies do not indicate that PMD is as strong of a candidate for countermeasures until some more promising data is produced. Finally, Etidronate (ETN) is a non-nitrogen bisphosphonate investigated for osteoporotic treatment. However, it was found that compared to the nitrogenous bisphosphonates (alendronate or risedronate), ETN has less, if any, reduction in mortality as well as a weaker effect on bone loss reduction [43]. Given that this directly compares ETN to others described and showed a weaker effect, unless more evidence is found for this drug, priority should be given to others.

There are many prospective treatments being studied that impact the cascade that leads to RANKL-induced activation of osteoclasts and bone reabsorption. One such prospective treatment is 4-acetylanthroquinonol B (4-AAQB). In microgravity models, 4-AAQB shows promise as a pharmaceutical intervention to prevent the bone loss experienced in space [44]. Another is isovaleric acid (IVA). When added to the drinking water of mice, it was shown to decrease bone destruction and osteoclast differentiation in the presence of RANKL-activated osteoclasts [45]. In another study, beta-hydroxy-beta-methyl butyrate was shown to promote bone growth in pigs [46]. Both IVA and beta-hydroxy-beta-methyl butyrate are leucine derivatives. This may indicate that a diet rich in leucine can act as a protective measure for bone health [45].

**Dietary**

Spaceflight requires different nutrition in comparison to lower-orbit aviation. Diets high in omega-3 fatty acids, derived from eating plentiful fish, is linked to increased bone density preservation from spaceflight [47,48]. Omega-3 fatty acid ingestion may also curb inflammation in spaceflight, further decreasing bone loss by immune regulation of osteoclasts [47,48]. Fish oil paired with curcumin is implicated to have benefits in maintaining skeletal muscle mass in spaceflight [49].

Other necessities in diet include to protect bone health are increased calcium and vitamin D intake [50]. On land, these are highly used to prevent osteoporosis. However, studies of their benefits in space show mixed results. It is vital to consume calcium for bone growth. Absorption of calcium from the gut tube relies on vitamin D. However, high intake of calcium did not impact bone turnover in bed rest studies [51]. When studied in astronauts, high intake of both calcium and vitamin D did not impact bone loss [52,53]. However, all of these studies were conducted in small sample sizes. Future studies with larger sample sizes may change our understanding. It is also important to note that aviators and astronauts are at higher risk for renal stone formation, and reducing bone degradation may decrease this risk, and urinary alkalinization with potassium citrate may reduce it even further [54].

The common intuitive step to prevent skeletal muscle breakdown is increased amino acid intake. Leucine derivatives may be protective for bone health [40,41]. Unfortunately, studies show increased protein intake is also linked to hypercalciuria [55,56]. This is due to higher acidity in diets high in amino acids, so one proposed solution is to supplement with alkaline agents. Potassium bicarbonate was used in a bed rest study in an attempt to prove the efficacy of such a treatment. Unfortunately, it failed to deter bone resorption [57]. Plant-based protein intake may have decreased associated bone resorption, though further studies need to be conducted [58].

**Post-Exposure Treatment**

Neck and low back pain in aviation and spaceflight occurs in 56-89% of flight crew [4,21]. The spine and its structures function via a concept known as tensegrity, perhaps better known as “core” [59-61].

The muscle tightness one feels does NOT indicate a need for static stretching, especially after prolonged positioning. Cervical and lumbar spine muscles turn off when they are...
Figure 6: Illustrates the cervical musculature and associated force velocity curves [74].
in pain and decrease their cross-sectional area [14,62]. A fatigued muscle warrants rehabilitation exercise more than stretching with static holds [61]. Strengthening of spine muscles does not happen with increased exposure to G-forces, but the muscles fatigue [4,63,64].

Airplanes and aircrew share a common limitation: the plane and the body have various regions where they can perform safely before reaching fatigue or failure [59].

**Physical therapy toolboxes**

Exercise is a broad term and needs to be defined for the aerospace organizations when discussing wholistic health and healing [65]. Aviation specific injuries need aviation specific interventions to deep spine muscles to effectively treat pain.

When deep neck flexors and extensors get stronger, neck pain reports go down [21,66,67]. When the neck is unloaded while activating deep spine stabilizers, aircrew reported minimal to no residual pain, and there was greater muscle activation. Prone positioning during isometric interventions feels better to the person, as confirmed by F/A-18 aircrew.

Low back pain can be mitigated by strengthening hip abductors, as pain was reduced and multifidus muscle size increased [68]. Multifidus activation was enhanced more with hip abduction interventions rather than flexion or extension activities. Sacroiliac pain and lumbar pain are reduced with activation of hip abductors as joint force closure is facilitated. When subjects were asked to stop stretching the hamstring to rest the S1 dural sheath, and to facilitate hamstring strength, they got better within the NASWI fast jet and rotary wing community.

F/A-18 aircrew confirm they were able to apply specific aviation biomechanical rehabilitation interventions independently and effectively while deployed. “I don’t always do these exercises. But when I hurt, I do them, and my pain goes away,” reported a VAQ 135 pilot. One session of specific spine stabilizing exercises reduced neck and back pain by 50-100% in five out of six F/A-18 aircrew following dynamic flights, and without equipment. Addressing the neurological fatigue of specific neck and low back muscles shortly after end of flight, prior to debrief, reduced pain, improved sense of wellness, and mitigated musculoskeletal risks to mission readiness. Loading of the spine in the Z-axis has significant consequences to astronauts, RWA, and HPJA.

The lumbar pain that occurs in flight with spinal elongation in microgravity and the subsequent post-flight risk of injury with degraded posterior neck and spinal musculature in astronauts is addressed with a well-defined inflight exercise program and post-flight rehabilitation schedule, which includes hydrotherapy, exercise, and multi-modalities to address extensor weakness and joint discomfort.

**Culture change for pain management**

Neck and low back pain after jet and space flight have been researched such that the evidence effectively anchors changes for future interventions. Consistency of interventions needs to be a priority, and so does trust. They no longer fear flight disqualification because they have developed trust that their spinal pain or injury can be treated effectively by providers [69,70]. This is a culture issue, and international aviation and spaceflight partners have designated mandated time in the workday for prehabilitation and rehabilitation. The NATO 2020 report on Aircrew Neck Pain Prevention and Management notes 24-hour access to aviation specialty physiotherapists with aviation specific training is imperative. The Aviation Physiotherapist and Astronaut Strength Condition and Rehabilitation (ASCR) specialist is able to deploy with the flight crew so the therapist's skilled resources are readily available, wherever duties take the flight crew.

Pain does not change with range of motion capacity, but less pain changes range of motion willingness. Pain does, however, correspond to neurological fatigue of muscles. Aviation members are mentally and physically exhausted after 12-14 hour shifts. Fighter Pilots had decreased symptoms and maintained endurance of spine muscles when compliance was integrated into the daily work culture. Those who had a culture that wasn’t reinforced got weaker over 6-8 months [71].

Flight crew are having their pain managed rather than being treated in the same fashion we would condition a non-painful athlete. Aircrew cannot be asked to manage neck or back pain well when they are placed in the slumped position or forward head posture before they leave the ground. The newer military fighter (e.g. F-35) seat allows for a reclined position.

**Conclusion**

The aerospace environmental stressors are unique with G-loading in some phases of flight and unloading in others, along with specific body posture configurations and in-flight tasking can render predictable symptoms and injuries in flight crewmembers. Countermeasures for muscle and bone mineral and architectural losses include dietary, pharmacologic, and targeted exercise approaches.

Fast jet aircrew are now empowered to use a specific combination of spine stabilizing strengthening exercises when they need to decrease neck and back pain. Successful
treatment is determined by the individual if pain is decreased. Interventions are done without equipment, in an unloaded position and isometric, painless, and affect the neurological inhibition of the spine stabilizers. A specific combination of exercises that facilitate activation of spine muscles have proven effective and efficient for reducing pain in many types of space, fixed-wing and rotary flight craft.

Dietary choices with designed protein sources that provide the optimal amino acid support will limit acid load (e.g. by monitoring sulfate moieties which reduce to sulfuric acid) that leaches valuable bone phosphate buffers, and thereby preserve bone mineral content [55].

The evidence base of safety and efficacy for the use of several medical agents, as studied in both bedrest analogs and spaceflight, is growing; such that bisphosphonates and potassium citrate can be employed during long duration space missions [1,54]. Additional studies with rank-ligand inhibitors should provide a safe alternative to bisphosphonates with additional study. Customized resistive exercise provides an effective means to preserve muscle mass, enhance structural stability and limit bone architectural changes, especially in trabecular bone. Fast jet and rotary wing communities are decreasing pain and improving mission readiness with customized stabilization protocols.

The aerospace medicine model of primary and secondary prevention can now be further expanded to include “whole person health with whole person healing” which will direct us towards the culture change needed to achieve maximal performance across our aerospace community.

Acknowledgements

We would like to acknowledge Sawan Dalal, Daniel O’Conor, Vignesh Ramachandran, Dr. Barry Shender, and Dr. Bethany Shivers for their assistance and support of projects associated with this manuscript.

References

1. Sibonga J, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford L, et al. Resistive exercise in astronauts on prolonged spaceflights provides partial protection against spaceflight-induced bone loss. Bone. 2019 Nov 1;128:112037.

2. Summerfield D, Raslau D, Johnson B, Steinkraus L. Physiologic challenges to pilots of modern high performance aircraft. Aircraft Technology. 2018 Sep 12:43-73.

3. Rintala H, Häkkinen A, Siitonen S, Kyröläinen H. Relationships between physical fitness, demands of flight duty, and musculoskeletal symptoms among military pilots. Military Medicine. 2015 Dec 1;180(12):1233-8.

4. Posch M, Schranz A, Lener M, Senn W, Äng BO, Burtscher M, et al. Prevalence and potential risk factors of flight-related neck, shoulder and low back pain among helicopter pilots and crewmembers: a questionnaire-based study. BMC Musculoskeletal Disorders. 2019 Dec;20(1):1-0.

5. Slungaard E, Green ND, Newham DJ, Harridge SD. Content validity of level two of the Royal air force aircrew conditioning programme. Aerospace Medicine and Human Performance. 2018 Oct 1;89(10):896-904.

6. Kikukawa A, Tachibana S, Yagura S. G-related musculoskeletal spine symptoms in Japan Air Self Defense Force F-15 pilots. Aviation, Space, and Environmental Medicine. 1995 Mar 1;66(3):269-72.

7. Lange B, Toft P, Myburgh C, Sjögaard G. Effect of targeted strength, endurance, and coordination exercise on neck and shoulder pain among fighter pilots: a randomized-controlled trial. The Clinical journal of pain. 2013 Jan 1;29(1):50-9.

8. Green ND. Acute soft tissue neck injury from unexpected acceleration. Aviation, space, and environmental medicine. 2003 Oct 1;74(10):1085-90.

9. Sovelius R, Mäntylä M, Heini H, Oksa J, Valtonen R, Tiitola L, et al. Joint helmet-mounted cueing system and neck muscle activity during air combat maneuvering. Aerospace Medicine and Human Performance. 2019 Oct 1;90(10):834-40.

10. Jones JA, Hart SF, Baskin DS, Effenhauser R, Johnson SL, Novas MA, et al. Human and behavioral factors contributing to spine-based neurological cockpit injuries in pilots of high-performance aircraft: recommendations for management and prevention. Military Medicine. 2000 Jan 1;165(1):6-12.

11. Kang KW, Shin YH, Kang S. Acute spinal injury after centrifuge training in asymptomatic fighter pilots. Aerospace Medicine and Human Performance. 2015 Apr 1;86(4):386-91.

12. Nachemson A. The effect of forward leaning on lumbar intradiscal pressure. Acta Orthopaedica Scandinavica. 1965 Jan 1;35(1-4):314-28.

13. Nachemson AL. Disc pressure measurements. Spine. 1981 Jan 1;6(1):93-7.

14. Escamilla RF, Lewis C, Pecson A, Imamura R,
26. Ramachandran V, Dalal S, Scheuring RA, Jones JA. Musculoskeletal injuries in astronauts: review of pre-flight, in-flight, post-flight, and extravehicular activity injuries. Current Pathobiology Reports. 2018 Sep;6(3):149-58.

27. Johnston SL, Campbell MR, Scheuring R, Feiveson AH. Risk of herniated nucleus pulposus among US astronauts. Aviation, Space, and Environmental Medicine. 2010 Jun 1;81(6):566-74.

28. Loehr JA, Lee SM, English KL, Sibonga J, Smith SM, Spiering BA, et al. Musculoskeletal adaptations to training with the advanced resistive exercise device. Medicine & Science in Sports & Exercise. 2011 Jan;43(1):146-56.

29. Hides JA, Lambrecht G, Sexton CT, Pruet C, Petersen N, Jaekel P, Rosenberger A, et al. The effects of exposure to microgravity and reconditioning of the lumbar multifidus and anterolateral abdominal muscles: implications for people with LBP. The Spine Journal. 2021 Mar 1;21(3):477-91.

30. Jones EJ, Kennett JE, Green DA. Spring-loaded body mass equivalent horizontal reactive countermovement jump ground contact and flight times, but not peak forces, are comparable to vertical jumping. Journal of Biomechanics. 2021 Feb 12;116:110206.

31. McNamara KP, Greene KA, Tooze JA, Dang J, Khattab K, Lenchik L, Weaver AA. Neck Muscle Changes Following Long-Duration Spaceflight. Frontiers in physiology. 2019 Sep 13;10:1115.

32. Salmon DM, Harrison MF, Sharpe D, Candow D, Albert WJ, Neary JP. Exercise therapy for improved neck muscle function in helicopter aircrew. Aviation, Space, and Environmental Medicine. 2013 Oct 1;84(10):1046-54.

33. Rausch M, Weber F, Kühn S, Ledderhos C, Zinner C, Sperlich B. The effects of 12 weeks of functional strength training on muscle strength, volume and activity upon exposure to elevated G z forces in high-performance aircraft personnel. Military Medical Research. 2021 Dec;8(1):1-9.

34. Murray M, Lange B, Sogaard K, Sjøgaard G. The effect of physical exercise training on neck and shoulder muscle function among military helicopter pilots and crew: A secondary analysis of a randomized controlled trial. Frontiers in Public Health. 2020;8.

35. Leblanc A, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford L, Smith SM, Evans H, Spector E, Ploutz-Snyder R, Sibonga J. Bisphosphonates as a supplement to
exercise to protect bone during long-duration spaceflight. Osteoporosis international. 2013 Jul;24(7):2105-14.

36. Jensen PR, Andersen TL, Chavassieux P, Roux JP, Delaisse JM. Bisphosphonates impair the onset of bone formation at remodeling sites. Bone. 2021 Apr 1;145:115850.

37. Hedvičáková V, Žižková R, Buzgo M, Rampačová M, Filová E. The Effect of Alendronate on Osteoclastogenesis in Different Combinations of M-CSF and RANKL Growth Factors. Biomolecules. 2021 Mar;11(3):438.

38. Wilches-Buitrago L, Viacava PR, Cunha FQ, Alves-Filho JC, Fukada SY. Fructose 1, 6-bisphosphate inhibits osteoclastogenesis by attenuating RANKL-induced NF-κB/NFATc-1. Inflammation Research. 2019 May;68(5):415-21.

39. Dhillon S. Zoledronic acid (Reclast®, Aclasta®): a review in osteoporosis. Drugs. 2016 Nov;76(17):1683-97.

40. Horikawa A, Miyakoshi N, Hongo M, Kasukawa Y, Kodama H, Shimada Y. A prospective comparative study of intravenous alendronate and ibandronate for the treatment of osteoporosis. Medicine. 2019 Feb;98(6).

41. Zanatta LB, Marcatto C, Ramos CS, Mañas N, Moreira C, Borba V. Use of pamidronate for osteoporosis treatment in public health care in Brazil. Revista brasileira de reumatologia. 2017 Dec;57(6):514-20.

42. Koo YA, Son KA, Choi SJ, Yoon BK. Effects of Adding Intravenous Pamidronate to Ongoing Menopausal Hormone Therapy in Postmenopausal Korean Women with Low Bone Mineral Density. Journal of Menopausal Medicine. 2019 Dec 1;25(3):117-22.

43. Bluuc D, Tran T, van Geel T, Adachi JD, Berger C, van den Bergh J, Eisman JA, Geusens P, Goltzman D, Hanley DA, Josse R. Reduced bone loss is associated with reduced mortality risk in subjects exposed to nitrogen bisphosphonates: A mediation analysis. Journal of Bone and Mineral Research. 2019 Dec 1;25(3):117-22.

44. Wu CH, Ou CH, Yen I, Lee SY. 4-Acetylantroquinonol B Inhibits Osteoclastogenesis by Inhibiting the Autophagy Pathway in a Simulated Microgravity Model. International Journal of Molecular Sciences. 2020 Jan;21(18):6971.

45. Cho KM, Kim YS, Lee M, Lee HY, Bae YS. Isovaleric acid ameliorates ovariectomy-induced osteoporosis by inhibiting osteoclast differentiation. Journal of Cellular and Molecular Science. 2021 May;25(9):4287-97.

46. Blicharski T, Tomaszewska E, Dobrowolski P, Hulas-Stasiak M, Muszyński S. A metabolite of leucine (β-hydroxy-β-methylbutyrate) given to sows during pregnancy alters bone development of their newborn offspring by hormonal modulation. PLoS One. 2017 Jun 15;12(6):e0179693.
SR, Biolo G, Smith SM. Effects of high-protein intake on bone turnover in long-term bed rest in women. Applied Physiology, Nutrition, and Metabolism. 2017;42(5):537-46.

57. Frings-Meuthen P, Bernhardt G, Buehlmeyer J, Baeker N, May F, Heer M. The negative effect of unloading exceeds the bone-sparing effect of alkaline supplementation: a bed rest study. Osteoporosis International. 2019 Feb;30(2):431-9.

58. Gao R, Duff W, Chizen D, Zello GA, Chilibeck PD. The effect of a low glycemic index pulse-based diet on insulin sensitivity, insulin resistance, bone resorption and cardiovascular risk factors during bed rest. Nutrients. 2019 Sep;11(9):2012.

59. Ingber DE, Wang N, Stamenović D. Tensegrity, cellular biophysics, and the mechanics of living systems. Reports on Progress in Physics. 2014 Apr 2;77(4):046603.

60. Kumar S, Maxwell IZ, Heisterkamp A, Polte TR, Lele TP, Salanga M, et al. Viscoelastic retraction of single living stress fibers and its impact on cell shape, cytoskeletal organization, and extracellular matrix mechanics. Biophysical Journal. 2006 May 15;90(10):3762-73.

61. Korhonen RK, Saarakkala S. Theoretical biomechanics. In: Theoretical biomechanics. Intech. 2011; pp. 5-130.

62. Wan Q, Lin C, Li X, Zeng W, Ma C. MRI assessment of paraspinal muscles in patients with acute and chronic unilateral low back pain. The British Journal of Radiology. 2015 Sep;88(1053):20140546.

63. Seng KY, Lam PM, Lee VS. Acceleration effects on neck muscle strength: pilots vs. non-pilots. Aviation, Space, and Environmental Medicine. 2003 Feb 1;74(2):164-8.

64. Sovelius R, Mäntylä M, Huhtala H, Oksa J, Valtonen R, Tiitola L, et al. Head movements and neck muscle activity during air combat manoeuvring. Aerospace Medicine and Human Performance. 2020 Jan 1;91(1):26-31.

65. Søgaard K, Jull G. Therapeutic exercise for prevention, treatment and rehabilitation of musculoskeletal pain and function. Manual Therapy. 2015 Oct 1;20(5):631-2.

66. Jull G, Falla D. Does increased superficial neck flexor activity in the cranio cervical flexion test reflect reduced deep flexor activity in people with neck pain?. Manual Therapy. 2016 Sep 1;25:43-7.

67. Blomgren J, Strandell E, Jull G, Vikman I, Röijezon U. Effects of deep cervical flexor training on impaired physiological functions associated with chronic neck pain: a systematic review. BMC Musculoskeletal Disorders. 2018 Dec;19(1):1-7.

68. Aboufazeli M, Afshar-Mohajer N, Jafaripisheh MS, Heidari M, Akbari M. Recovery of the lumbar multifidus muscle size in chronic low back pain patients by strengthening hip abductors: A randomized clinical trial. Journal of Bodywork and Movement Therapies. 2021 Apr 1;26:147-52.

69. Salmon DM, Harrison MF, Neary JP. Neck pain in military helicopter aircrew and the role of exercise therapy. Aviation, Space, and Environmental Medicine. 2011 Oct 1;82(10):978-87.

70. Truszczyńska A, Rapała K, Łukawski S, Trzaskoma Z, Tarnowski A, Drzal-Grabiec J, et al. Evaluation of functional outcomes in individuals 10 years after posterior lumbar interbody fusion with corundum implants and decompression: a comparison of 2 surgical techniques. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2014;20:1400-1406.

71. Alricsson, MA, Harms-Ringdahl K, Larsson B, Linder J, Werner S. Neck muscle strength and endurance in fighter pilots: effects of a supervised training program. Aviation, Space, and Environmental Medicine. 2004 Jan 1;75(1):23-8.

72. Strimpakos N. The assessment of the cervical spine. Part 2: strength and endurance/fatigue. Journal of Bodywork and Movement Therapies. 2011 Oct 1;15(4):417-30.

73. Norris CM. Managing sports injuries. A guide for students and clinicians. 4th ed. Butterworth Heinemann; 2011. p. 261.

74. Kuo C, Sheffels J, Fanton M, Yu IB, Hamalainen R, Camarillo D. Passive cervical spine ligaments provide stability during head impacts. Journal of the Royal Society Interface. 2019 May 31;16(154):20190086.