National Aeronautics and Space Administration

Human Research Program

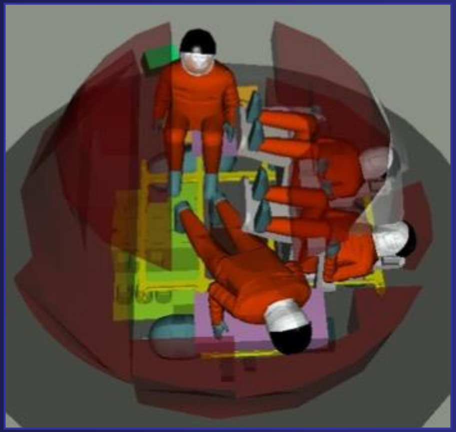
Steven H. Platts, Ph.D.

Acting Chief Scientist

humanresearch.jsc.nasa.gov

Human Research Program

- The Human Research Program (HRP) focuses on applied research
- Program goals
  - Perform research necessary to understand and reduce spaceflight human health and performance risks in support of exploration
  - Enable development of human spaceflight medical and human performance standards
  - Develop and validate technologies that serve to characterize and reduce medical risks associated with human spaceflight



An Applied Research Program

Characteristics of HRP

- Composed of five Elements
  - Exploration Medical Capability
    - *Medical care for deep-space missions*
  - Human Factors and Behavioral Performance
    - *Interfaces between humans, vehicles & habitats*
    - *Individual and interpersonal*
  - Human Health Countermeasures
    - *Physiology*
  - Space Radiation
    - *Biological effects of radiation exposure*
  - Research Operations and Integration
    - *Infrastructure for flight and analog experiments*

- Funds Translational Research Institute for Space Health (TRISH) through cooperative agreement to pursue disruptive, breakthrough approaches that reduce risks to human health and performance
- Collaborates with NASA Space Biology to understand causal cellular and other mechanisms that underlie adaptation to fractional gravity levels in cells, microorganisms, plants, and animals

Venues for Conducting Research

International Space Station

NASA Space Radiation Lab

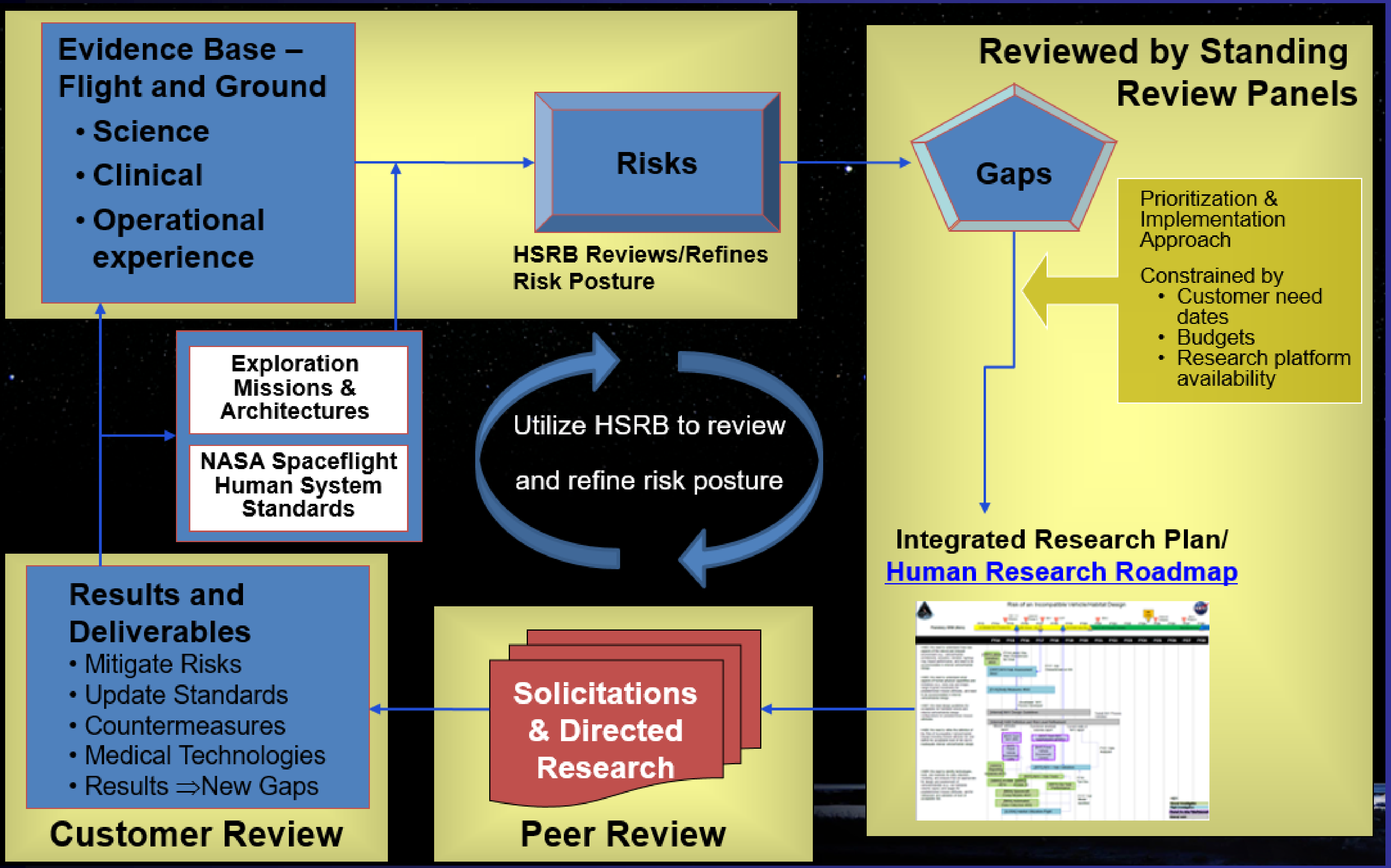
Parabolic Flight

:envihab

Antarctica

Human Exploration Research Analog

HRP Continuous Review & Evaluation of Priorities




Radiation
Isolation & Confinement
Distance from Earth
Gravity fields
Environments

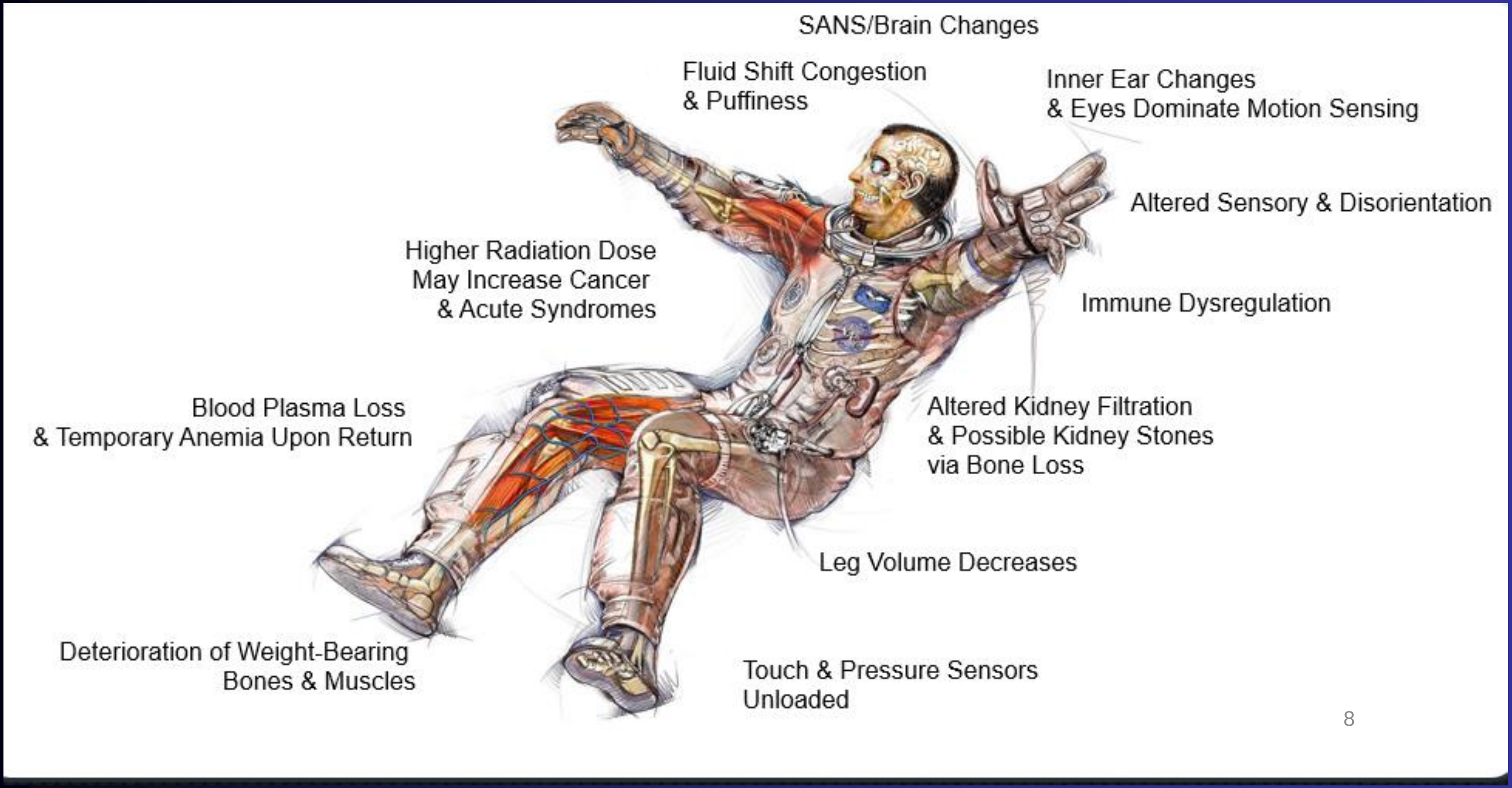
Human System Risk Summary – Risks by Hazard

Human Spaceflight Risks	Low Earth Orbit (Long) 30 D - 1 Y	Lunar Orbital (Short) < 30 D	Lunar Orbital (Long) 30 D - 1 Y	Lunar Orbital + Surface (Short) < 30 D	Lunar Orbital + Surface (Long) 30 D - 1 Y	Mars (Preparatory) < 1 Y	Mars (Planetary) 730-1224D
Radiation							
Non-Ionizing Radiation	A	A	A	A	A	AO	AO
Radiation Carcinogenesis **(LTH)**	RC	A	RC	A	RC	RM	RM
Distance from Earth							
Inadequate Human Systems Integration Architecture	A	RM/SR	RM/SR	RM	RM	RM	RM
Inflight Medical Conditions	A	A	RM	RM	RM	RM	RM
Inadequate Food and Nutrition	A	A	RM	A	RM	RM	RM
Ineffective or Toxic Medications	A	A	A	A	A	A	RM
Isolation and Confinement							
Cognitive or Behavioral Conditions	RM	AM	RM	RC	RM	RM	RM
Psychosocial Adaptation within a Team	AM	AM	RM	AM	AM	RM	RM
Altered Gravity							
Bone Fracture	A	A	RC	A	RC	RC	RC
Cardiac Rhythm Problems	AM	AM	AM	AM	AM	RM	RM
Concern of Venous Thromboembolism (VTE)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Host-Microorganism Interactions	AM	AM	AM	AM	AM	AM	RM
Orthostatic Intolerance	A	A	A	A	A	A	A
Reduced Aerobic Capacity	AM	AO	AO	AO	AO	AO	AO
Reduced Muscle Size	AM	AO	AM	AO	AO	AO	AO
Renal Stone Formation	A	A	A	A	A	RM	RM
SANS	A	A	A	A	A	A	RM
Sensorimotor Alterations	RM/SR	AM	RM/SR	RM/SR	RM/SR	RM/SR	RM/SR
Urinary Retention	A	A	A	A	A	A	A
Crew Egress	AM	RC	RC	RC	RC	RC	RC
Cardiovascular Adaptations	AM	A	AM	AO	AO	AM	RM
Hostile Closed Environment							
Altered Immune Response	AM	AM	AM	AM	RM	RM	RM
Carbon Dioxide Exposure	A	A	A	A	A	RM	RM
Celestial Dust Exposure	N/A	A	A	A	RM	N/A	TBD
Decompression Sickness	A	RM	RM	RM	RM	RM	RM
Dynamic Loads	AM	AM	AM	RM	RM	AM	RM
Electrical Shock	A	A	A	RC	RC	RC	RC
EVA Risk	A	AO	AO	RM	RM	AO	RM
Hearing Loss **(LTH)**	AM	AM	RC	AM	AM	RC	RC
Hypoxia **(LTH)**	RM	A	RM	A	RM	RM	RM
Sleep Loss	AO	AO	AO	AO	RM	RM	RM
Toxic Exposure	AM	AM	AM	AM	AM	AM	AM

Notes:

- Risk ratings are approved at the Human System Risk Board
- Risk ratings are for In-mission operations unless otherwise noted for Long-Term Health (LTH)
- Risk text color:
  - Current risk ratings
  - Risk ratings under review
  - Proposed to be approved
  - To be transferred to another risk
- Risk colors:
  - High LxC
  - Mid LxC
  - Low LxC
- Risk Dispositions
  - **A** – Accepted
  - **AM** – Accepted with monitoring
  - **AO** – Accepted with optimization
  - **RM** – Requires Mitigation
  - **RM/SR** – Requires Mitigation/ Standard Refinement
  - **RC** – Requires Characterization

Space Flight Effects on the Human Body



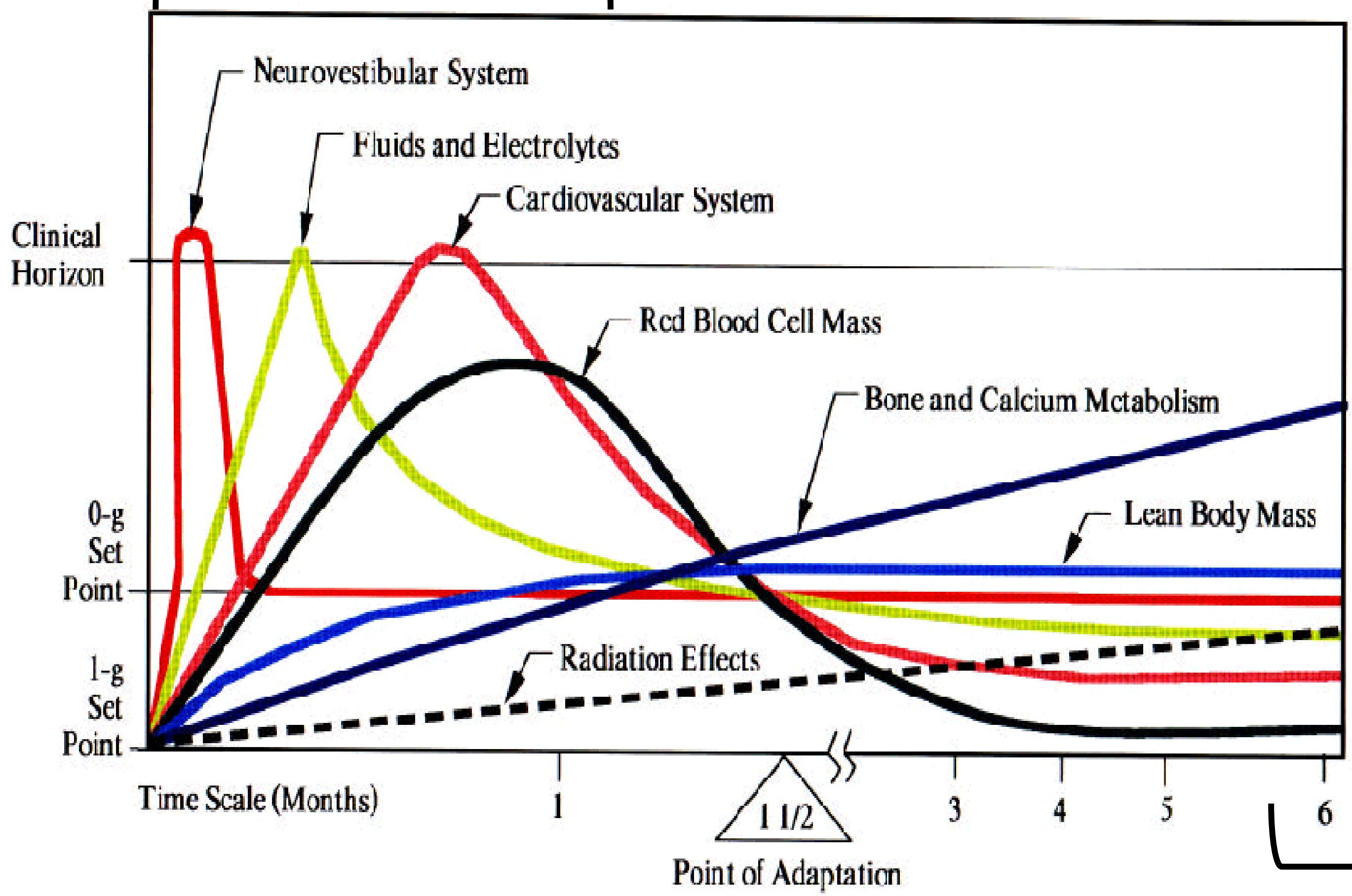
One Year Mission

Time Course of Physiological Changes During Weightlessness

This is notionally how the body adapts to Spaceflight, most notably microgravity

Note that there are acute and chronic processes at work

Still unclear if there are bimodal responses

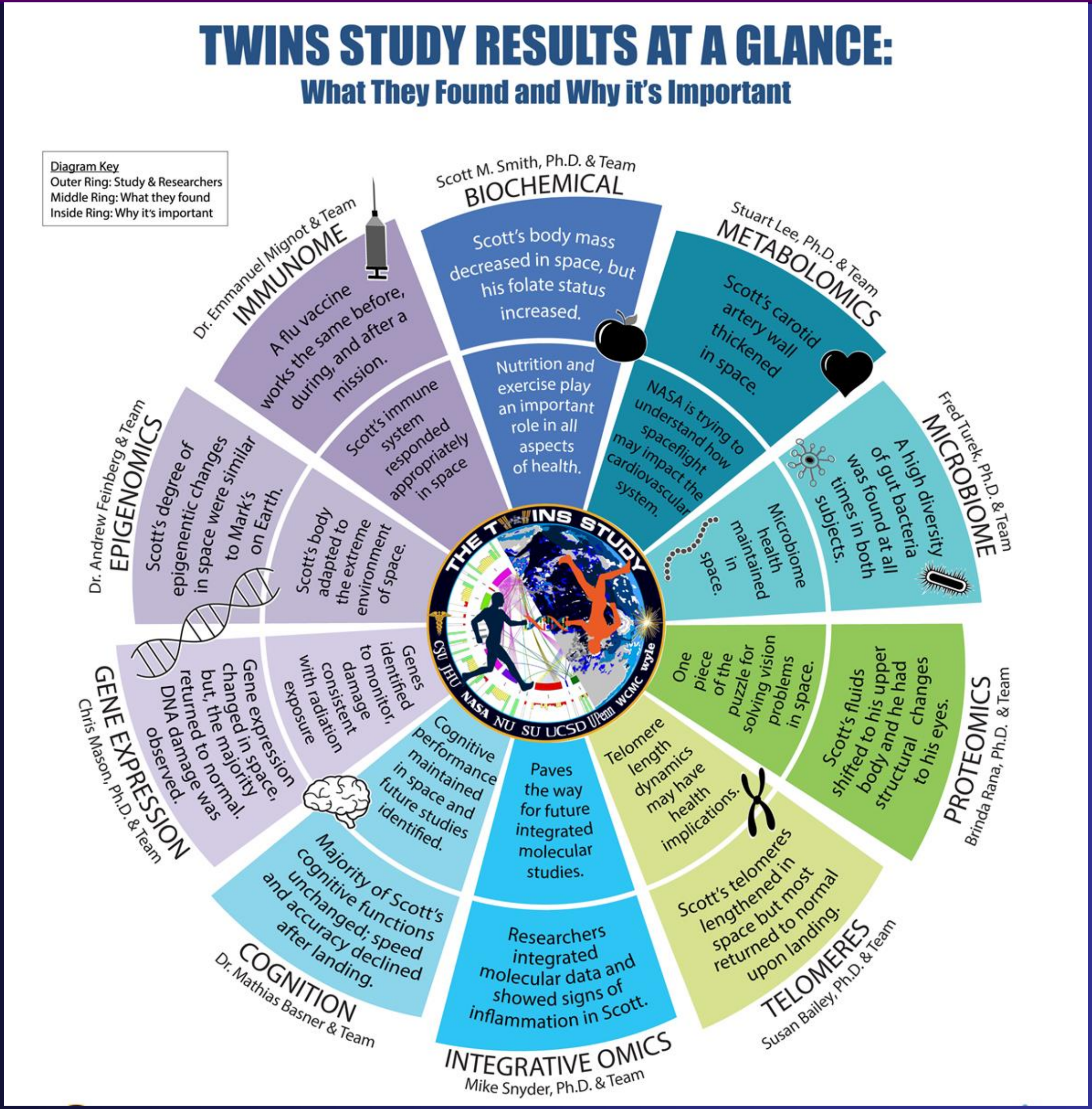


A. Nicogossian et al, Space Physiology and Medicine

Therefore, the body has a process by which it readapts to gravity. These processes will have acute and chronic elements as well

Mission Overview

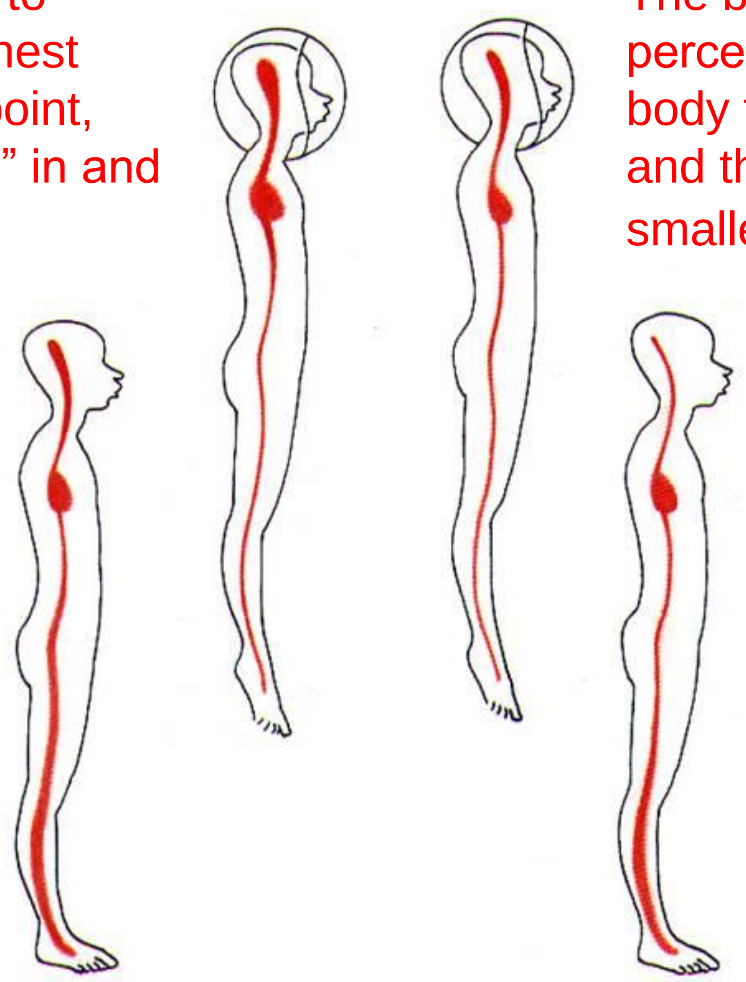
- Launch: March 27, 2015
- Landing: March 1, 2016
- Duration: 340 days
- Earth Orbits: ~5440 orbits
- Miles traveled: ~143,846,525
- Other Interesting Facts:
  - Including the HRP studies, over 400 total investigations were conducted during the 1YM across all disciplines.
  - Kelly/Kornienko saw the arrival of 6 resupply spacecraft during their mission - SpX-6, 60P, HTV5, 61P, OA-4, 62P


TWINS STUDY RESULTS AT A GLANCE:
What They Found and Why it's Important
Diagram Key
Outer Ring: Study & Researchers
Middle Ring: What they found
Inside Ring: Why it's important
Scott M. Smith, Ph.D. & Team
BIOCHEMICAL
Scott's body mass decreased in space, but his folate status increased.
Nutrition and exercise play an important role in all aspects of health.
Stuart Lee, Ph.D. & Team
METABOLOMICS
Scott's carotid artery wall thickened in space.
NASA is trying to understand how spaceflight may impact the cardiovascular system.
Fred Turek, Ph.D. & Team
MICROBIOME
A high diversity of gut bacteria was found at all times in both subjects.
Microbiome health maintained in space.
Brinda Rana, Ph.D. & Team
PROTEOMICS
Scott's fluids shifted to his upper body and he had structural changes to his eyes.
One piece of the puzzle for solving vision problems in space.
Susan Bailey, Ph.D. & Team
TELOMERES
Scott's telomeres lengthened in space but most returned to normal upon landing.
Telomere length dynamics may have health implications.
Mike Snyder, Ph.D. & Team
INTEGRATIVE OMICS
Researchers integrated molecular data and showed signs of inflammation in Scott.
Paves the way for future integrated molecular studies.
Dr. Mathias Basner & Team
COGNITION
Majority of Scott's cognitive functions unchanged; speed and accuracy declined after landing.
Cognitive performance maintained in space and future studies identified.
Chris Mason, Ph.D. & Team
GENE EXPRESSION
Gene expression changed in space, but, the majority returned to normal. DNA damage was observed.
Genes identified to monitor damage consistent with radiation exposure
Dr. Andrew Feinberg & Team
EPIGENOMICS
Scott's degree of epigenetic changes in space were similar to Mark's on Earth.
Scott's body adapted to the extreme environment of space.
Dr. Emmanuel Mignot & Team
IMMUNOME
A flu vaccine works the same before, during, and after a mission.
Scott's immune system responded appropriately in space
THE TWINS STUDY
CSU JHU NASA NU SU UCSD UPenn WCMC Wyle

Fluid Shifts during Space Flight

In space, the fluid tends to redistribute toward the chest and upper body. At this point, the body detects a “flood” in and around the heart.

The body rids itself of this perceived “excess” fluid. The body functions with less fluid and the heart becomes smaller.



On Earth, gravity exerts a downward force to keep fluids flowing to the lower body.

Upon return to Earth, gravity again pulls the fluid downward, but there is not enough fluid to function normally on Earth.

Lujan and White (1995)

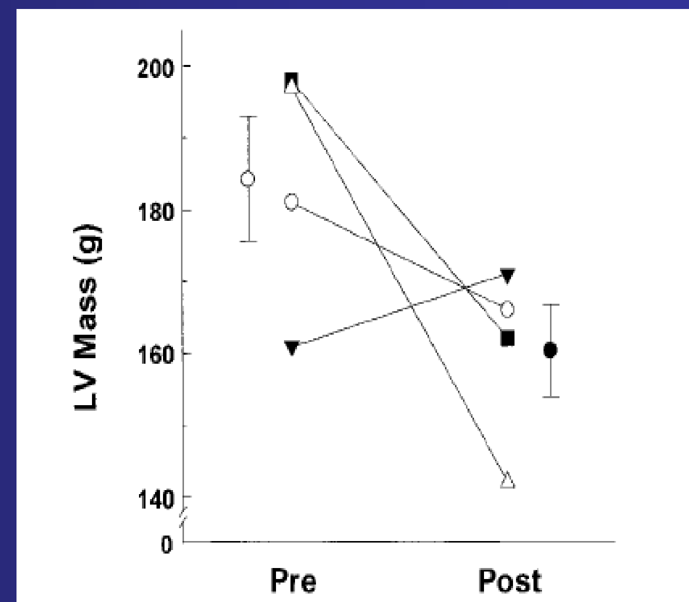
Fluid Shifts: Puffy Head - Chicken Leg Syndrome

- Lack of gravity - no downward pull of fluids
- Fluids make headward shift
- Feeling different
  - Less Thirsty
  - Urinate frequently
  - Stuffy nose
  - Dull sense of taste
- Looking different
  - Puffy face
  - Thin legs

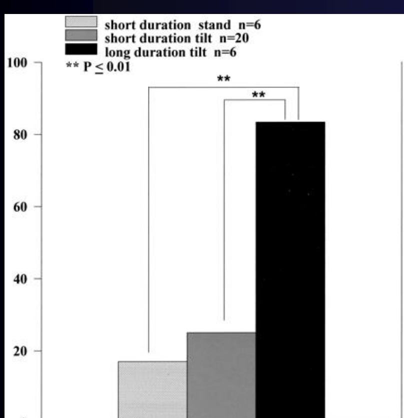
vs.

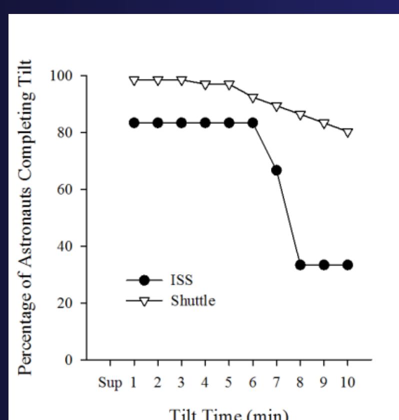
Cardiovascular System

- Spaceflight has significant effect on cardiovascular system
  - Blood pressure control
  - Heart size
  - Vascular function
  - SANS



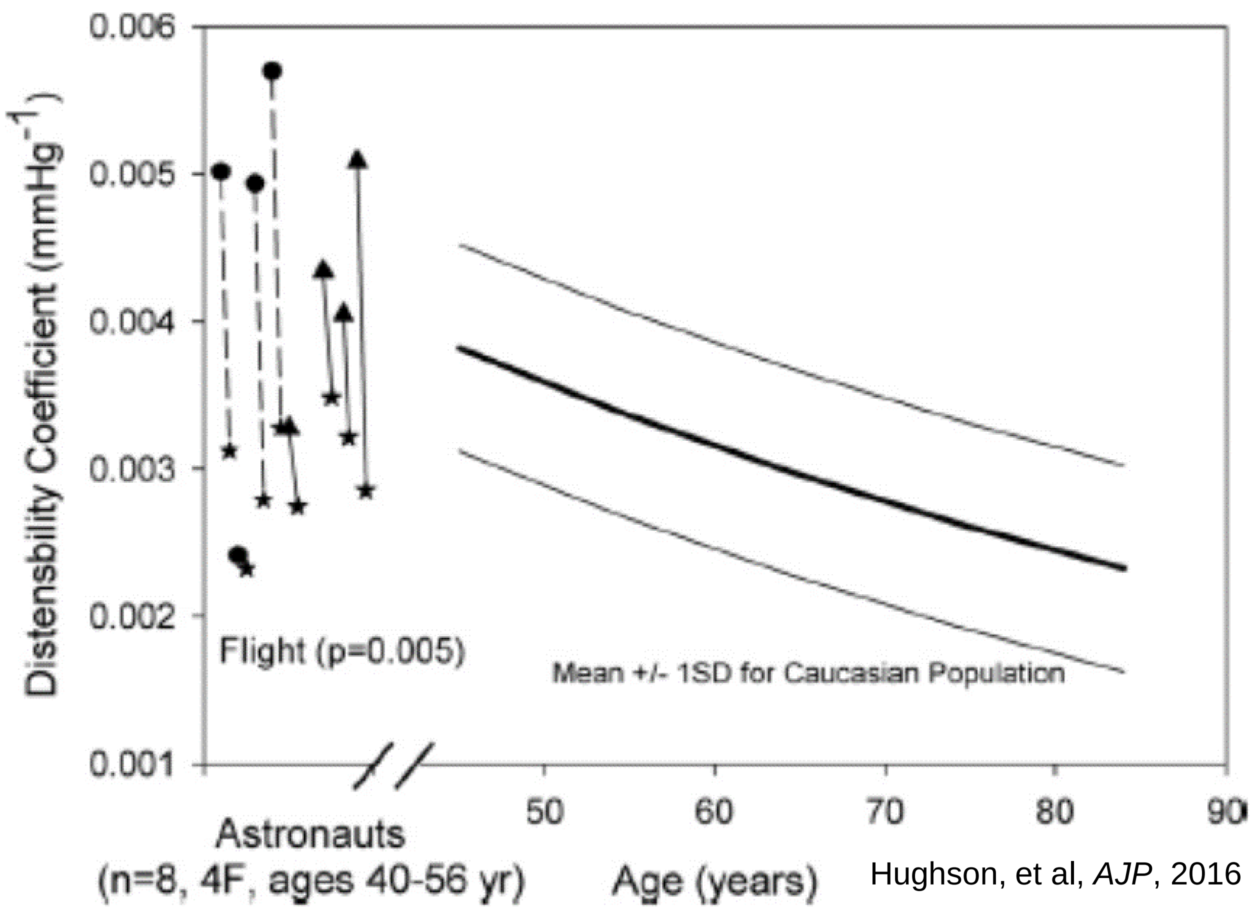
Perhonen, *JAP*, 2001





Meck, Psychosom Med, *2001*

Effects of spaceflight on arterial system



Hughson, et al, *AJP*, 2016

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Spaceflight Associated Neuro-ocular Syndrome (SANS)

Human Research Program

Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-duration Space Flight

Thomas H. Mader, MD,[1] C. Robert Gibson, OD,[2] Anastas F. Pass, OD, JD,[3] Larry A. Kramer, MD,[4] Andrew G. Lee, MD,[5] Jennifer Fogarty, PhD,[6] William J. Tarver, MD,[6] Joseph P. Dervay, MD,[6] Douglas R. Hamilton, MD, PhD,[7] Ashot Sargsyan, MD,[7] John L. Phillips, PhD,[8] Duc Tran, DO,[2] William Lipsky, MD,[2] Jung Choi, OD,[2] Claudia Stern, MD, PhD,[9] Raffi Kuyumjian, MD,[10] James D. Polk, DO[6]

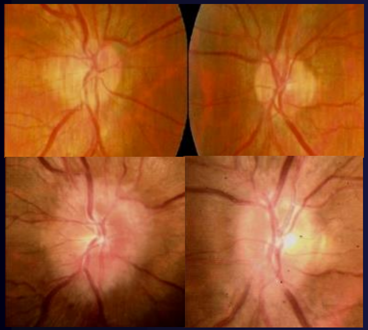
Hyperopic Shifts

Up to +2.00 diopters

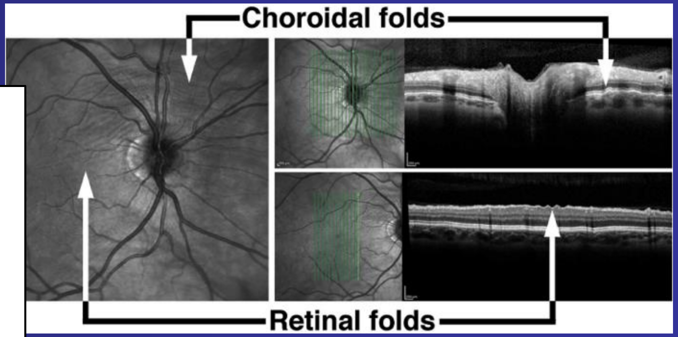
Optic Disc Edema

Pre

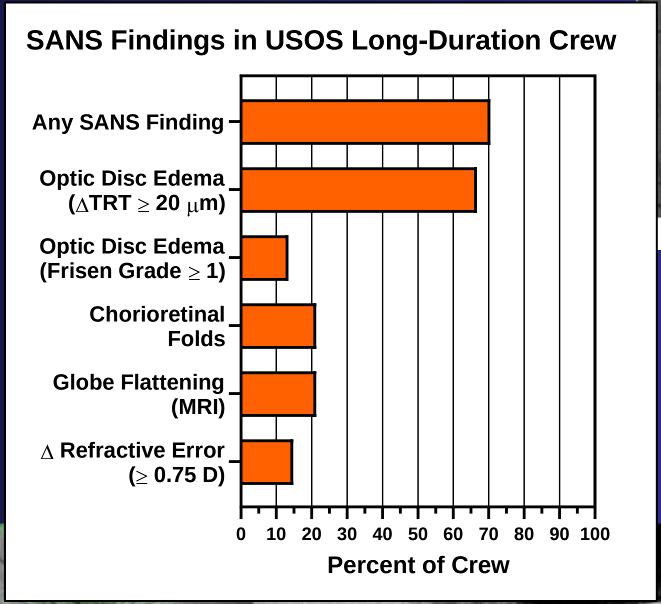
Post

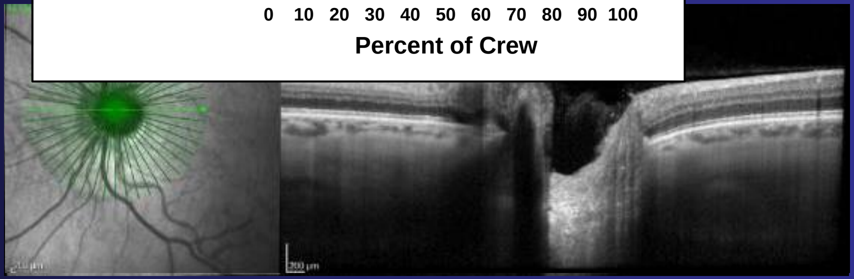


Right Left

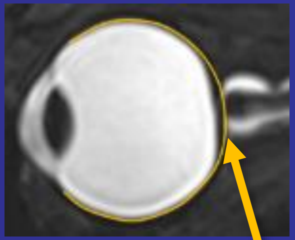


Mader, J Neuro-Ophthalmol, 2016



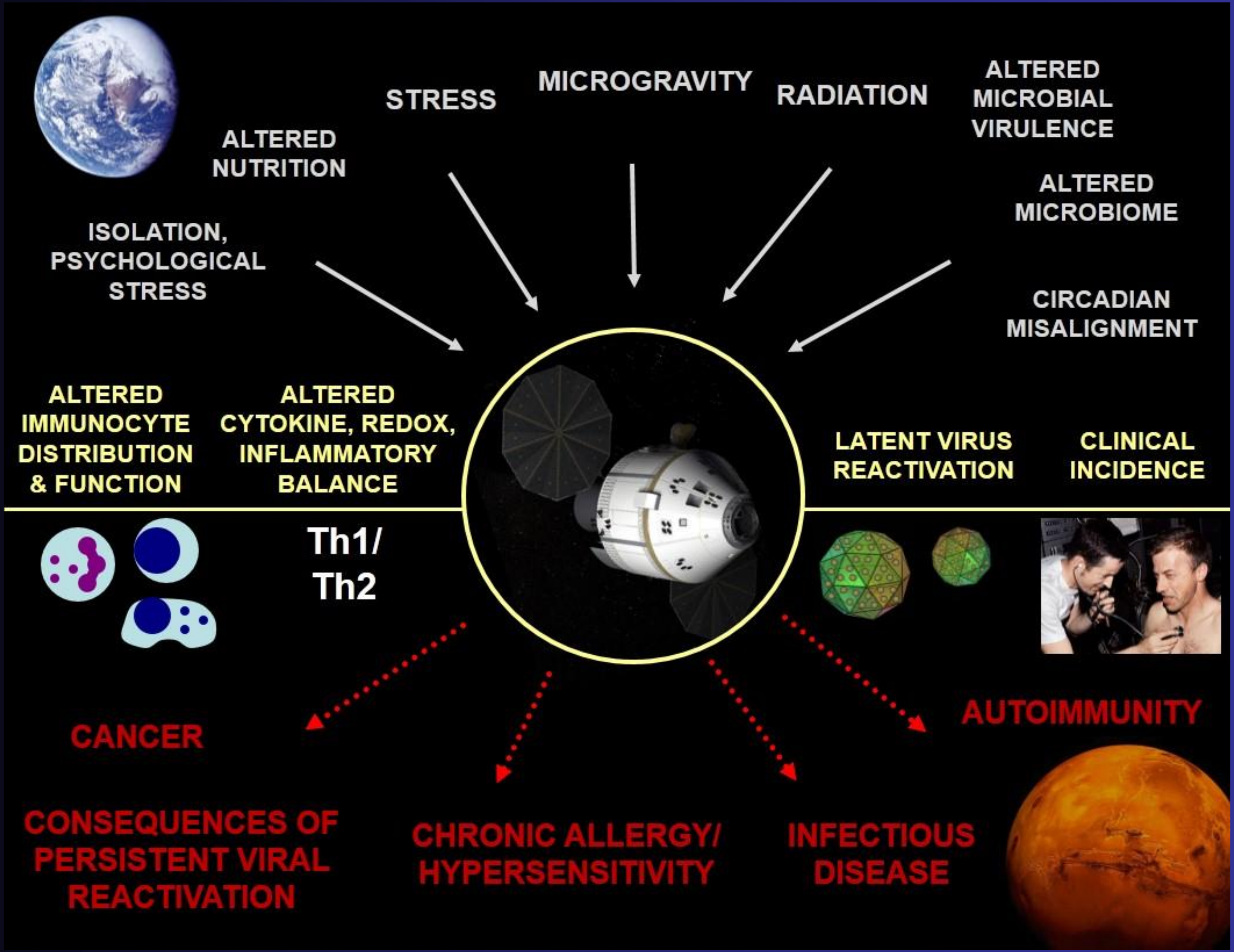


Globe Flattening



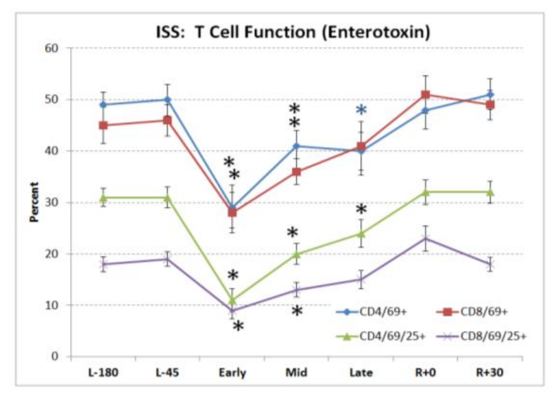
Pre-flight shape

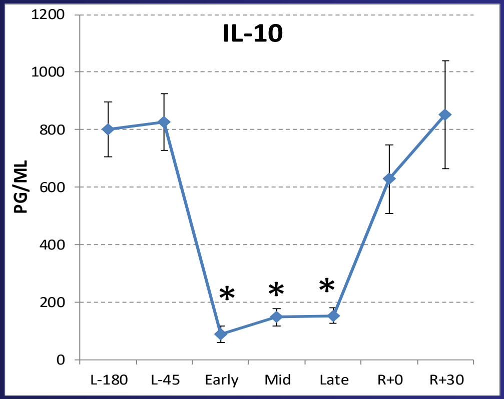
Immunology

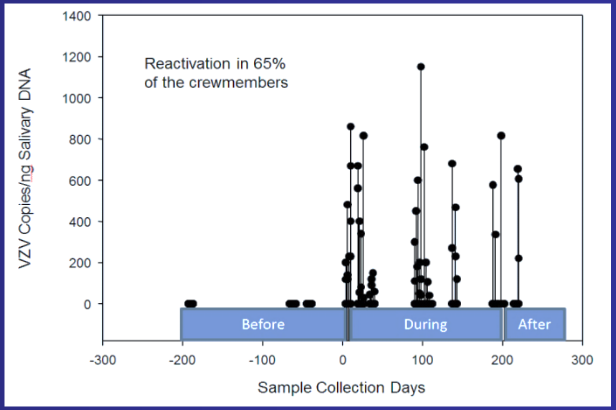

ALTERED NUTRITION
STRESS
MICROGRAVITY
RADIATION
ALTERED MICROBIAL VIRULENCE
ALTERED MICROBIOME
ISOLATION, PSYCHOLOGICAL STRESS
CIRCADIAN MISALIGNMENT
ALTERED IMMUNOCYTE DISTRIBUTION & FUNCTION
ALTERED CYTOKINE, REDOX, INFLAMMATORY BALANCE
Th1/ Th2
LATENT VIRUS REACTIVATION
CLINICAL INCIDENCE
CANCER
AUTOIMMUNITY
CONSEQUENCES OF PERSISTENT VIRAL REACTIVATION
CHRONIC ALLERGY/ HYPERSENSITIVITY
INFECTIOUS DISEASE

Science Findings from ‘Integrated Immune Study’ of 22 ISS Astronauts

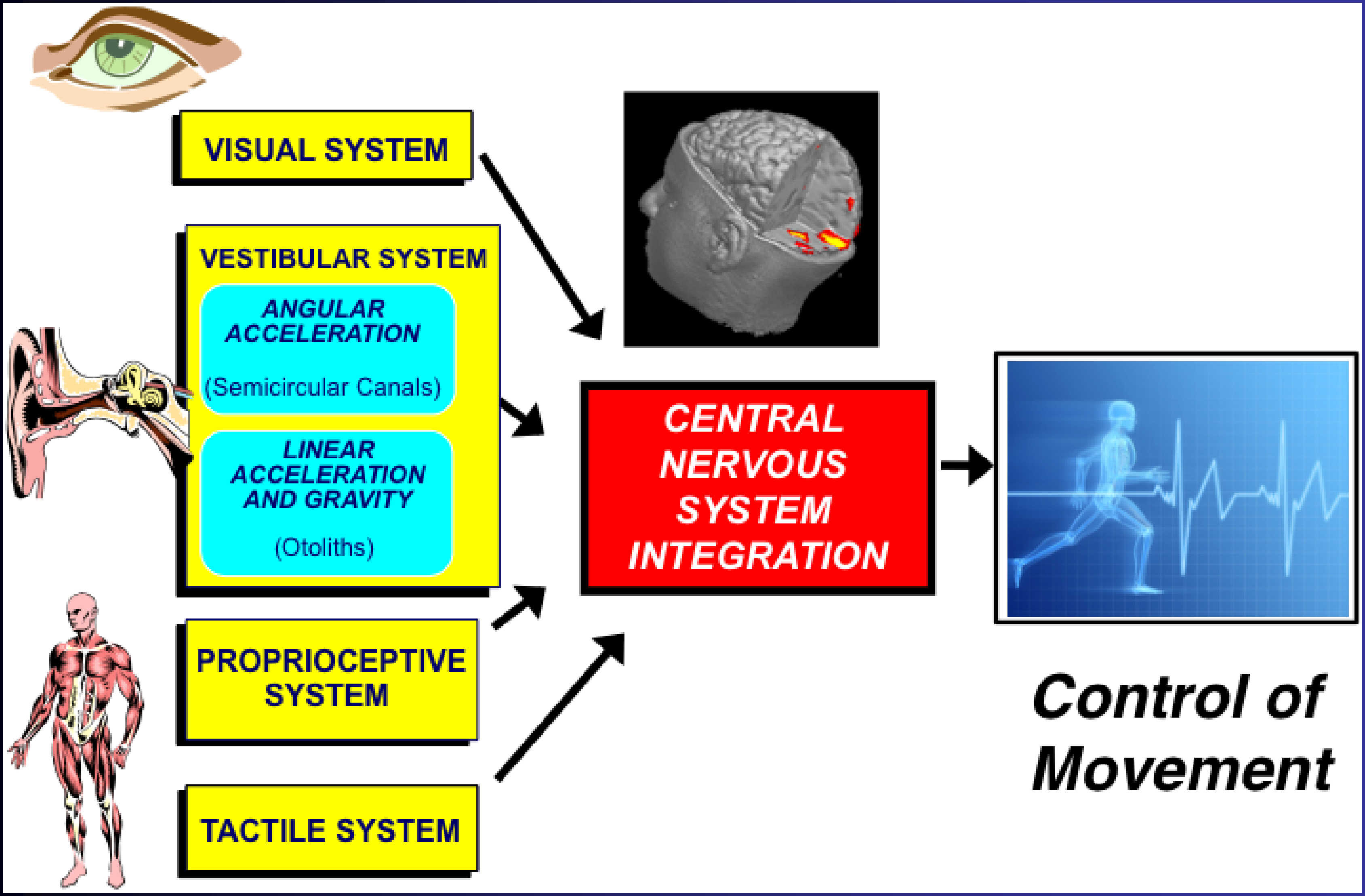
- Altered (1) peripheral leukocyte distribution, (2) T cell function, (3) mitogen-stimulated cytokine which persist for the duration of a 6-month ISS mission.
- Latent herpesviruses, including VZV, EBV, CMV, reactivate for the duration of a 6-month ISS mission.
- Appears to be a pan-suppression of adaptive function, including viral specific T cells.
- Circadian misalignment occurs, difficult to regain a ‘normal’ circadian rhythm. (Sleep meds most commonly prescribed Rx)
- Clinical events include some infectious disease. Some crews manifest persistent allergy symptoms, dermatitis, hypersensitivity reactions.







Central Nervous System Integrates Multiple Sensory Inputs to Control Movement



Sensorimotor Disturbances Caused by G-transitions

Transit

Transit

Earth Preflight

Planetary Surface Operations

Earth Postflight

G-transitions

G-transitions

ISSUES:

Postural and gait instability
Visual performance changes
Manual control disruptions
Spatial disorientation
Motion sickness

OPERATIONAL IMPACT:

Vehicle control
Vehicle egress
Planetary EVAs

Space Motion Sickness (SMS)

- Incidence
  - Affects approximately 79% of all crewmembers
  - ~33% Require medication
  - 10% of cases are severe
- Symptoms
  - From loss of appetite to nausea and vomiting
- Time Course
  - Onset from MECO to 24 hours; peak
  - symptoms at 24 to 48 hours;

  symptoms resolve at 72 to 96 hours

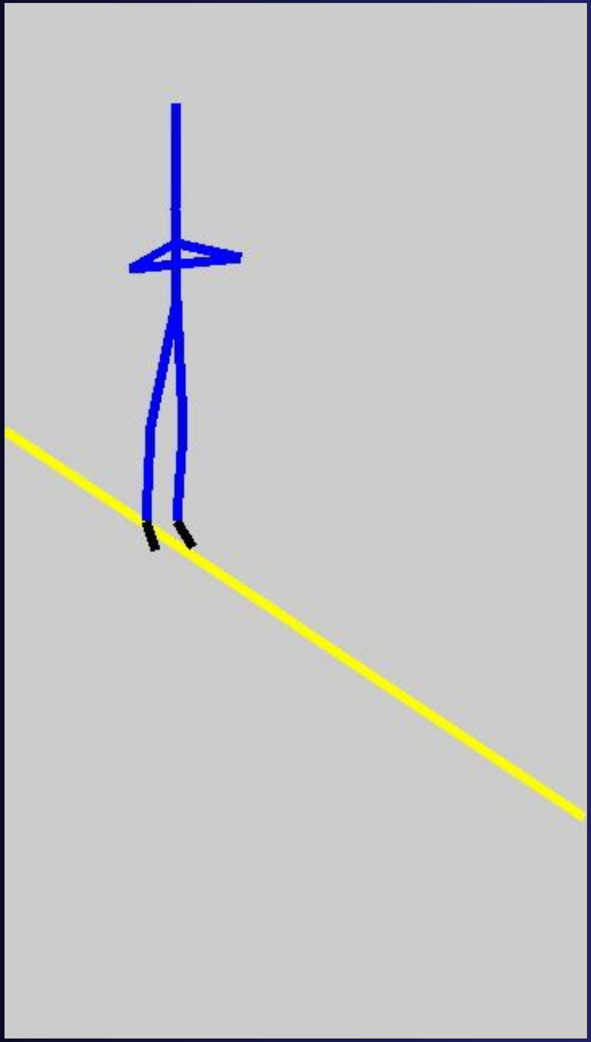
Space Motion Sickness (SMS)

- Causes (possible)
  - Neurovestibular
    - Otolith mismatch
    - Sensory conflicts
  - Fluid shift
- Countermeasures
  - Inactivity
  - 1-G orientation
  - Medication (Phenergan IM)
  - Preflight training and prophylaxis

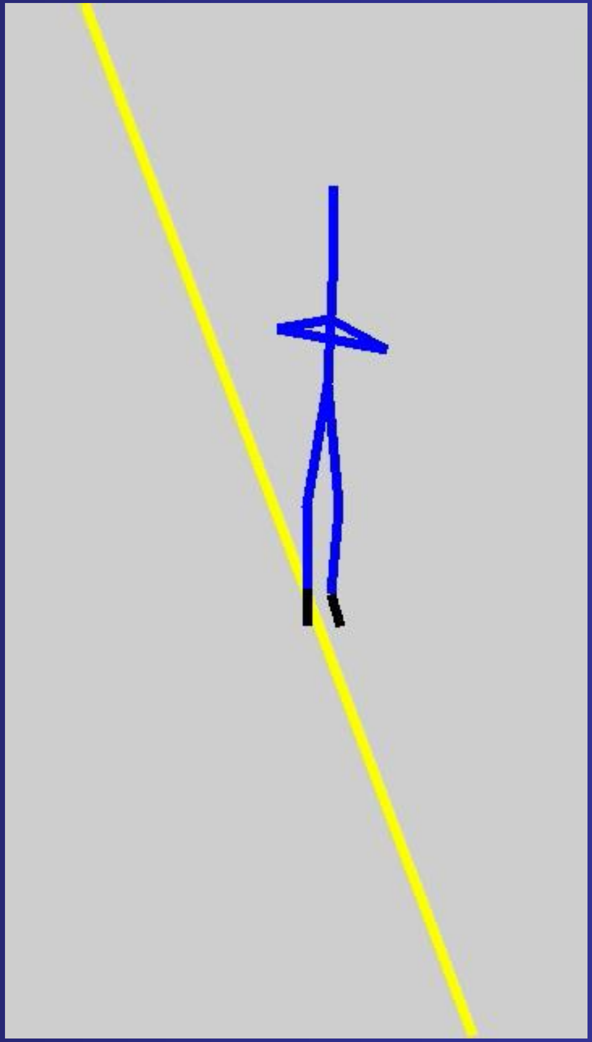
Tandom Walk

Postflight R+0

Tandem Walk Test: Pre/Post ISS



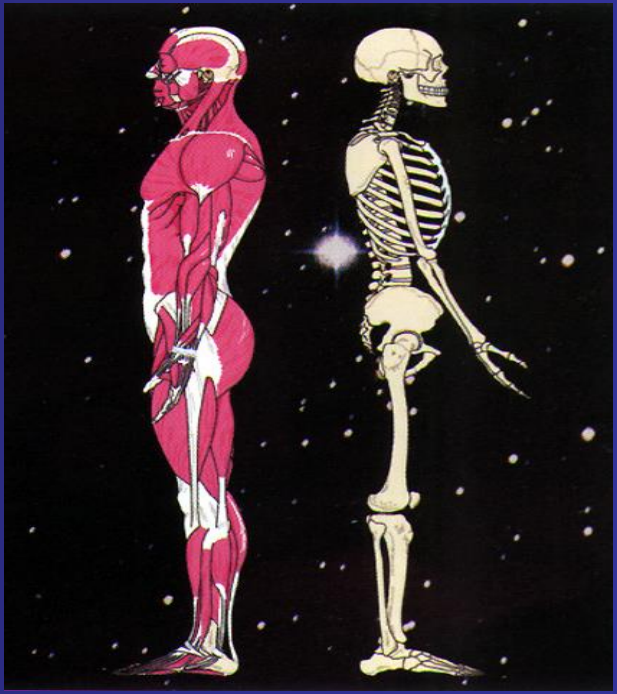
Preflight



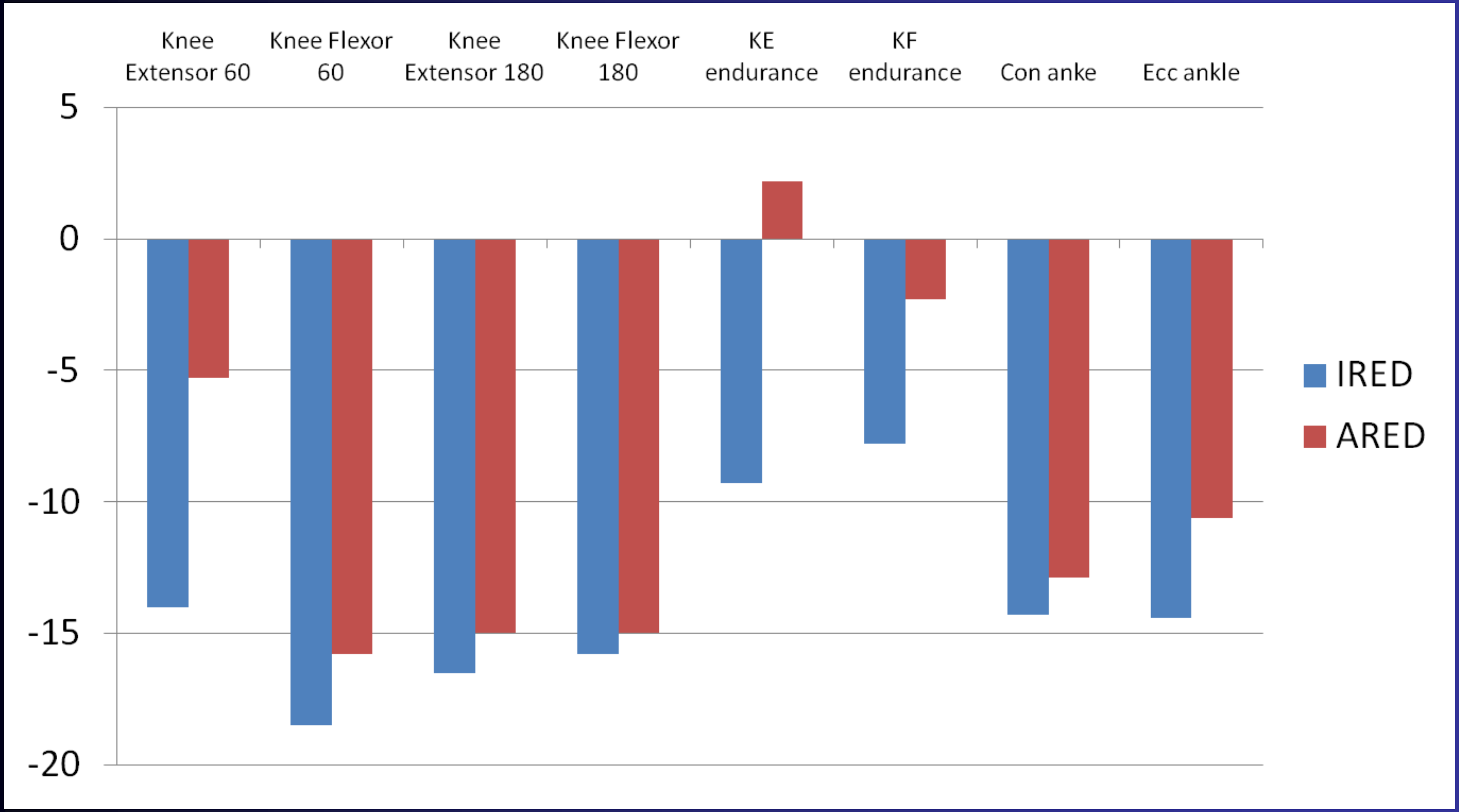
Postflight (ISS, R+1)

Musculoskeletal

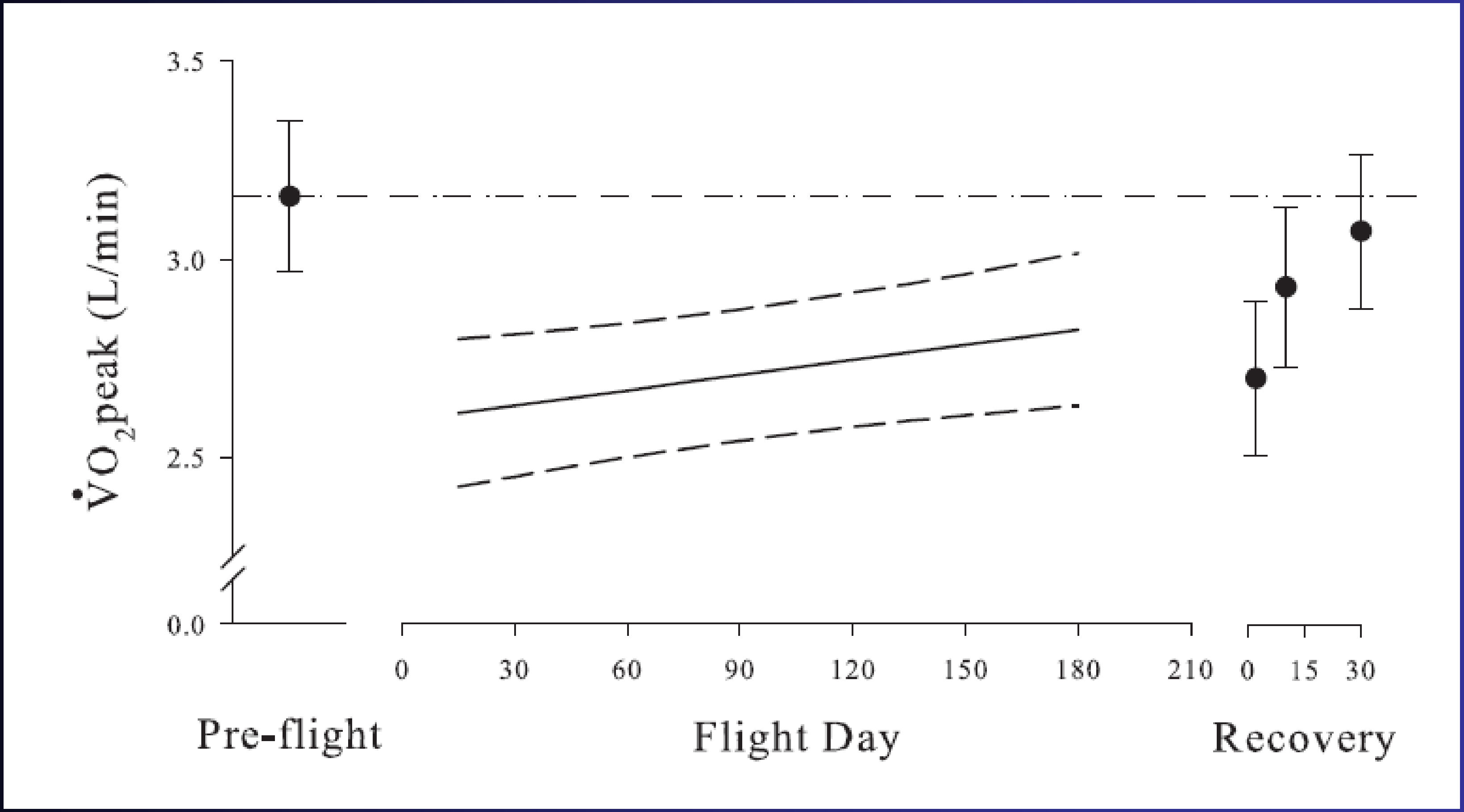
- Changes in antigravity muscles, bone and calcium metabolism
- Incidence
  - All crewmembers are affected
- Symptoms
  - Acute – short term
    - Postural change with stretching of tendons and ligaments
    - Height increases on orbit by 2-6 cm
    - Back pain (70 – 90% incidence)
    - Fatigue (less flexibility and endurance)
  - Chronic – long term
    - Muscle atrophy
    - Loss of total body calcium
    - Loss of bone density



Isokinetic Muscle Function



Aerobic detraining



Moore, A. et al. 2014

Aerobic conditioning:
In-Flight → Post-Flight

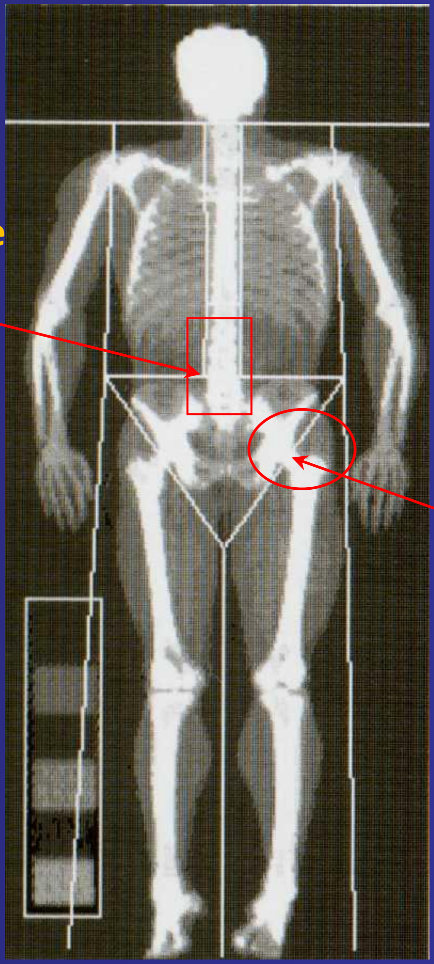
- Deconditioning effects
  - Decreased maximum power outputs during exercise.
  - Oxygen uptake less during exercise
  - Less circulating blood volume upon return to Earth
  - Decreased standing blood pressure

- Countermeasures on ISS largely effective……exploration?

Bone mineral density losses are regional and rapid

Areal BMD g/cm2	%/Month Change ± SD
Lumbar Spine	-1.06±0.63*
Femoral Neck	-1.15±0.84*
Trochanter	-1.56±0.99*
Total Body	-0.35±0.25*
Pelvis	-1.35±0.54*
Arm	-0.04±0.88
Leg	-0.34±0.33*

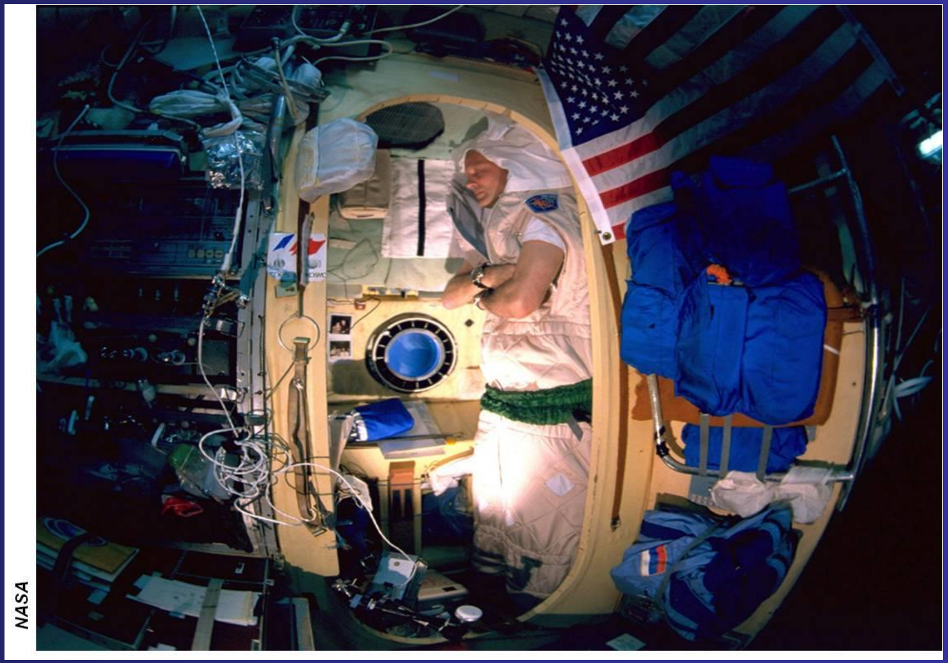
*p<0.01, n=16-18



LeBlanc et al, J Musculoskeletal 2000

Behavioral/Psycho-social

- Changes in crew mood, morale, and circadian rhythm
- Symptoms
  - Fatigue and irritability
- Causes
  - Work load
  - Sleep habits and facilities
  - Temperature
  - Noise
  - Odors
  - Atmosphere
  - Diet
  - Lack of family contact
  - Crew personalities, cultural differences, and “crew space”



Behavioral Health & Team Dynamics

SIRIUS 21

8-month mission simulating lunar transit and exploration activities

HRP focus on autonomy, isolation, and confinement impacts on psychology, physiology, and team dynamics in a mixed gender, international crew

BHP & HRP Standard Measures

Biomarkers Stress & Resilience

Team Task Switching

Components of Successful Autonomy




SIRIUS 19 CrewCrew

Behavioral/Psycho-social

- Countermeasures

Team Building Training

Communications

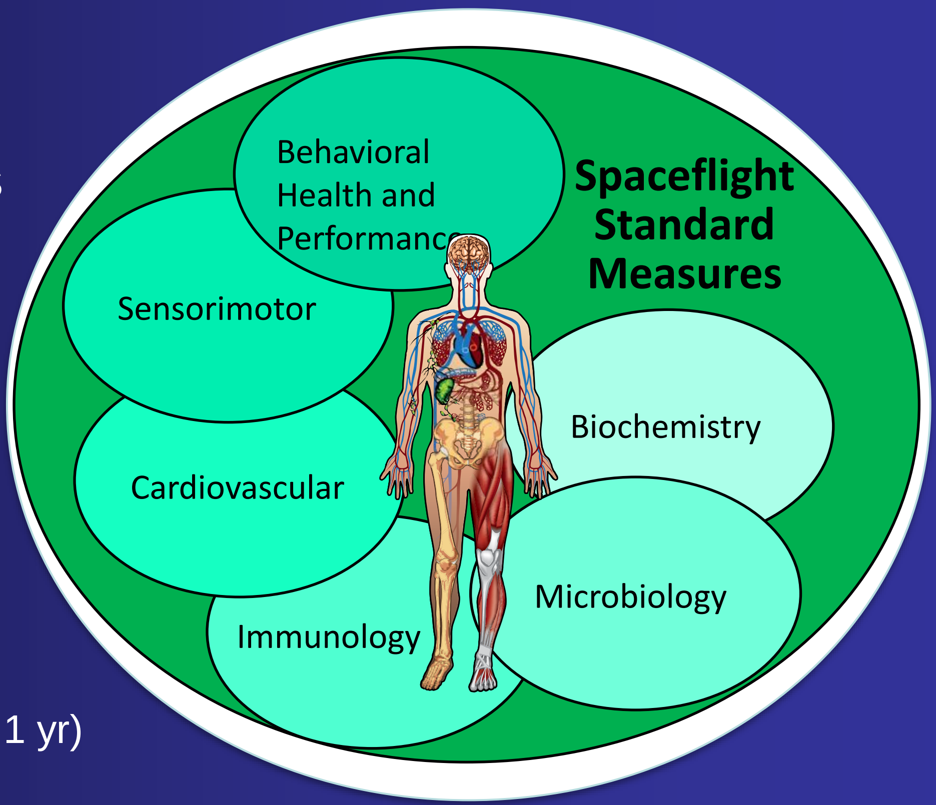
Crew Care Packages

Spaceflight Standard Measures

Objectives

- Ensure minimal measures consistently from ISS crew
- Data storage and sharing to
  - Provide context for data
  - Support or develop hypotheses
  - Evaluate effectiveness countermeasures
  - Compare population responses to various

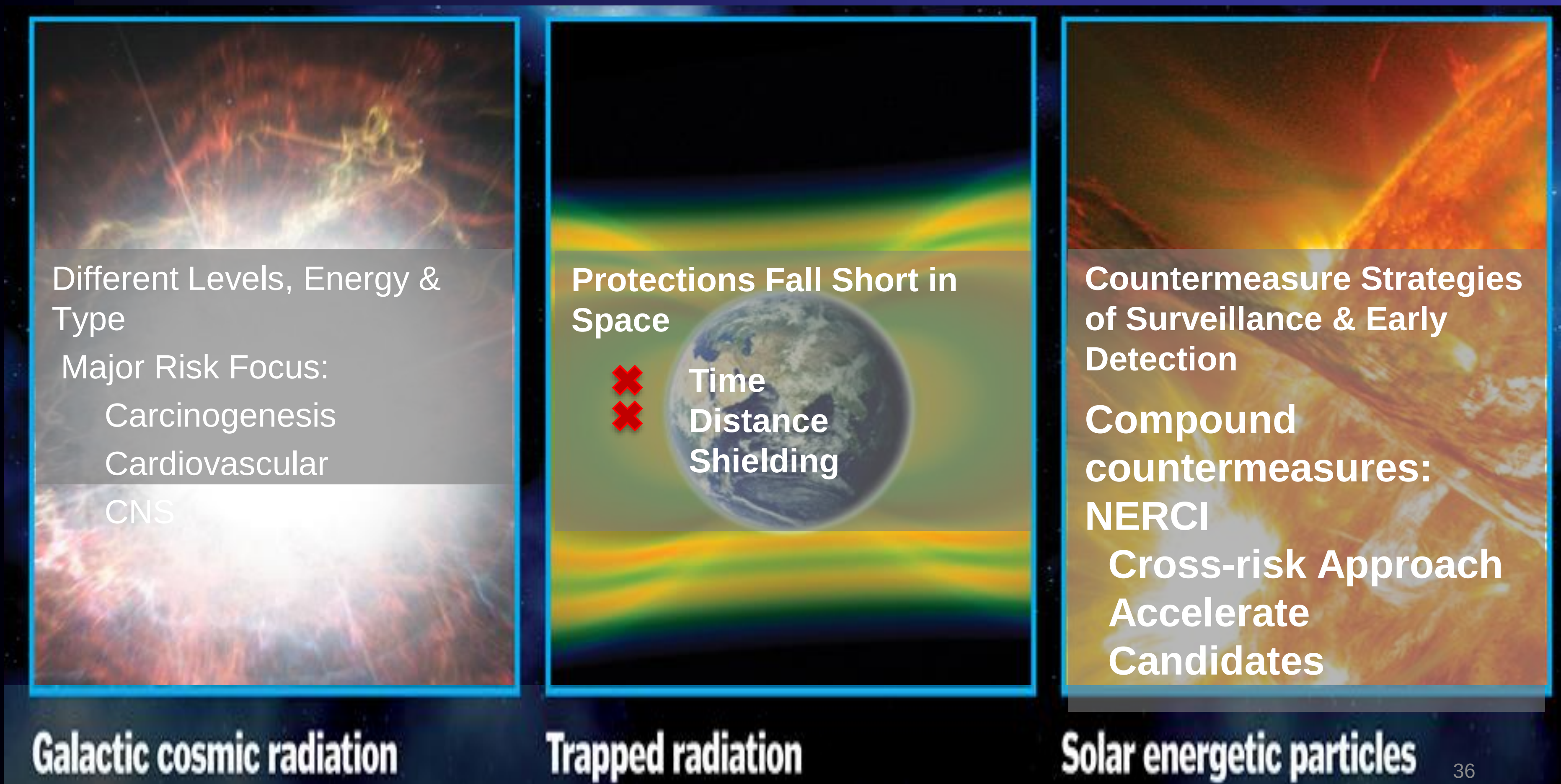
  mission platforms and durations (6 wk, 6 mo, 1 yr)



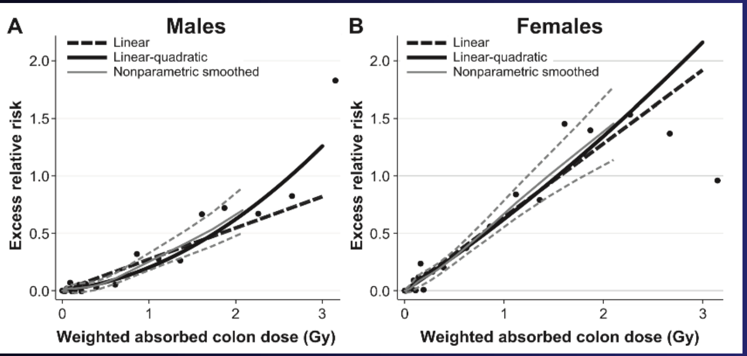
Radiation

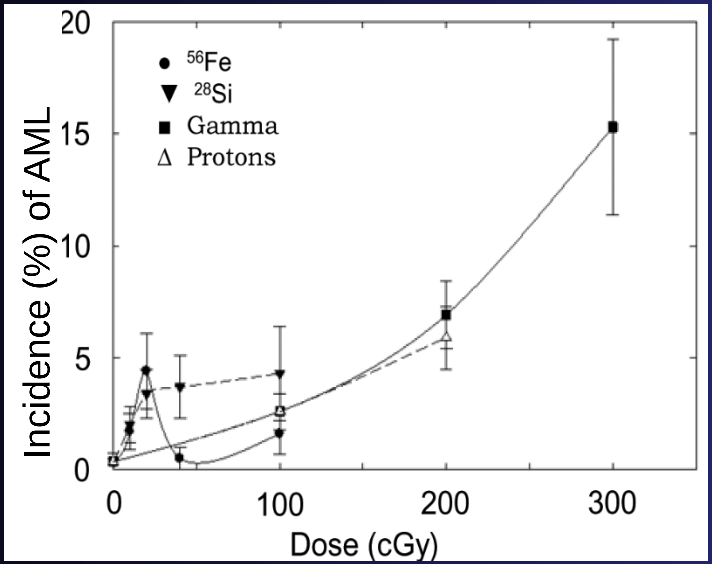
- Exposure based on orbital altitude/inclination, duration, and solar activity
- Crewmembers are radiation workers
  - Limits for mission and career exposure are set by the National Council on Radiation Protection
- As Low As Reasonably Achievable (ALARA) principle for mission planning
- Exposure monitored by active and passive dosimeters
- Radiation effects on cells
  - Is there an acute in-mission risk such decreased cognitive function?
  - Is there a long-term risk such as an increased incidence of cancer?

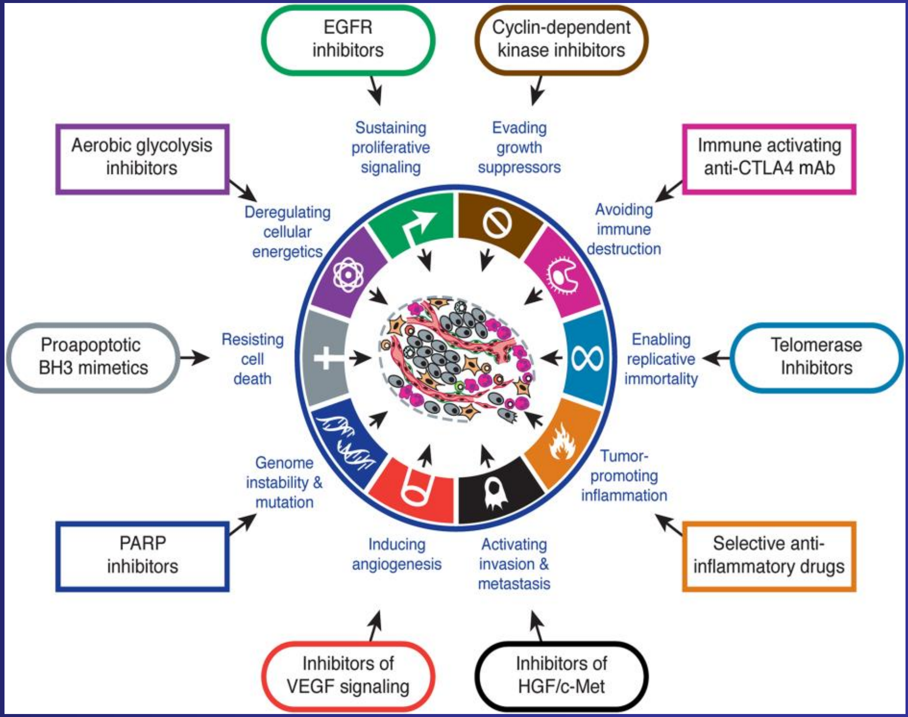
Space Radiation



Space Radiation Element: Carcinogenesis





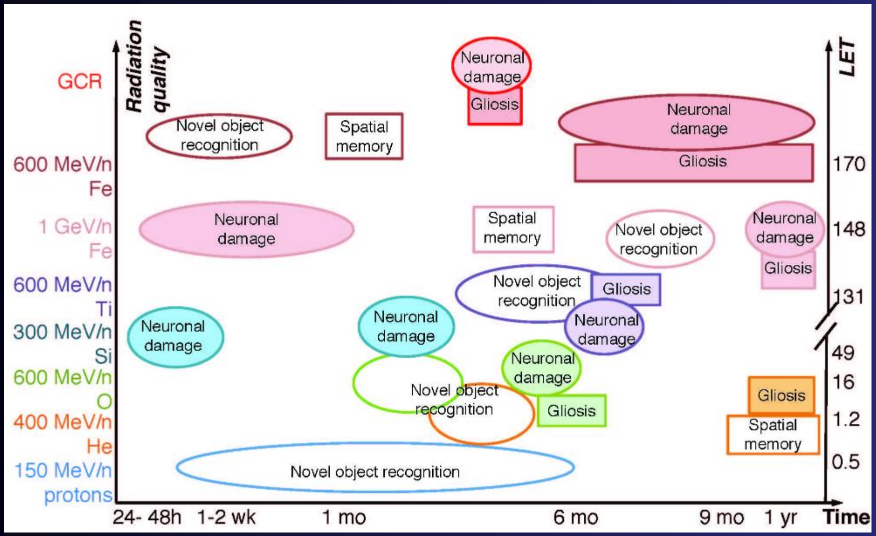


Hallmarks of Cancer & Corresponding Therapeutics

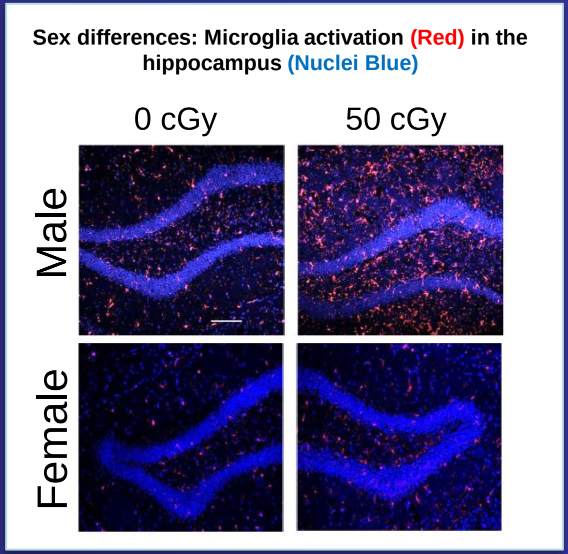
Hanahan and Weinberg (2011) *Cell* 144(5), 646-74

Space Radiation Element: Central Nervous System Changes

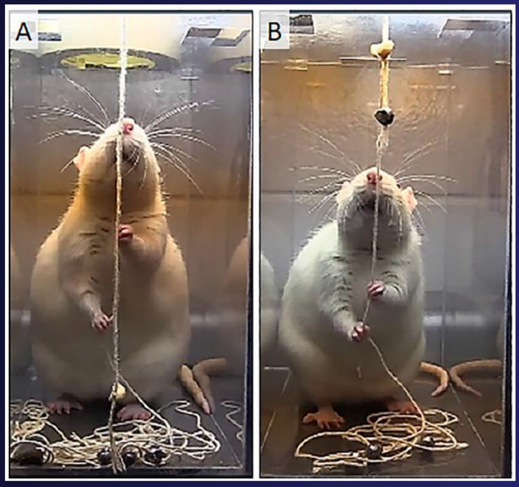
Literature Review Summary of Space Radiation effects on the CNS

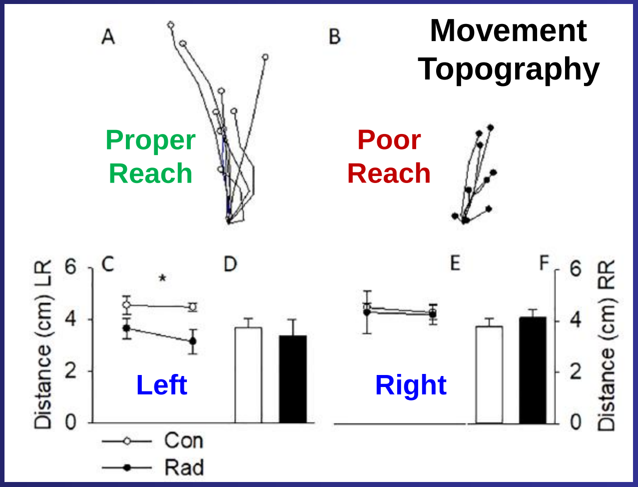


Cekanaviciute, et al. (2018) *International Journal of Molecular Sciences*. 19(11), 3669



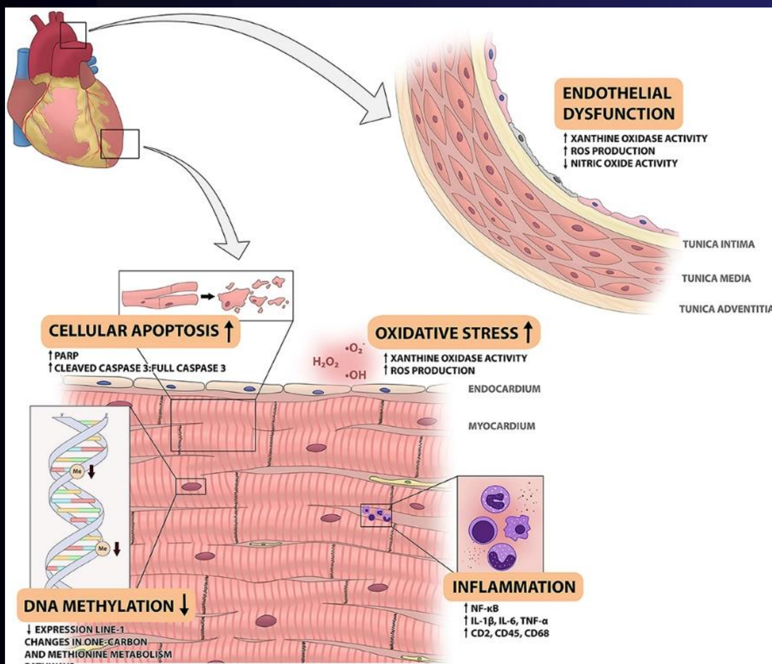
Krukowski et al. (2018) *Brain, Behavior, and Immunity*





Blackwell et al. (2020) *Behavioral Brain Research* 400,113010

Space Radiation Element: Cardiovascular Disease



Meerman, et al. (2021) *Front. Cardiovasc. Med.* 8:631985.

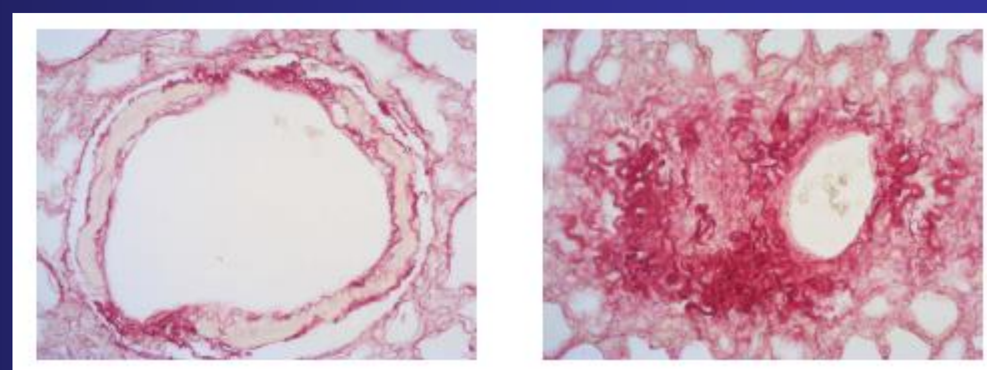
Cardiovascular Risk from Low Dose Radiation Exposure Review and Scientific Appraisal of the Literature

Circulatory Disease Category	ERR/Sv	95% CI:
CVD Mortality		
Japanese Atomic Bomb Survivors – LSS	0.11	0.050, 0.170
Mayak Production Association Workers	0.05	0.000, 0.110
U.S. Peptic Ulcer Study	0.082	0.031, 0.140
French Uranium Miners	0.60	-1.80, 3.5
INWORKS (note 90% CI)	0.22	0.08, 0.37
Canadian + Mass. TB-Fluoroscopy study < 0.5 Gy (50 rads)	0.246	0.036, 0.469
U.S. Power Reactor Workers	8.32	2.3, 18.2
U.S. Nuclear Power Plant Workers	0.06	-0.50, 0.40
U.S. Industrial Radiographers	0.02	-0.03, 0.08
U.S. Mound Workers	-0.40	-3.9, 3.2

Electric Power Research Institute. Technical Report 2020

Lung Fibrosis

15 months after 1 GeV/u ^{40}Ca ions



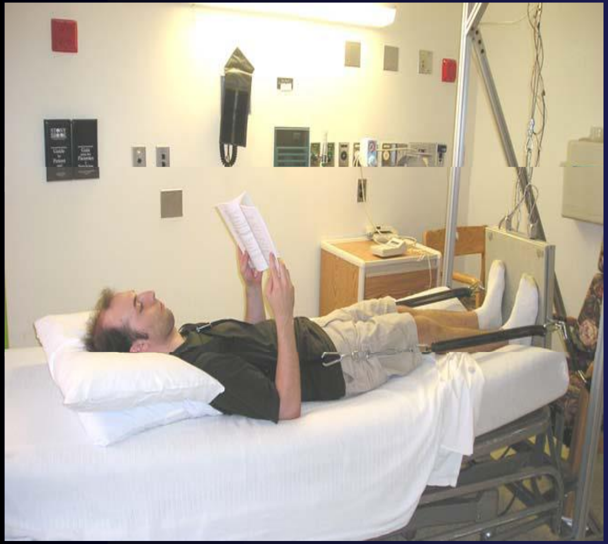
Control

40 cGy(3 fractions; 1f/day)

Azzam, HRP IWS 2020

Countermeasures

Research



Operational

Artificial Gravity

- Many of the negative effects on human physiology associated with spaceflight are caused or exacerbated by lack of gravity.

- Continuous exposure to artificial gravity may prevent or attenuate deconditioning during space flight, and integration with other countermeasures may enhance their effectiveness.

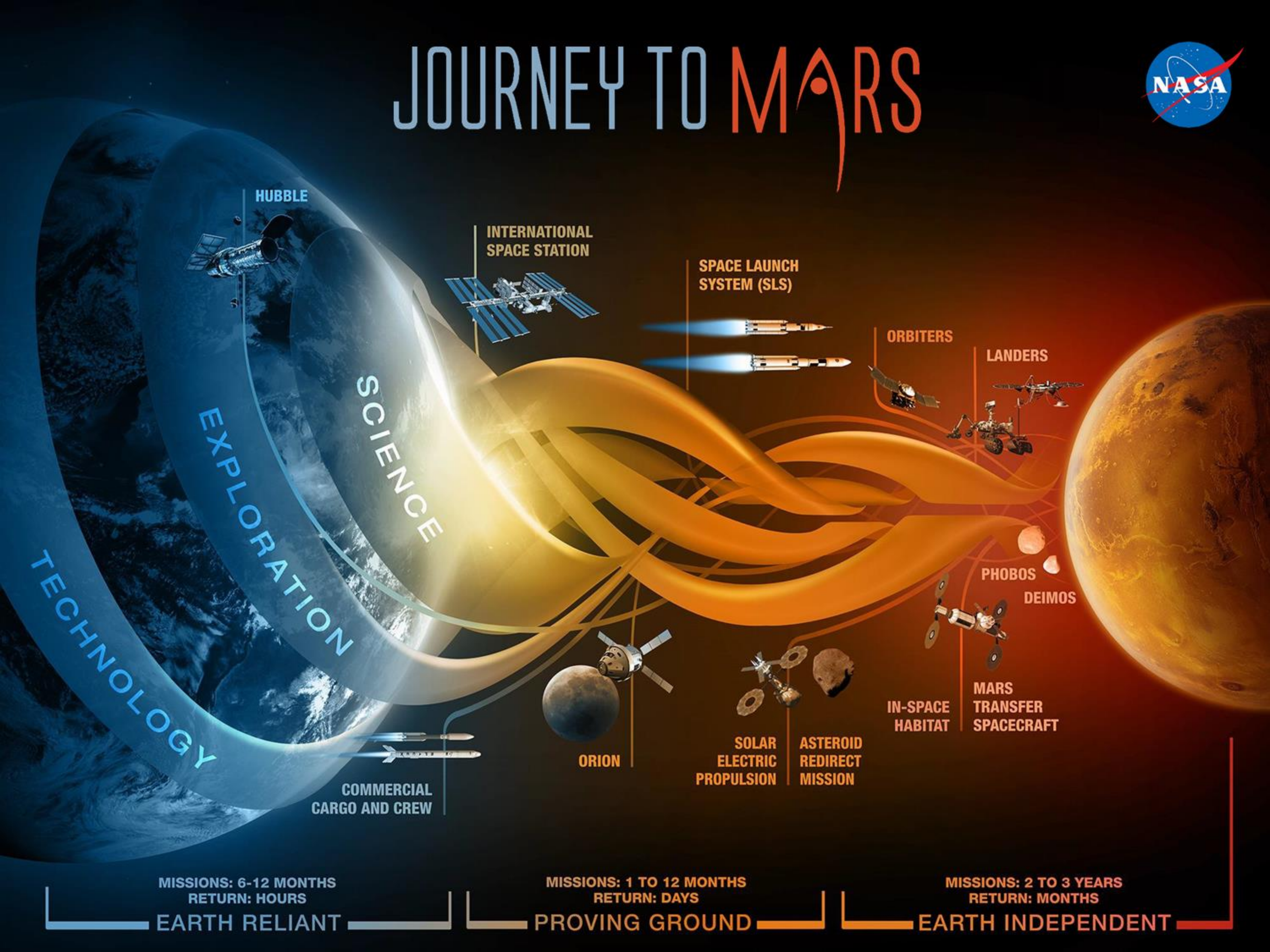
- Artificial gravity may reduce requirements for other countermeasures and/or reconditioning after space flight.

- Artificial gravity alone or in combination with another countermeasure can be used to combat multiple system deconditioning: bone, muscle, cardiovascular, sensorimotor, etc.


09:56:48
07/14/99
0.040 Gz

Thank you for Listening!

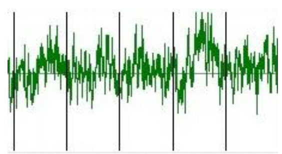
Questions?


JOURNEY TO MARS
NASA
HUBBLE
INTERNATIONAL SPACE STATION
SPACE LAUNCH SYSTEM (SLS)
ORBITERS
LANDERS
SCIENCE
EXPLORATION
TECHNOLOGY
PHOBOS
DEIMOS
ORION
SOLAR ELECTRIC PROPULSION
ASTEROID REDIRECT MISSION
IN-SPACE HABITAT
MARS TRANSFER SPACECRAFT
COMMERCIAL CARGO AND CREW
MISSIONS: 6-12 MONTHS
RETURN: HOURS
EARTH RELIANT
MISSIONS: 1 TO 12 MONTHS
RETURN: DAYS
PROVING GROUND
MISSIONS: 2 TO 3 YEARS
RETURN: MONTHS
EARTH INDEPENDENT

Mechanistic Understanding

ISS Fluid Shift study
looking at fluid shifts,

ISS 1 Carbon Metabolism study looking at genetic mutations and relation to astronaut vision issues.



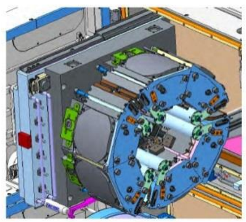
HRP funded rat study looking at fluid shifts, ICP, ocular changes and gene expression

GeneLab

Open Science
for Exploration

Biospecimen sharing with Space Biology for Gene lab and looking at other physiological systems (bone, IVD, cardiovascular)

AG translational research

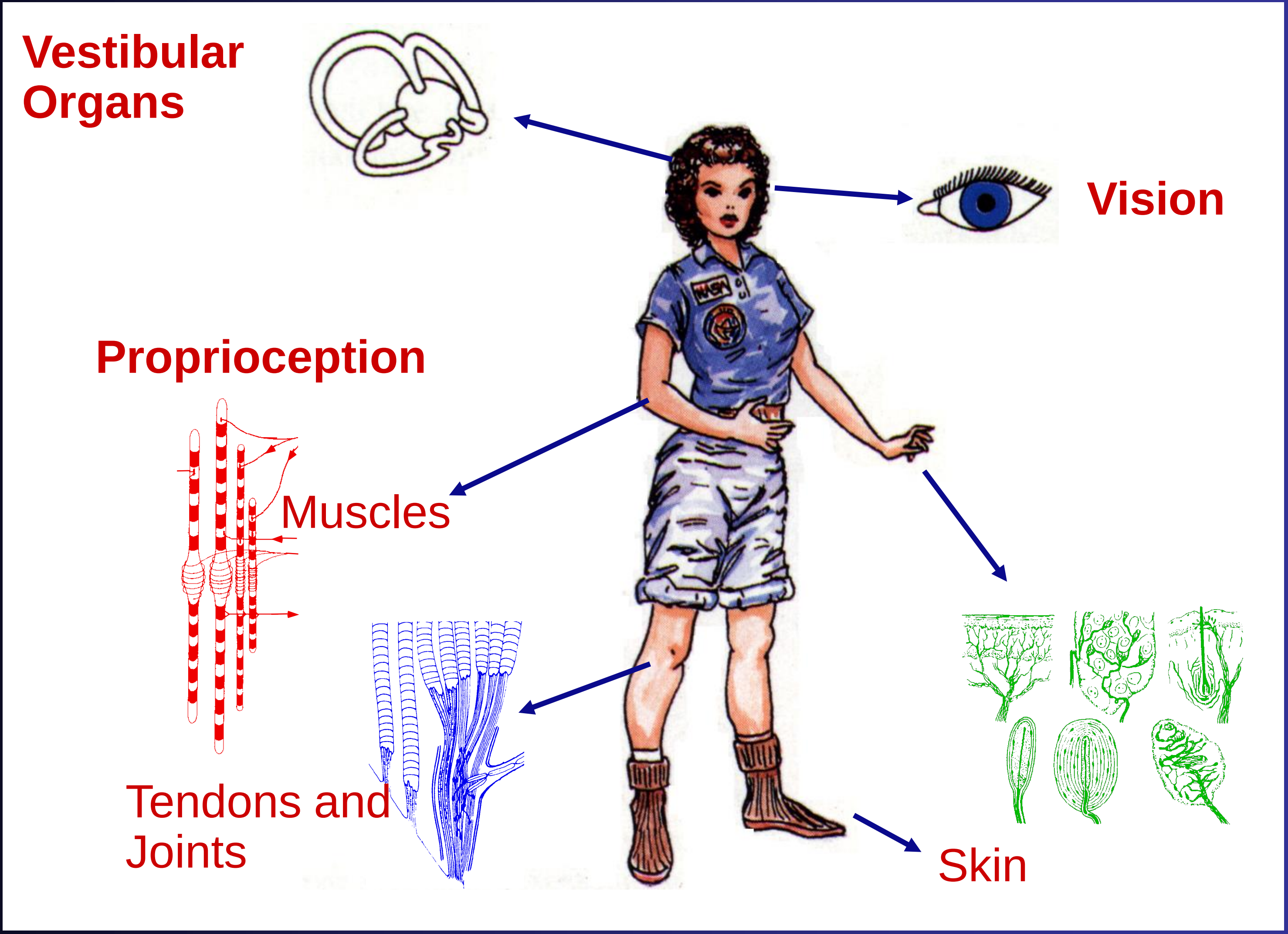


ISS hypo and artificial gravity mouse studies
Collaborations between JAXA, Space Biology and HRP

Human bedrest and AG (centrifuge studies)
Collaborations between DLR, Space Biology and HRP

Neurovestibular

- The sense of motion



Human Response to Spaceflight

Astronauts experience a spectrum of adaptations in flight and post flight

Exposures:

Launch & Landing Loads

Microgravity

Closed Environment (air and water)

Confined Habitat

Radiation Exposure

Balance disorders
Cardiovascular deconditioning
Decreased immune function
Muscle atrophy
Bone loss

- Neurovestibular
- Cardiovascular
- Skeletal
- Muscular
- Immunological
- Nutritional
- Behavioral

Musculoskeletal

- Countermeasures
  - Exercise
  - Pharmacologic treatment

Preflight

In flight

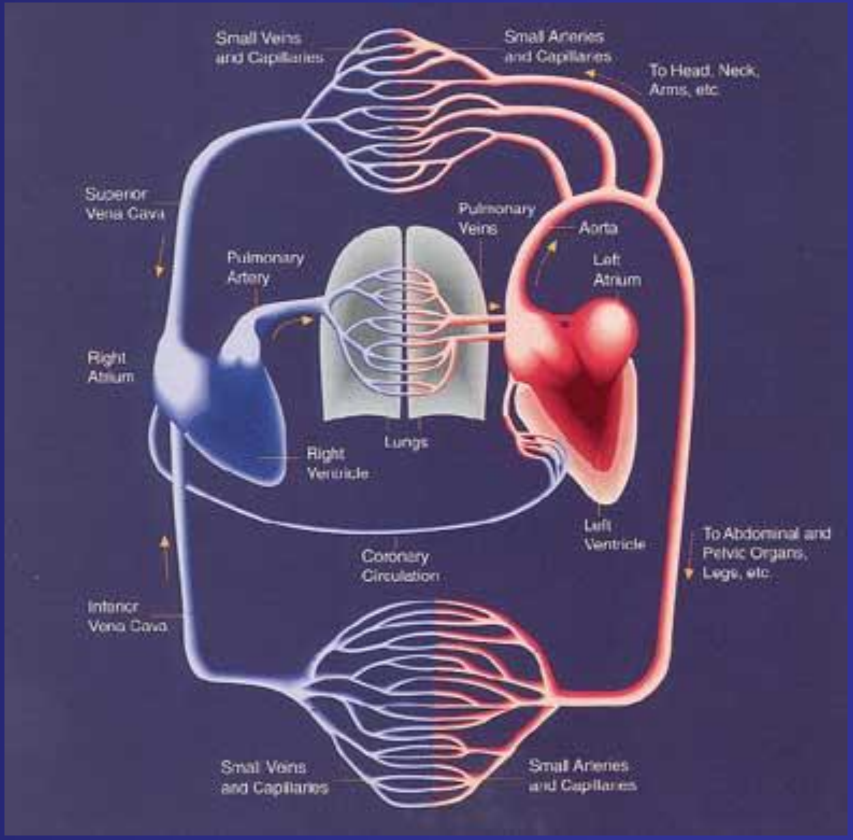
Postflight

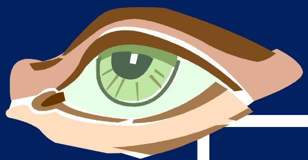
Cardiovascular: Preflight

- The heart is about the size of your fist and has to work hard to move blood through the body on Earth – it has to work less to pump blood throughout the body in the absence of gravity
- The blood vessels in the upper and lower body dilate and constrict depending on the blood flow needs of the organs they feed – these vessels behave differently during and after space flight

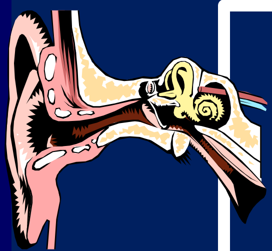
Altered heart rate and contractility

Total Blood Volume is reduced



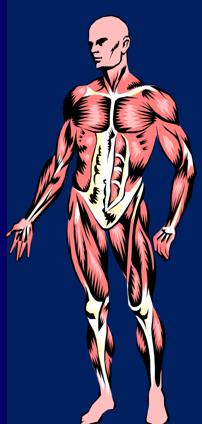


VISUAL SYSTEM



VESTIBULAR SYSTEM

Balance organs of the inner ear



PROPRIOCEPTIVE SYSTEM

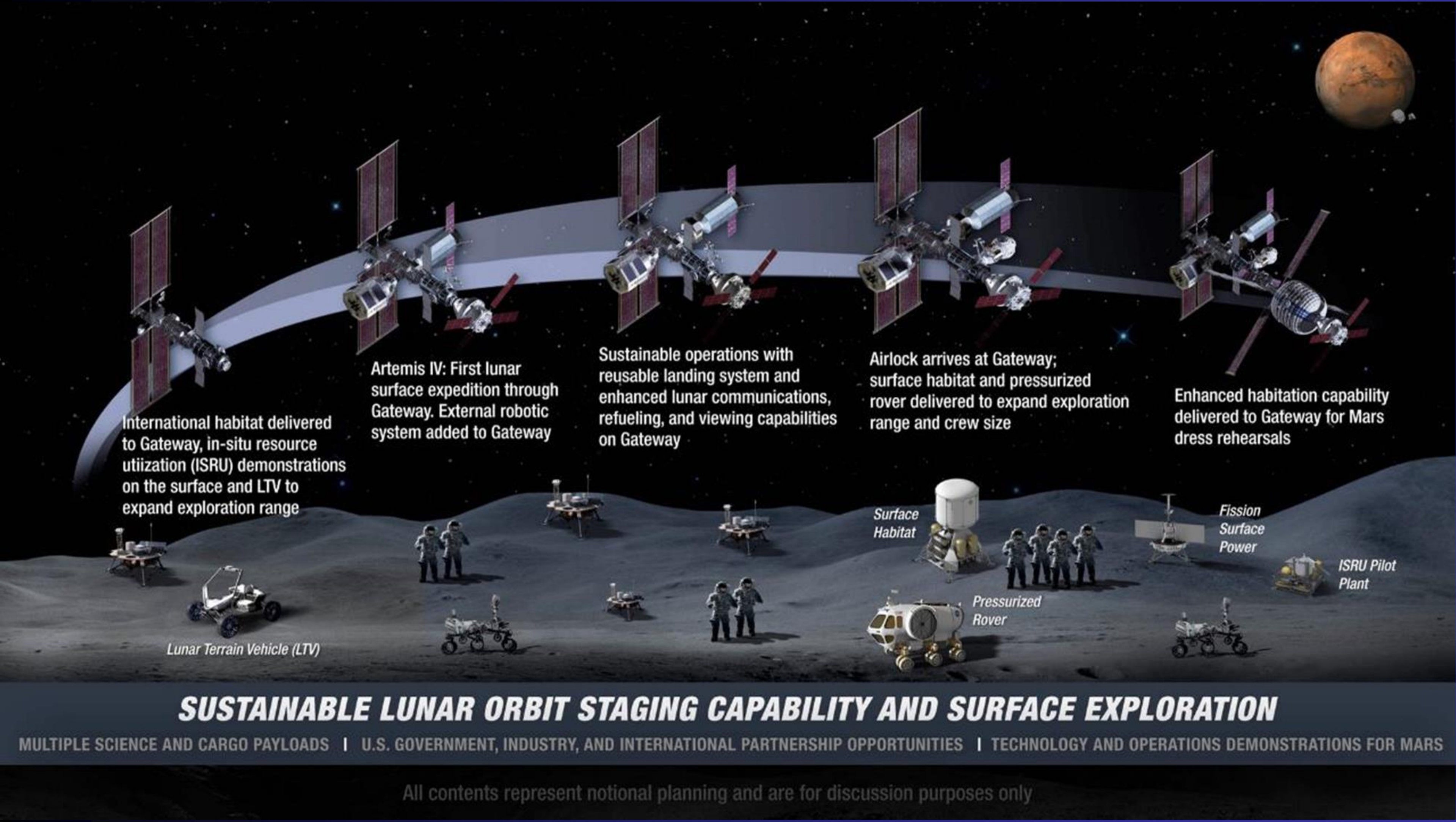
Muscle, tendon, skin receptors

CENTRAL REINTERPRETATION OF SENSORY INPUT

Control of movement in 0-g

Control of movement in 1-g

Planned Exploration Activities



Hazards of Space Flight

Radiation

Altered Gravity Fields
- Microgravity
- Planatary gravity (1/6, 3/8, 1)

Space Environment
- Vacuum
- Debris

Hostile Closed Environment
- Noise and Vibration
- Closed loop environment (life support)
- Payloads and construction activities
- Waste production

Isolation and Confinement
- Launch and reentry Forces
- Remoteness and communication access
- Circadian rhythms and crew schedule changes
- Extravehicular Activity (EVA)