



18th Meeting of the US/Russian Joint Working Group on Space Biomedical and Biological Sciences Research

**Moscow, Russia
December 8, 2016**

NASA Flight Research Overview

**NASA
HUMAN RESEARCH PROGRAM (HRP)
INTERNATIONAL SPACE STATION MEDICAL PROJECTS (ISSMP)
Steven H. Platts, Ph.D.
ISSMP Element Scientist**

Eighteen Active NASA ISS Research Studies

Biochem Profile
Bishposphonate Controls
Body Measures
Cardio OX
Dose Tracker
Field Test
Fine Motor Skills
Fluid Shifts
Functional Immune
Habitability
Intervertebral Disc Damage
Lighting Effects
Medical Consumables Tracking
NeuroMapping
Repository
Rx Metabolism
Sprint (Active)
Telomeres



Four Recently Completed NASA Research Studies

**Cognition
Microbiome
Ocular Health
Salivary Markers**

Six Research Studies Completing In-Flight Operations During the Current Increment 49-50 Mission

**Bisphosphonates (Control)
Body Measures
Cardio Ox
Fluid Shifts
Habitability
Telomeres**

Five Upcoming NASA Research Studies

**Behavioral Core Measures
Occupant Protection
One Carbon Poly
Spaceflight Standard Measures
Vertebral Strength**

Three Joint Research Studies



**Field Test
Fluid Shifts
MARES (Sarcolab 3)**



POCKOCMOC

Current NASA Research Studies

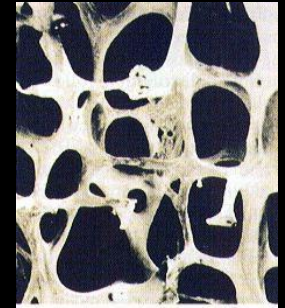


Bisphosphonates Controls

Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss

Adrian LeBlanc, Ph.D. and Toshio Matsumoto, M.D., Ph.D.

Addition of control subjects to determine the amount of bone protection on subjects using the ARED alone versus those using the ARED and taking Bisphosphonates. Subjects will complete DXA scans, peripheral (limb) QCT scans, high resolution QCT scans, blood draws with 24-hr urine collections, and ultrasound imaging for assessment of renal stones.



Biochemical Profile

Scott Smith, Ph.D. NASA JSC



Blood and urine are commonly used to assess an astronaut's health as well as conduct research in physiological disciplines by measuring key biomarkers found in these fluids. In support of research studies, this project collects blood and urine samples during the preflight, in-flight and postflight phases of ISS missions. Postflight analysis will yield a database of metabolic profiles of the effects of spaceflight on human physiology.

Body Measures

Quantification of In-flight Physical Changes – Anthropometry and Neutral Body Posture

Sudhakar Rajulu Ph.D. NASA JSC

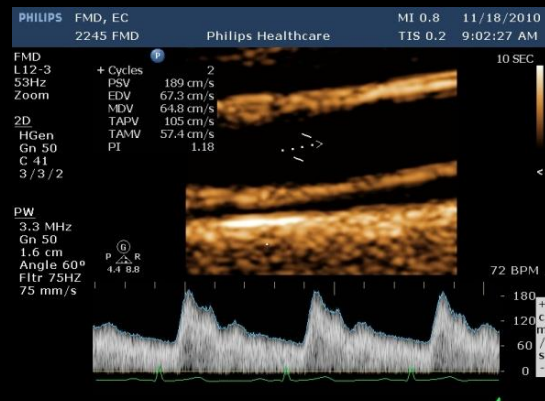
Study to gather in-flight anthropometric measurements, such as lengths, depths, breadths, and circumferences to determine the changes to body shape and size due to microgravity effects. It is anticipated that by recording the potential changes to body shape and size, a better suit sizing protocol will be developed to ensure optimal crew performance, fit, and comfort. This study uses digital still and video data, to perform photogrammetric analyses to determine the changes.



Cardio Ox

Defining the Relationship Between Biomarkers of Oxidative and Inflammatory Stress and the Risk for Atherosclerosis in Astronauts During and After Long-duration Spaceflight

Steven H. Platts, Ph.D. and Stuart Lee, NASA/JSC

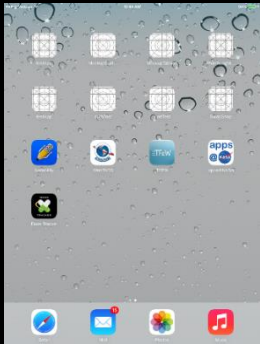


Purpose is to identify biomarkers of oxidative and inflammatory stress and to correlate them to indices of atherosclerosis risk before, during, and after long-duration spaceflight. Analyses of blood and urine biomarkers will be performed. Arterial structure and function via ultrasound measures of carotid intima-media thickness, arterial stiffness, and brachial artery flow-mediated dilation are measured.

Dose Tracker

Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effect During Missions

Virginia E. Wotring, Ph.D. Baylor College of Medicine



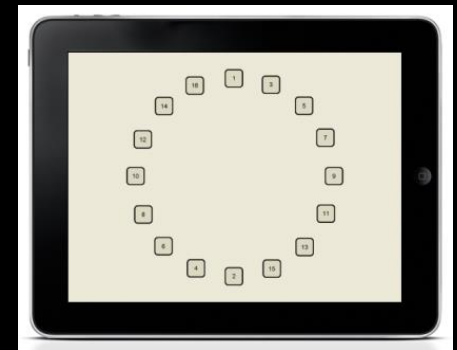
This observational epidemiological study uses a tablet- or handheld device-based questionnaire to permit fast and efficient collection of data regarding crewmembers' medication use on a near real-time basis. The data collection process uses a computerized survey application that leverages the limited medication choices aboard, the doses available, typical dosing frequency, and side effects associated with each medication to provide an individualized short questionnaire for each medication use by the crewmember. Post-flight each participating crewmember will repeat recording their medication usage, so that their ground medication usage frequencies, doses, and perceptions may be compared to those recorded during flight.

Fine Motor Skills

Effects of Long Duration Microgravity on Fine Motor Skills

Kritina Holden, Ph.D. NASA/JSC

This investigation measures the fine motor performance of crewmembers through a series of interactive tasks on a touch screen tablet (an iPad). Fine Motor Skills is the first complete study of fine motor performance to include different phases of microgravity adaptation, long-term microgravity, and sensorimotor recovery after transition to Earth gravity. Fine motor skills are critical for interaction with touch technologies, and any measured changes could affect crew safety and efficiency in future space exploration missions.



Functional Immune

Functional Immune Alterations, Latent Herpesvirus Reactivation, Physiological Stress and Clinical Incidence Onboard the International Space Station

Brian E. Crucian, Ph.D., NASA/JSC

The Functional Immune experiment is a comprehensive immunity investigation that will use longitudinally repeated measures to assess several aspects of immunity during long-duration spaceflight. Blood (ambient, live) and saliva samples will be collected before, during, and following spaceflight. Previously uninvestigated live cell assays will be performed to assess cellular function during spaceflight. Specialized preservatives will be utilized to assess comprehensive immunophenotype, gene expression, and proteomics. Measures of inflammation, stress, antimicrobial activity, etc. will be assessed in blood, saliva, and/or urine. The reactivation of a panel of herpesviruses will be assessed both during flight, and post-flight until shedding resolves. Array technology will be utilized to allow maximal information to be derived from minimal in-flight samples.



Habitability

Habitability Assessment of International Space Station

Sherry S. Thaxton, Ph.D., Lockheed Martin

For crew members on long-duration space missions, a spacecraft is their only home and work space, so cabin designs must balance comfort and efficiency. This study collects observations about the relationship between crew members and their environment on the ISS through an iPad application called iSHORT. The iSHORT application allows crew members to record videos of specific tasks, perform tours on the ISS for human factors engineers to study, and complete questionnaires. These observations can then help spacecraft designers understand how much habitable volume is required, and whether a mission's duration impacts how much space crew members need.



IVD

Risk of *Intervertebral Disc* Damage After Prolong Spaceflight

Alan Hargens, Ph.D., University of California San Diego



Among many space-related health changes, crewmembers frequently report back pain while in orbit and when they return to Earth, which physicians believe is related to changes in the astronauts' intervertebral discs. Crewmembers participating in the Intervertebral Disc Damage experiment completed a battery of six tests before, and after spaceflight, so doctors can determine how the discs change, and whether this correlates to the pain those crewmembers experience.

Lighting Effects

Testing solid state lighting countermeasures to improve circadian adaptation, sleep, and performance during high fidelity analog and flight studies for the International Space Station

George Brainard, Ph.D., Jefferson Medical College

Steven Lockley, Ph.D., Brigham and Women's Hospital

This study will generate quantitative data and knowledge for the benefit of crew health, habitability, environment, and human factors in the design of future human space flight vehicles and habitats. The study also will provide guidance for flight surgeons, flight psychologists, and astronauts to help optimize sleep and circadian regulation during space exploration.



Medical Consumables Tracking

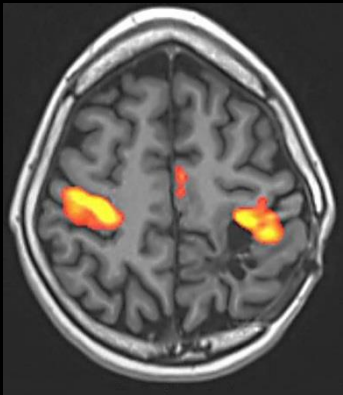
John Zolak, Ph.D., Zin Technologies NASA/GRC

The Medical Consumables Tracking (MCT) System is a battery-powered system that utilizes a Radio Frequency Identification (RFID) system comprised of a reader/scanner/interrogator, antennas, a transponder, and a single board computer. The MCT system will track RFID-tagged medications and medical supplies located in a CHeCS RSR (Resource Supply Rack) locker on ISS to provide a baseline for medication and medical consumables planning for long duration missions. The system is designed to perform an automated inventory cycle every 30 days and provides the capability to manually initiate an inventory cycle. When a cycle is complete, an inventory report of RFID tagged items detected within the locker is transmitted wirelessly to the ground.

Neuromapping

Spaceflight Effects on Neurocognitive Performance: Extent, Longevity and Neural Bases

Rachel Seidler, M.D., University of Michigan



Assess changes in neurocognitive functions such as perception, motor control, memory, language, etc. following long duration space flight. These changes will be measured using behavioral assessments as well as neuroimaging assessments. The central hypothesis proposes that measures of brain structure, function, and network integrity will change from pre to post flight in crewmembers. In addition, these changes will correlate with indices of cognitive, sensory, and motor function in a neuroanatomically selective fashion.

Repository

NASA Biological Specimen Repository
Kathleen McMonigal, M.D., NASA/JSC

Biological specimens provide a means for investigating the physiological responses to spaceflight. Blood and urine are collected before, during and after long-duration flight in order to establish an archive of human biological samples. This archive, which ultimately will include samples from many different flights, will provide a potential population for future research activities and will serve as a valuable resource with which future investigators can validate clinical hypotheses, study spaceflight-related physiological changes, and investigate physiological markers.



Sprint

An Integrated Resistance and Aerobic Training Study for the Validation of an Exercise Countermeasures Regimens Aboard the International Space Station

Lori Ploutz-Snyder, Ph.D., NASA/JSC



Evaluates the use of high intensity, low volume exercise training to minimize loss of muscle, bone, and cardiovascular function in ISS crewmembers during long-duration missions.

Telomeres

Assessing Telomere Lengths and Telomerase Activity in Astronauts Susan Bailey, Ph.D., University of Colorado

This research is needed to establish how the combined stresses of long-duration space flight influence telomere shortening and changes in telomerase activity in blood samples from crewmembers collected pre-, in- and post-flight. This research is needed in order to better evaluate the impact of future space flight, specifically in regard to changes in telomere length and telomerase activity, which have the potential to contribute to accelerated aging, reduced immune function, cardiovascular disease, and cancer.



Current NASA Human Research Program Flight Investigations

Investigation	Subjects (thru Increment 47-48)		
	Required	Completed	In Progress
Biochem Profile	All USOS	12	9
Bishposphonate Controls	10	9	1
Body Measures	9	7	2
Cardio OX	12	9	4
Dose Tracker	24	2	7
Field Test	15	3	5
Fine Motor Skills	8	4	5
Fluid Shifts	5 (USOS)	1	4
Functional Immune	10	0	1
Habitability	6	3	3
IVD	12	6	4
Lighting Effects	6	0	3
Medical Consumables Tracking	N/A		
NeuroMapping	13	4	5
Repository	All USOS	44	9
Rx Metabolism	6	0	0
Sprint (Active)	12	7	2
Telomeres	10	4	6

A photograph of Earth from space, showing the curvature of the planet and the blue atmosphere. The sun is visible on the left side, creating a bright lens flare effect. The text "Recently completed NASA research studies" is overlaid on the right side of the image in a bold, yellow font.

**Recently
completed NASA
research studies**

NASA Twins Study

The NASA Twins Study was a collaborative effort between 10 investigations designed to compare the effects of space flight accumulated over one year and observe changes in the genetic makeup between twin brothers. These studies focused on the use of integrated human -omic analyses to better understand the biomolecular responses to the physical, physiological, and environmental stressors associated with space flight. The project emphasized on the collection of biological specimens and psychological testing from one twin in orbit on the ISS and the collection of corresponding samples and data from his twin on the ground.

Sample collection and data analysis occurred before, during and after the one-year mission. This study focused on the comparison of blood, urine, fecal, saliva and buccal samples collected. Physiological and cognitive testing also was conducted on the brothers before, during and after the mission.

Subjects Completed - 2



NASA Twins Study Investigators

- **Biochemical Profile: Homozygous Twin Control for a 12 Month Space Flight Exposure**
S. Smith, Ph.D., NASA, Houston, TX
- **Metabolomic and Genomic Markers of Atherosclerosis as Related to Oxidative Stress, Inflammation, and Vascular Function in Twin Astronauts**
S. Lee, M.S., Wyle Integrated Science and Engineering, Houston, TX
- **Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue**
M. Basner, Ph.D., University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.
- **Comprehensive Whole Genome Analysis of Differential Epigenetic Effect of Space Travel on Monozygotic Twins**
A. Feinberg, M.D., MPH, Johns Hopkins Medical Center, Baltimore, MD.
- **The Landscape of DNA and RNA Methylation Before, During and After Human Space Travel**
C. Mason, Ph.D., Cornell University, Ithica, NY.

NASA Twins Study Investigators

- **Metagenomic Sequencing of the Bacteriome in GI Tract of Twin Astronauts**
F. Turek, Ph.D., Northwestern University, Evanston, IL
- **Immunome Changes in Space**
E. Mignot, M.D., Ph.D., Stanford University School of Medicine, Palo Alto, CA.
- **Longitudinal Integrated Multi-Omic Analysis of the Biomolecular Effects of Space Travel**
M. Snyder, Ph.D., Stanford University School of Medicine, Palo Alto, CA.
- **Proteomic Assessment of Fluid Shifts and Association with Visual Impairment and Intracranial Pressure in Twin Astronauts**
B. Rana, Ph.D., University of California San Diego, San Diego, CA.
- **Assessing Telomere Lengths and Telomerase Activity in Astronauts**
S. Bailey, Ph.D., University of Colorado, Ft. Collins, CO.

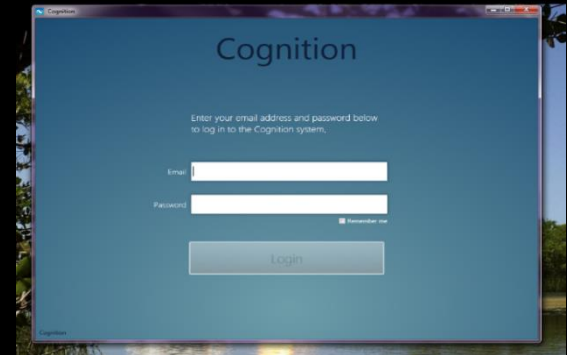
Cognition

Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue

Mathias Basner, MD, Ph.D. University of Pennsylvania

Cognition was a battery of tests that measured how spaceflight-related physical changes, such as microgravity and lack of sleep, can affected cognitive performance. Cognition included a set of brief computerized tests that covered a wide range of cognitive functions, and allowing for real-time measurement of cognitive performance in space.

Subjects Completed - 7



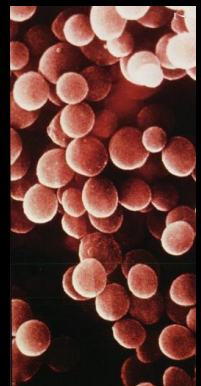
Microbiome

Study of the Impact of Long-Term Space Travel on the Astronaut's Microbiome

Hernan Lorenzi, Ph.D., J. Craig Venter Institute

The study determined how the composition of the human microbiome changed during long-term space exploration and evaluated its potential impact on a crewmember's health including associations with health status, environmental stress, and exposure to space conditions. This experiment characterized the prokaryotic and viral microbiome from various body sites of astronauts who traveled to space at several time points before, during, and after a space mission. Also, the astronauts' immune function was assessed before, during, and after the mission by analyzing saliva samples for reactivated latent viruses and cortisol levels as well as cytokines from blood samples.

Subjects Completed - 9



Ocular Health

Prospective Observational Study Of Ocular Health In ISS Crews Christian Otto, M.D., Universities Space Research Association

The study mimicked current medical ocular testing performed pre, in, and post-flight. The study added two blood pressure readings and a vascular compliance activity (EKG and cardiac ultrasound) to accurately assess changes that occurred in the visual, vascular, and central nervous systems upon exposure to microgravity and induction of fluid shifting.

Subjects Completed - 13



Salivary Markers

The Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity Richard J. Simpson, Ph.D., University of Houston

The study determined if spaceflight induced immune system dysregulation increases infection susceptibility or poses a significant health risk to crewmembers onboard the ISS. Analysis included salivary antimicrobial proteins (AMPs), latent viral reactivation, antibacterial properties of saliva, and blood markers associated with innate host immune defense. Results were also made to establish relationships between salivary and cellular immune markers, viral reactivation and other stressors associated with spaceflight including mood state disturbances, circadian desynchronization, sleep loss/disruption, stress biomarkers) using serial data.

Subjects Completed - 7



Journals – Six Crew
Behavioral Issues Associated with isolation and Confinement: Review and Analysis of Astronaut Journals
Jack Stuster, Ph.D., Anacapa Sciences, Inc.

Study focused on collecting information on behavioral and human issues that are relevant to the design of equipment and procedures and sustained human performance during extended-duration missions. Study results will provide information to help prepare for future missions to low-Earth orbit and beyond.

Subjects Completed - 10





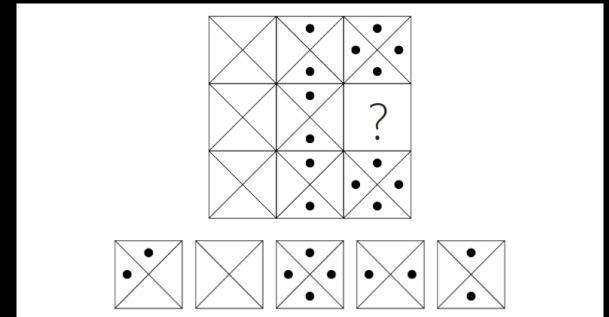
Upcoming NASA research studies

Behavioral Core Measures

Standardized Behavioral Measures for Detecting Behavioral Health Risks During Exploration Missions

David Dinges, PhD; University of Pennsylvania, Mathias Basner, MD, PhD, University of Pennsylvania, Ruben Gur, PhD; University of Pennsylvania, Daniel Mollicone, PhD; Pulsar Informatics and Jack Stuster, PhD, Anacapa Sciences

Isolated and confined environments anticipated during exploration missions will include stressors such as small teams living and working in extreme conditions for prolonged periods separated from family, friends; loss of the day/light cycle; loss or delay of communications with ground; partial gravity; and limited space, privacy, and food selection. The overarching goal of this project is to build on a successful record of unobtrusive, software-based measurement of behavioral health indicators (e.g., mood, cognitive function, physical and mental fatigue, sleep quality) to develop an integrated standardized suite of behavioral core measures (BCM) that would be quite feasible to implement within the constraints of spaceflight research, ground-based analogs (both short- and long-duration), and prolonged missions in isolated, confined, extreme environments lasting up to 12 months or longer. Achievement of this goal would permit a more rapid and reliable assessment and quantification of the Risk of Adverse Behavioral Conditions Psychiatric Outcomes for exploration class missions.



Occupant Protection

Soyuz Occupant Risk Characterization

Nate Newby, KBRwyle, Jeff Somers, KBRwyle, Jessica Wells, Leidos

Currently it is unknown how Soyuz landing accelerations and numbers and types of associated injuries relate to the new NASA occupant protection requirements levied upon future space vehicles. Understanding this relation will allow better quantification of the risk of injury for future spacecraft designs. An accurate estimation of the occurrences of injury during Soyuz landings will be determined using self-reported survey data from retrospective and prospective U.S. crewmembers, as well as information stored on NASA databases. This study consists of obtaining acceleration data from the instrumented seats of the Soyuz vehicle and US astronaut landing injury data.

The vehicle seat acceleration data will be used to drive computer simulations of a finite element model of an anthropometric test device (ATD). Human injury metrics have been ascribed to the ATD for head, neck, and spine injuries. Simulations of injurious and non-injurious Soyuz landings will help refine the ATD injury metrics that form the basis for our current occupant protection standards.

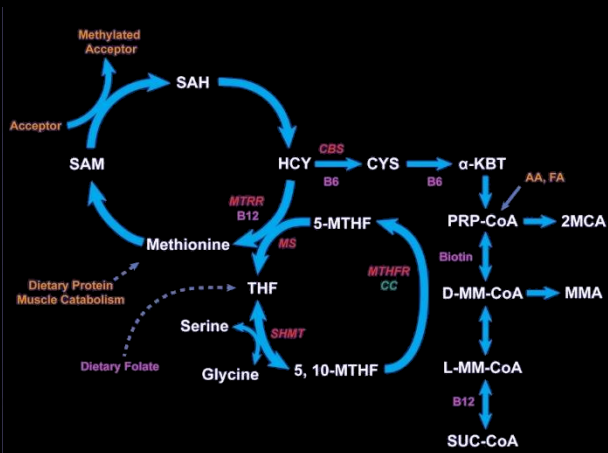


One Carbon Poly

One Carbon Metabolism: Expanded Polymorphism Evaluation

Scott M. Smith, Ph.D, NASA JSC, Sara R. Zwart, Ph.D./UTMB, Jesse F. Gregory, Ph.D, University of Florida, Steven Zeisel, M.D., Ph.D, University of North Carolina at Kannapolis, C. Robert Gibson, O.D., Coastal Eye Associates, Thomas Mader, M.D./US Army (retired) and Robert Ploutz-Snyder, Ph.D, University of Michigan

We have documented a genetic predisposition for some astronauts to develop ophthalmologic issues, often referred to as VIIP (vision impairment/intracranial pressure). From a limited study of 5 single-nucleotide polymorphisms (SNPs), we found one SNP associated with a greater risk of choroidal folds and cotton wool spots, and another SNP that was associated with optic disc edema. In light of these findings, we propose here to evaluate a wider range of SNPs to clarify and verify the relationship of genetics in some astronauts that may predispose to ophthalmic



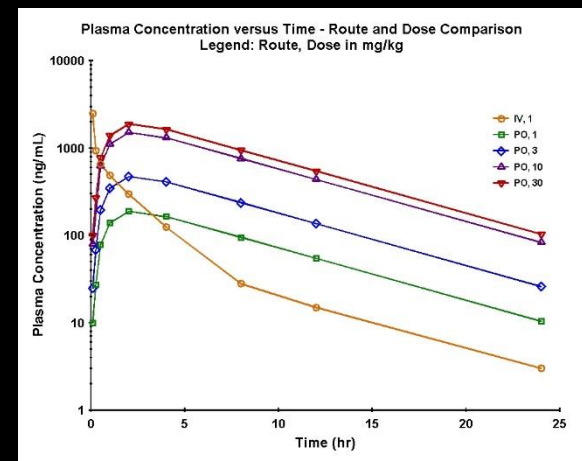
issues during space flight. The primary goal of this study is to extend the one-carbon pathway SNP assessment as related to astronaut ophthalmologic findings. While this studies alone will not identify the mechanism(s) of VIIP, we aim to clarify the genetic relationship to ophthalmic findings. This line of research may ultimately allow for the definition of the mechanism of and means to prevent or treat these potentially vision-threatening processes in astronauts.

Rx Metabolism

Inflight Pharmacokinetic and Pharmacodynamic Responses to Medications Commonly Used in Spaceflight

Virginia Wotring, Ph.D., Baylor College of Medicine

Crewmembers on spaceflight missions use medications to treat spaceflight-associated conditions like space adaptation syndrome as well as common ordinary complaints. They do so under the remote guidance of their flight surgeons, who base prescriptions on their knowledge and experience in terrestrial medicine. However, even after decades of spaceflight missions, we do not know if medications act the same in the spaceflight environment as they do on Earth. Aspects of the spaceflight environment (low gravity, radiation exposure, closed environment, stress) have been shown to alter human physiology. Anecdotal data have suggested that, at least for certain medications or indications, inflight medication efficacy is poor, and spaceflight crew use high doses, repeated doses, or even experience apparent treatment failures. This study will determine if the LEO environment of the International Space Station alters the actions of three common medications.



Spaceflight Standard Measures

NASA/JSC

A multi-disciplinary set of measurements with emphasis on addressing the risks to human spaceflight. Data collected will be based on existing bed-rest measures when possible (international agreement). Results will establish a baseline for testing of in-flight countermeasures and enable comparison of one-year and six-month missions. Assessment will be based on validated and established outcome measures.



Vertebral Strength

Quantitative CT and MRI-based Modeling Assessment of Dynamic Vertebral Strength and Injury Risk Following Long-Duration Spaceflight

Ashley Weaver, PhD, Wake Forest University Health Sciences

Prolonged exposure of astronauts to microgravity during long-duration spaceflight can degrade the musculoskeletal system, increasing the risk of structural failure of these tissues when they experience dynamic loads. Quantitative computed tomography (qCT) can measure changes in bone morphology, volumetric bone mineral density (vBMD), and cortical thickness as a means to quantify skeletal degradation from prolonged spaceflight. Magnetic resonance imaging (MRI) can measure volumetric changes in spinal musculature occurring as a result of prolonged spaceflight. These musculoskeletal measurements derived from qCT and MRI pre- and post-flight crewmember scans can be integrated and applied in our dynamic simulations that will quantify vertebral strength changes during spaceflight. Our proposed approach has relevance in quantifying the risks associated with long-duration spaceflight, including vertebral injury from dynamic loads, vertebral fracture, early onset vertebral osteoporosis due to spaceflight, and impaired performance due to reduced spinal muscle mass, strength and endurance.



Joint research studies



Field Test

Recovery of Functional Sensorimotor Performance Following Long Duration Space Flight

Millard Reschke, Ph.D., NASA/JSC

Inessa B. Kozlovskaya, M.D., RAS/IBMP

Astronauts and cosmonauts that live in space for six months to a year experience physical changes that have noticeable effects once they return to Earth's gravity, including changes to vision, balance, coordination, blood pressure, and the ability to walk, which impact their ability to perform basic tasks. The Field Test investigation includes several studies designed to investigate the complexity, severity, and duration of these changes, with an aim toward improving recovery time and developing injury prevention methods for future missions.

Current crews land on Earth with immediate access to medical assistance and rehabilitation facilities, but future crews traveling to Mars, or other destinations won't have these resources or much time to recover from the changes upon arrival.



Fluid Shifts

Fluid Shifts Before, During and After Prolonged Space Flight and Their Association with Intracranial Pressure and Visual Impairment (Fluid Shifts)

Michael B. Stenger, Ph.D, KBRWyle

Alan R. Hargens, Ph.D., University of California San Diego

Scott A. Dulchavsky, M.D., Ph.D., Henry Ford Hospital

Valeri V. Bogomolov, MD, Ph.D., RAS/IBMP

Irina Alferova, MD, RAS/IBMP

Changes in vision and eye structure are thought to be the result of space flight-induced headward fluid shifts and transiently elevated intracranial pressure. The purpose of this investigation is to characterize the space flight-induced fluid shift, including intra- and extravascular shifts, intra- and extracellular shifts, changes in total body water and lower vs. upper body shifts. Lower body negative pressure will be investigated pre- and in-flight for its ability to mitigate some of the effects of the space flight-induced fluid shift. Results from this investigation will help to define the causes of the ocular structure and vision changes associated with long duration space flight and assist in the development of countermeasures.



SarcoLab 3

Myotendinous and Neuromuscular Adaptation to Long-Term Spaceflight

Jörn Rittweger, PhD, Institute of Aerospace Medicine, German Aerospace Center (DLR)

Mitzi Laughlin, PhD, University of Houston

Inessa Kozlovskaya, PhD, Institute for Biomedical Problems (RAS/IBMP)

Exposure to actual and simulated microgravity is known to lead to loss of muscle mass, function and motor control, and to alterations in tendon material and mechanical properties. The loss in muscle strength notably exceeds the loss in muscle size, thus demonstrating that there both muscle quantity and 'quality' are compromised. While these effects have been studied in some detail, it is largely how the molecular mechanisms are underpinning the functional and structural changes in the muscle-tendon complex. The objective of the Sarcolab study is to investigate the adaptations of the calf muscle and tendon to long-term spaceflight, at the macroscopic and molecular levels.

Sarcolab 3 involves measurements that help us to quantify the various aspects of muscle deterioration, and allow us to unravel the responsible mechanisms. This is important, as establishing the mechanisms involved in space-related muscle deterioration will help us to devise optimized countermeasure strategies.



Thank you

