Human Research Program
Human Health Countermeasures Element

Evidence Book

Risk of Intervertebral Disc Damage

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Lyndon B. Johnson Space Center
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I. PRD Risk Title: Risk of Intervertebral Disc Damage

Description: Extended exposures to microgravity (and possibly fractional gravity) may lead to an increased risk of spinal nerve compression and back pain.

II. Executive Summary

There is an increased incidence of back pain expressed by crewmembers in space. Additionally, herniated Intervertebral Discs (IVD) have been diagnosed in returning Skylab and Shuttle astronauts on landing day, and after varying periods of time in the postflight period. Such injuries in astronauts, however, may be related to their careers as aviators (either high performance jet pilots and/or helicopter pilots). However, the evidence of IVD injuries raises the concern that astronauts are at increased risk during loading scenarios experienced during exploration missions (for example, re-entry to a gravitational field, activities on planetary surfaces).

To date, flight data related to potential back injuries have focused upon spine elongation and the well-established effects of mechanical unloading on intervertebral discs (IVDs). IVDs are the articulating connective tissue between vertebral bodies of the spinal column where the IVD acts as a shock absorber to the mechanical loads experienced in the axial direction. The connective tissue of joints is devoid of vasculature so the exchange of nutrients and waste products is accomplished by the influx and efflux of fluid. In general, the diurnal fluctuations in IVD volume of the spine are induced as the individual transitions between sleep (supine) and ambulation (upright), although the spine is subjected to a variety of mechanical forces with daily activities in 1 G. However, during prolonged bed rest or spaces flight, the absence of axial and muscular loading to the spine causes the IVDs to swell with increased fluid intake. Consequently, the changes in IVD volume are a major factor for the elongation of the spine, the increase in height, and the loss of lordotic curvature. It may also account for the occurrence of back pain, although the exact cause for the latter is not well defined. Tissue analyses of animals, mechanically unloaded in space and ground-based models, reveal changes in IVD biochemical composition. Spaceflight-induced changes to IVDs may predispose the IVD to injury during reloading. Currently there is no effective way to introduce axial loads to the human spine, during real or simulated weightlessness, as a means of restoring the diurnal changes in IVD volume. Restoration of IVD volume, after spaceflight and bed rest, has been observed with return to upright position in a 1-G environment, but the recovery time course has not been systematically assessed. Likewise, IVD biochemical and biomechanical properties, before and after spaceflight, have not been investigated.

In brief, extended exposures to microgravity are associated with increased reports of back pain during flight and may be related to the occurrence of disc herniations in astronauts after flight. The etiology for these observations may be multi-factorial given the number of documented physiological risk factors induced in space, which include muscle atrophy, tissue degeneration, bone fracture and accelerated bone loss. Thus, evidence to define the risk need further investigation.

Background

In a questionnaire survey of astronauts who had flown in space, sixty-eight percent of the population reported generalized back pain, with some astronauts rating the pain between severe to moderate (Wing, 1991). This discomfort is considered most painful early during the spaceflight but is attenuated as flight duration progresses. At face value, the cause of back pain in space may be associated to the elongation of the vertebral column by IVD expansion or to other causes. Lower back pain in humans, for example, is also associated with trunk muscle weakness (Dvir, 2003; Ho, 2005) suggesting that the reduced biomechanical forces from space-induced atrophy of lower back muscles may be a contributing factor. Alternatively, pain caused by IVD changes may be related to increased strain of proximal facet joint capsules (Moneta, 1994), fractured innervated vertebral end-plates (Boos, 1995; Hicks, 2002), disc degeneration (Straus, 2002), or herniation of annulus fibrosis (Collacott, 2000).

Irrespective of the exact cause of back pain, there may be an increased risk for IVD injury or damage when the swollen IVDs of crewmembers (under the weightlessness of transit) are subjected to excessive forces or torques while performing work on planetary surfaces. Exploration missions on planetary surfaces may introduce habitability issues that could induce excessive torsional stress, an established risk factor for herniation of annulus fibrosus (Farfan, 1970). For instance, excessive axial rotation could occur while carrying large masses in the partial G environment by a crewmember with de-conditioned back muscles and may consequently subject IVDs to lateral shear forces. Regardless, there are minimal data (medical evaluations or research) that characterizes the biomechanical and biochemical changes in IVDs in crewmembers during or after flight to assess how such changes predisposes the IVDs to injury under re-loading.

However, herniated nucleus pulposus *is* known to occur in aviators exposed to high G environments (Mason, 1996) and has occurred in astronauts after a mission. There were three separate occurrences of IVD injury on the day of landing as determined by chart reviews and personal communication with crewmembers and flight surgeons (medical chart reviews, personal communication). The relative risk rate of IVD injury in the astronaut population has only recently been evaluated (Johnston, manuscript in revision 2009). There is no evidence, however, connecting the origin of an IVD injury with changes in IVDs as a result of spaceflight – that is, morphological and biochemical changes in IVD composition.

Nevertheless, the results of this retrospective characterization of IVD injury in the astronaut population raises the concern that the spaceflight-induced changes to IVDs require further analyses. Additional evidence would describe the spaceflight-induced changes and elucidate how these morphological and biochemical changes predispose the nucleus pulposus to herniation during compressive loading. Based upon the IVD tissue analyses of unweighted animals, biochemical changes to the nucleus pulposus during spaceflight will affect the ability of the osmotic pressure and elasticity of the nucleus pulposus to resist compressive loading (Pedrini-Mille, 1992; Morey-Holton; 2002; Hutton, 2002). Biochemical changes in the IVDs of crewmembers after flight have not been identified. However, there is in vitro research with bovine cartilage explants to use magnetic resonance technology to correlate changes in IVD proteoglycan content with the T_{1rho} relaxation rates of protons (Wheaton, 2005). This biomarker will enable non-invasive monitoring of proteoglycan content as a method of assessing the biochemical impact of weightlessness.

Evidence-to-Date

Spaceflight Evidence

An early quantification of spine elongation during weightlessness was performed in a single astronaut during the 84-day Skylab 4 mission (Thornton, 1987). Changes in height were monitored during weightlessness (to the 1/16 in.) which described an asymptotic increase in height during flight that appeared to plateau 29 days into the flight. The absolute height change was 1.5 inches at the end of the mission. The increase in spine elongation is presumed associated with the expansion of IVDs during axial unloading. There was also a reported case of spine pain on landing day which was associated with herniated IVD (personal medical communication).

Astronaut Chart Review

The reports of several astronauts developing cervical or lumbar herniated nucleus pulposus (HNP) in the immediate period following landing on earth prompted a retrospective review by NASA flight surgeons to evaluate the incidence of IVD damage in the astronaut population (S. Johnston, manuscript in revision, 2009). The review sought to clarify whether spaceflight increased the risk for IVD damage because of (a) the exposure to both low- and high G environments during a mission; (b) the extended periods in an abnormal posture; and/or (c) the changes to IVD structure due to its expansion in the absence of axial loading in space. Specifically, this retrospective study compared the incidence of herniated nucleus pulposus (IVD damage) in astronauts to an age-matched control population of persons who have not flown in space. Although the postflight incidence of IVD damage in astronauts is apparent, it is unclear whether the spaceflight-induced changes predispose the IVDs to injury. In particular, evidence indicates that many of the injured astronauts had previous, multiple exposures to excessive G forces (between 6-20 G) as high performance jet pilots or to vibrating forces as helicopter pilots.

Notably, the pathophysiology of IVD injury after spaceflight has not been clearly identified. The documented expansion of disc volume after spaceflight, together with the IVD injuries after reloading in Earth's gravity, suggests that the adaptive changes of the IVD in weightlessness disrupts the balance between osmotic pressure of the nucleus pulposus and the resistive collagen structure of the annuli fibrosus, thereby reducing the ability of the IVD structure to withstand re-exposure to G forces. Repeated, previous exposures to excessive G forces in high performance jets, however, may have also weakened IVD structures, particularly in the cervical vertebrae, increasing the susceptibility of these IVDs to damage. Thus, the relative risk of spaceflight-induced IVD injury needs to be delineated by comparing the absolute risks of the astronaut population with that of a terrestrial control cohort with similar pilot flight history.

Ground-based Evidence

IVD volume changes were quantified by magnetic resonance imaging in response to varying scenarios of axial unloading (LeBlanc, 1994). The cross-sectional areas and the transverse proton relaxation constants (T2) of IVDs were indices used to monitor adaptive

changes of the IVDs to overnight bed rest (over 5 weeks and 17 weeks) and after 8 days of spaceflight. The averaged expansion of IVDs with bed rest appeared to reach an equilibrium anywhere between 9 hours and 4 days of unloading with the expansion ranging between 10-40% of baseline, pre-bed rest values (mean=22%). There were mild increases in T2 relaxation times relative to increases in disc area. Restoration of IVD volumes after unloading was not evaluated systematically but the Table (below) provides a relative comparison of the elapsed time in 1 G at which time the measured IVD volumes were no different from baseline measurements; the relative periods of recovery appear to lengthen as the period of IVD adaptation to unloading increases.

Table. Relative comparison of the elapsed time in 1 G

Period of Unloading	Relative Time before Recovery
8 days spaceflight	< 24 hours
5 weeks bed rest	days
17 weeks bed rest	> 6 weeks

Computer-Based Simulation Information

The literature reports the application of Finite Element Modeling (FEM) to IVDs under the lower osmotic pressure of the space environment. Under this scenario, FEM shows that the appearance of a crack in the IVD experiencing lower osmotic pressure will increase the IVD risk for injury (Wognum, 2006). Likewise, FEM was used to demonstrate that static loading alone will not promote fluid extrusion from IVDs swollen during bed rest or weightlessness. Fluid expulsion will increase with the increased frequency of loading (Cheung, 2003). Future work in this simulation capability needs to be pursued.

Risk in Context of Exploration Mission Operational Scenarios

Although evidence to define the etiology of back and IVD injury *remains an open issue*, the following assumptions and presumptions were consider when the risk was first evaluated in the context of exploration missions.

1. The absence of axial loading and of forces due to atrophy of back muscles may predispose crewmembers to IVD injury;
2. The risk of detrimental changes to back and to IVD structure and biochemistry will increase with increasing unloaded periods in weightlessness;
3. The risk for back injury and for IVD damage will be greater with the larger G forces experienced during re-entry, landing and surface activities.

Conclusion

In sum, reports in the literature suggest that adaptation to the space environment can directly or indirectly induce back pain and may increase the risk for injury when crewmembers are re-subjected to gravity enhanced mechanical forces and torques. Back pain is commonly reported by crewmembers during spaceflight and a chart review of 321

astronauts suggested there may be an increased risk for IVD injury in astronauts but this finding needs to explored further before an increased risk for injury during exploration missions can be defined. Mechanical unloading with spaceflight is associated with distortions in IVD morphology, alterations in biochemistry (proteoglycan and collagen content) and in reduced biomechanical forces of muscles. More evidence (clinical and bench research data) needs to be acquired in order to establish whether the lengthening of the spinal column with space adaptation syndrome, the atrophy of back muscles, the accelerated loss of bone mass and the degeneration of both skeletal and IVD tissue, due to space exposure, exacerbate the risk for back injury during and after spaceflight. Knowledge regarding the various loading activities during exploration missions and during return to earth needs to be well defined; identification of loads and torques shall be used in computer modeling to assess the probability of back and/or IVD injury.

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List of Acronyms

EVA	Extravehicular activity
FEM	Finite element modeling
GAG	Glycoaminoglycan
HNP	Herniated nucleus pulposus
IVD	Intervertebral discs
LSAH	Longitudinal Study of Astronaut Health
mRNA	Messenger Ribonucleic Acid
NASA-JSC	National Aeronautics Space Administration- Johnson Space Center
PRD	Program Requirements Document