Neuroscience Overview

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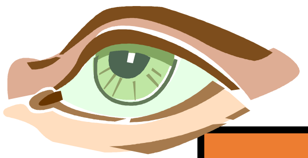
Sensorimotor Risk

Given that altered gravity transitions leads to changes in sensorimotor / vestibular function that manifest in motion sickness, spatial disorientation, decrements in postural control and locomotion, and fine motor control deficits, there is a possibility that crew will experience performance decrements in manual / vehicle control, extravehicular activities, and egress during and following these transitions.

Manual Control

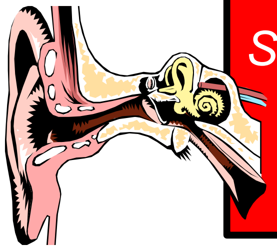
Early EVA

Crew Egress



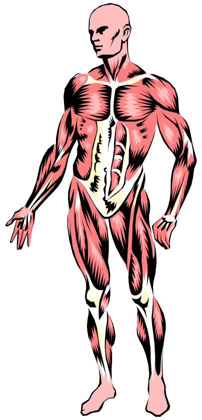
VISUAL
Central (foveal)
Peripheral

Control of Movement



INNER EAR
Semi-circular canals
Otoliths
Auditory

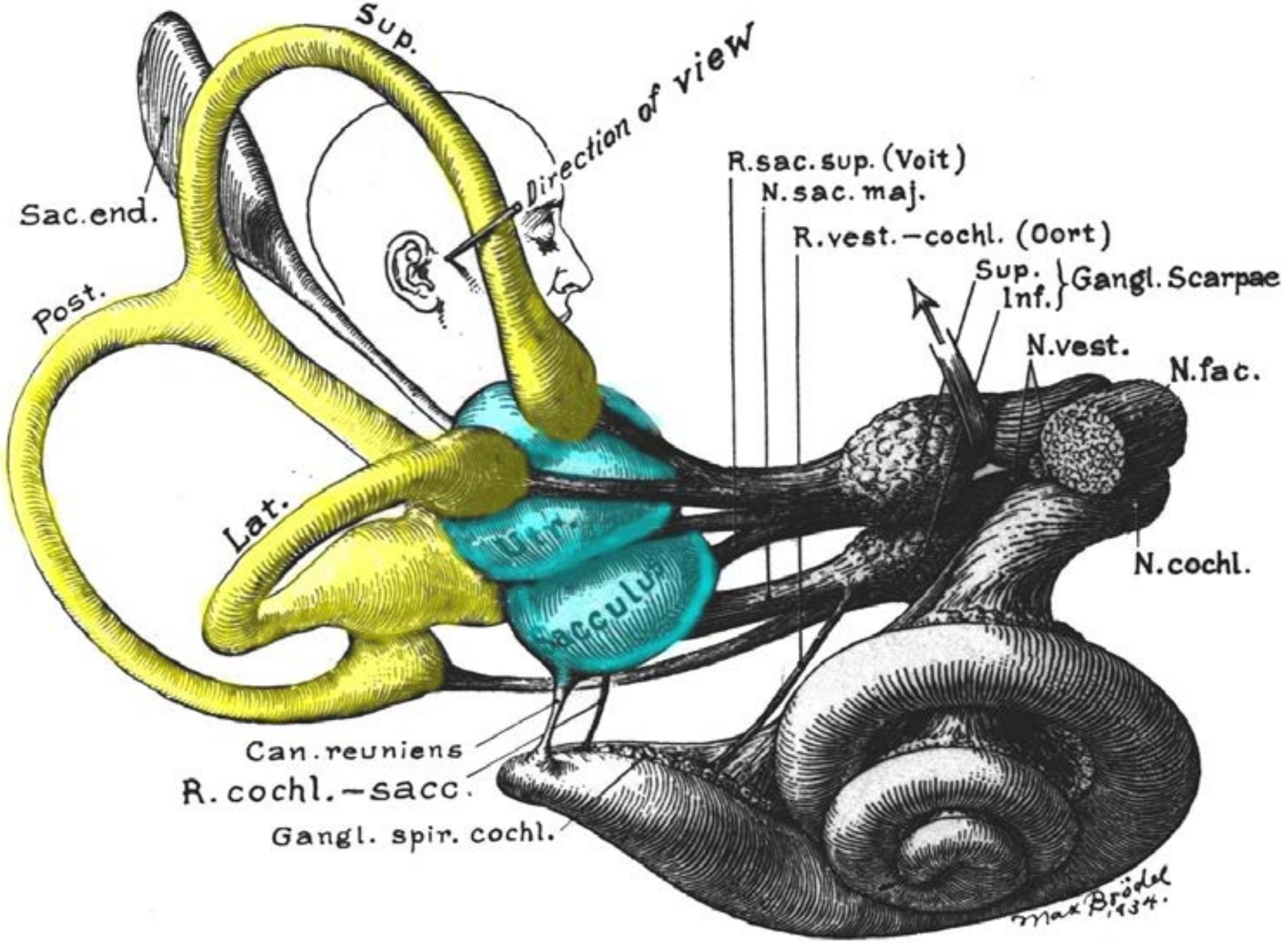
CENTRAL <u>INTEGRATION</u> OF SENSORY INPUT



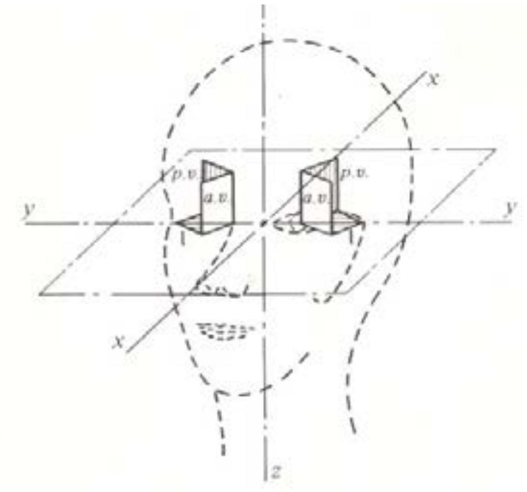
SOMATOSENSORY
Proprioception (body),
Exteroception (tactile),
Interoception (viscera)

Our ability to sense and control motion depends on a learned ability to interpret the continuous input of multiple sensory signals

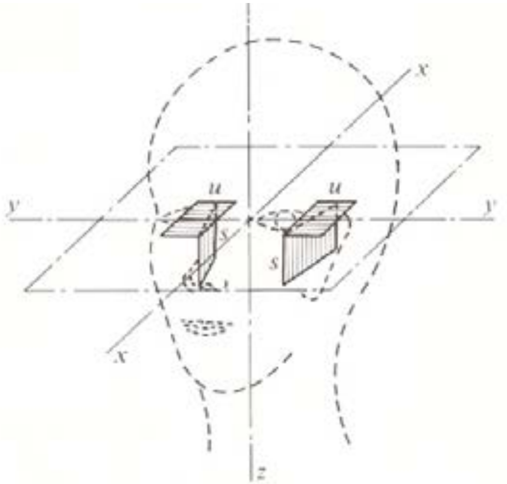
Vestibular structure



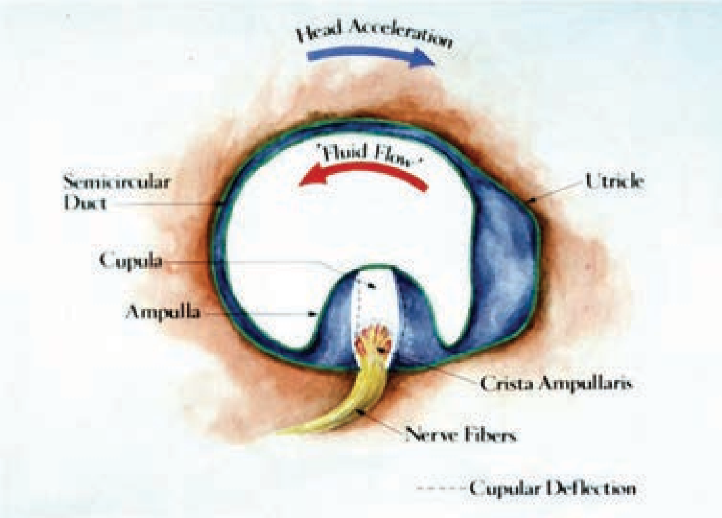
Semicircular canals - angular

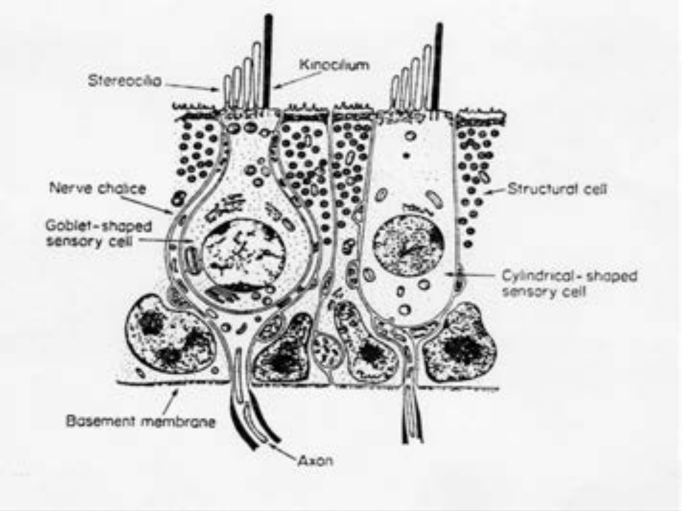


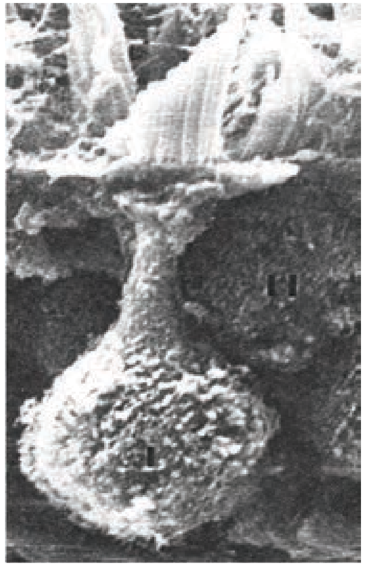
Otoliths - linear

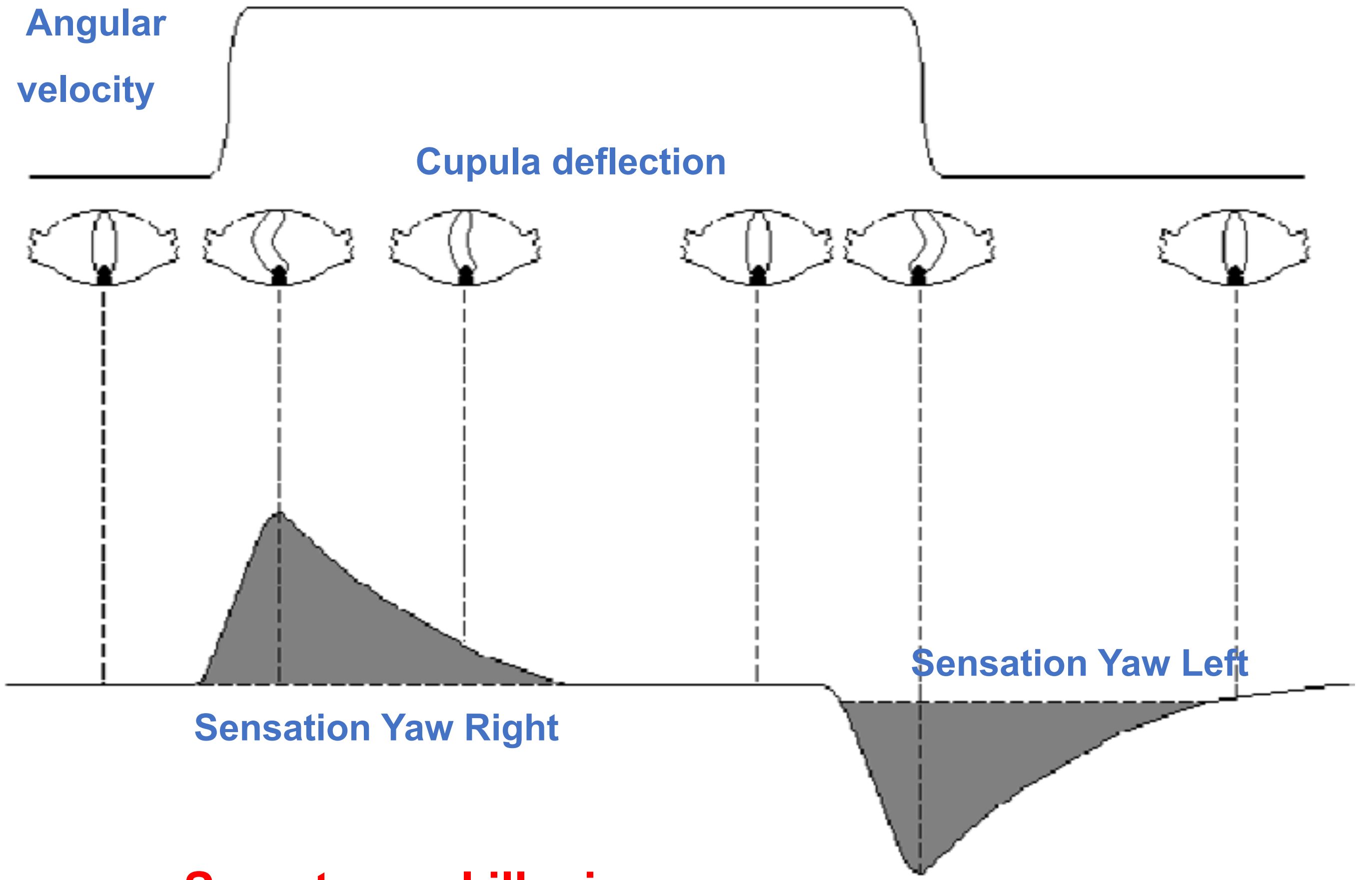


Semicircular canals: angular







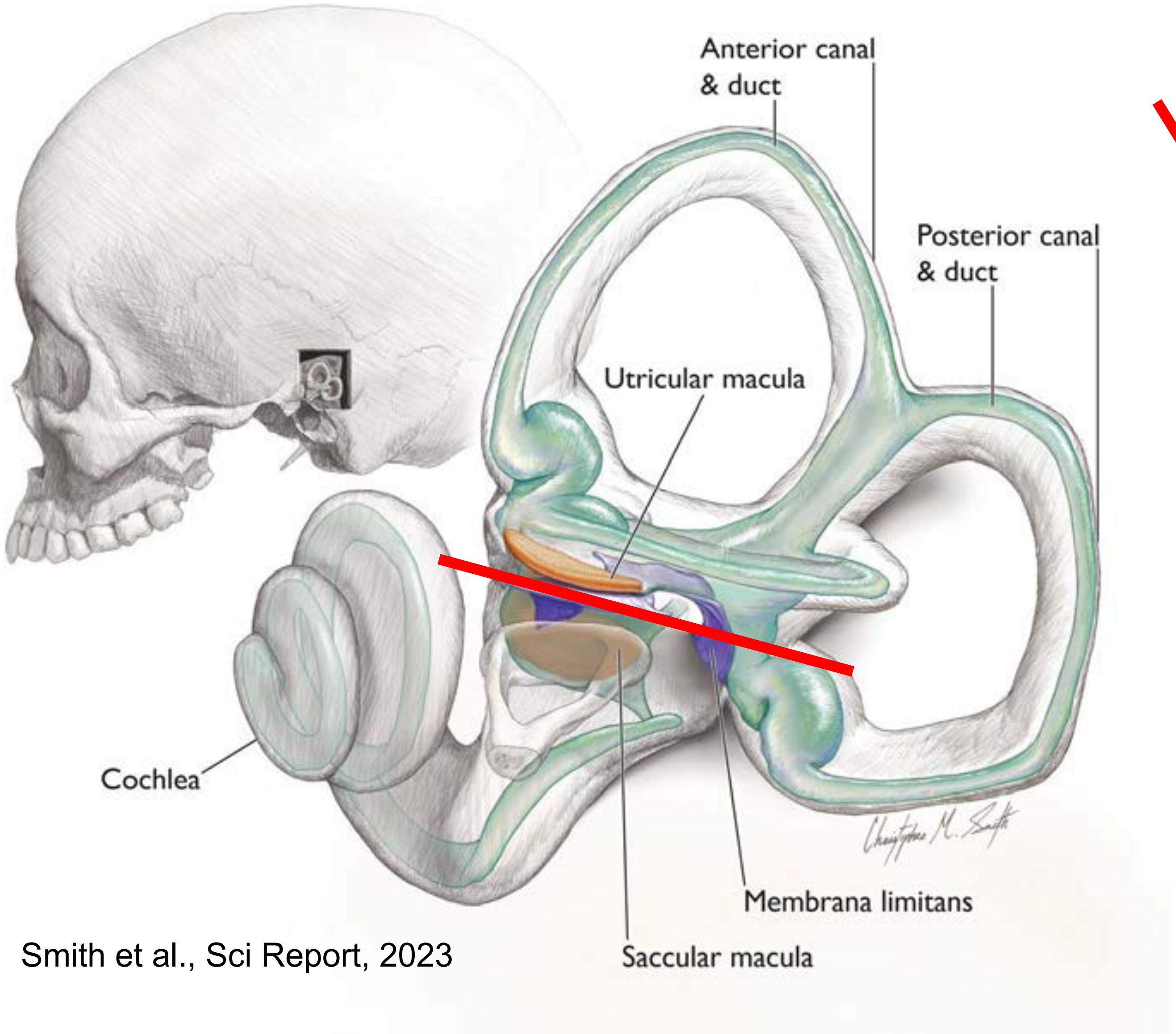


Somatogyral illusion
Graveyard spin

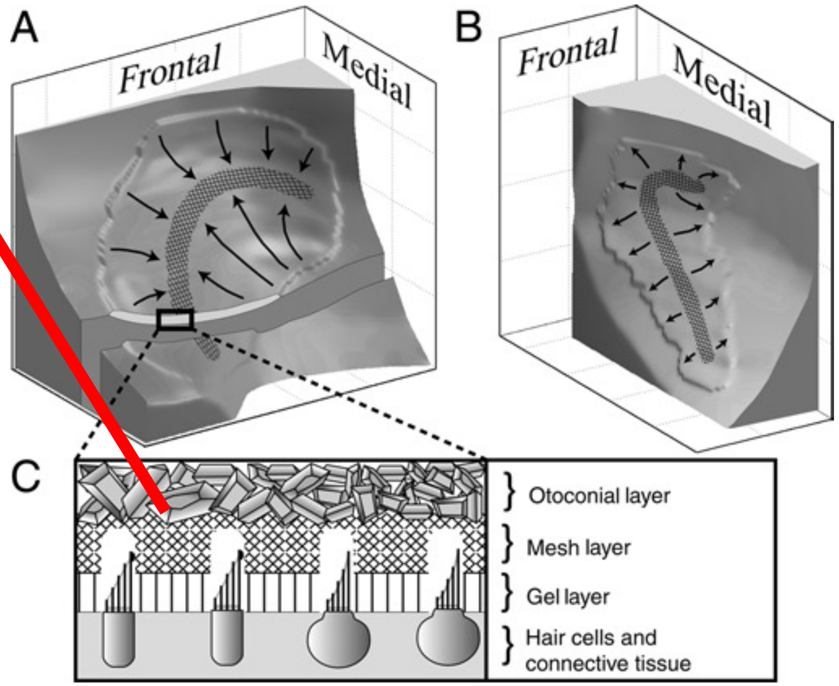
Oculogyral illusion

Gemini VIII stuck thruster

Otoliths: linear acceleration

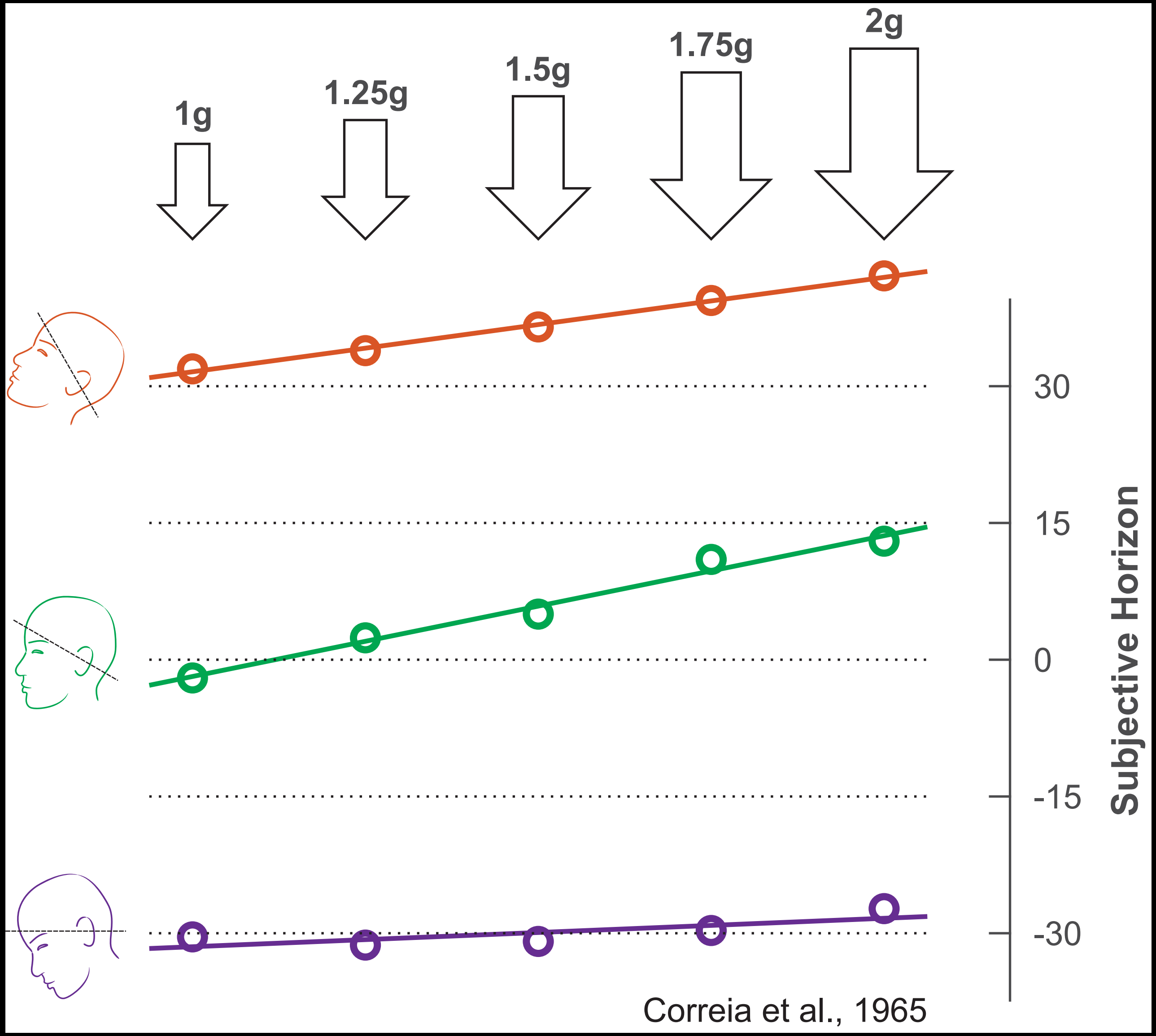


Smith et al., Sci Report, 2023



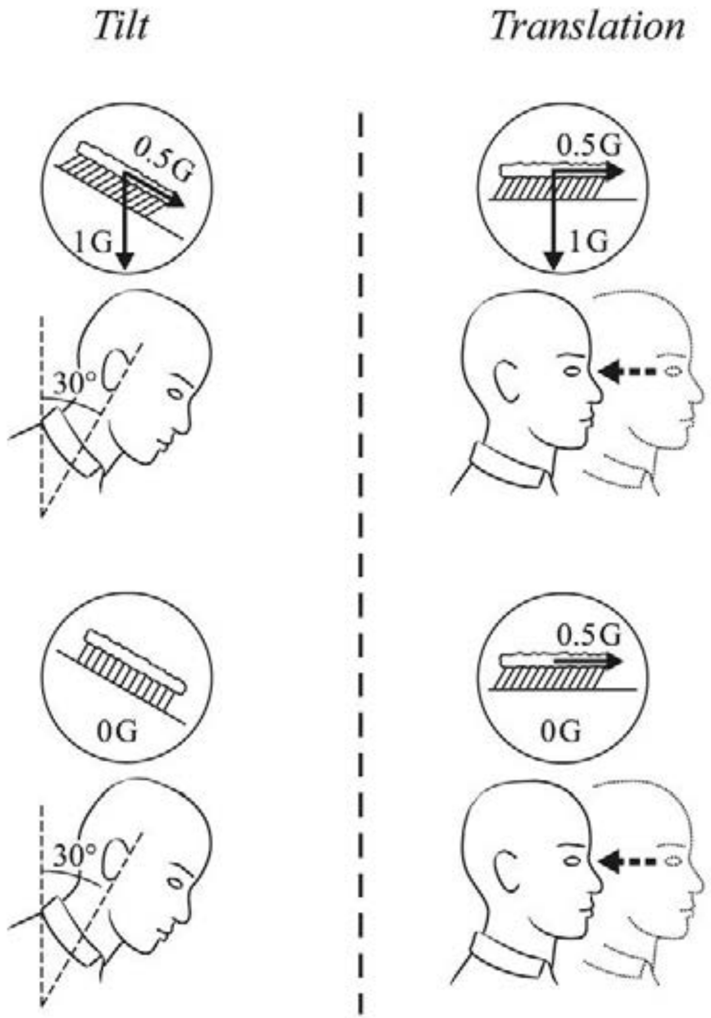
Jaeger & Haslwanter, Biol. Cybern 2004

G-excess tilt illusion



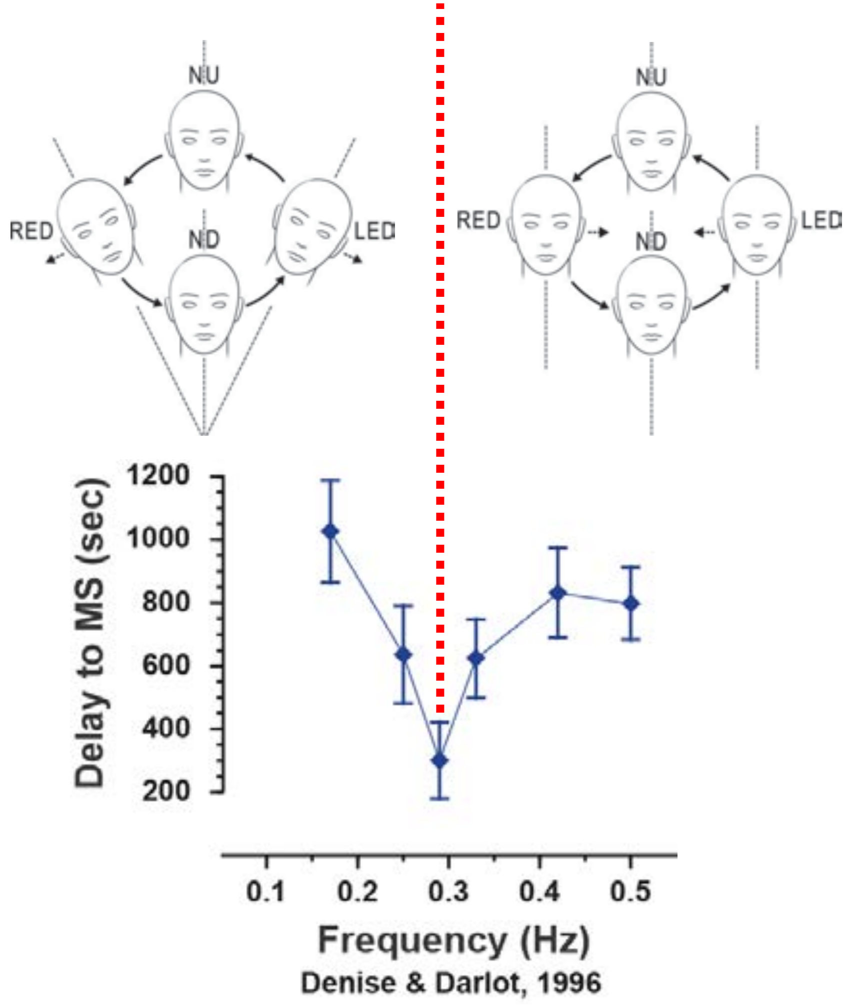
- G-excess effect is a false or exaggerated sensation of body tilt that can occur when exposed to hypergravity
- A similar effect can occur following transition from 0g to 1g
- This is the result of increased shear along the utricular plan
- Pitching the head forward to reduce the shear effect can reduce the G-excess or vertigo

Tilt-Translation Ambiguity



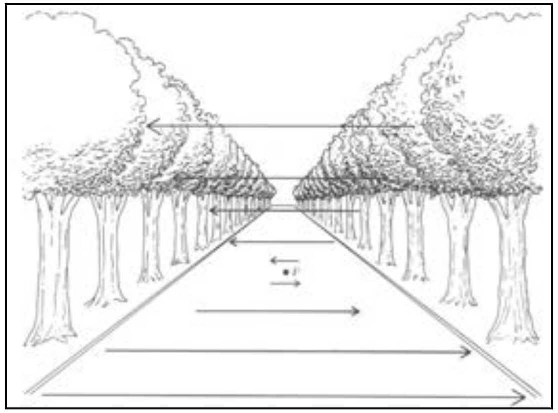
Somatogravic illusion
Pitch up during takeoff

Tilt-translation illusions can be experienced following transition from micro-g



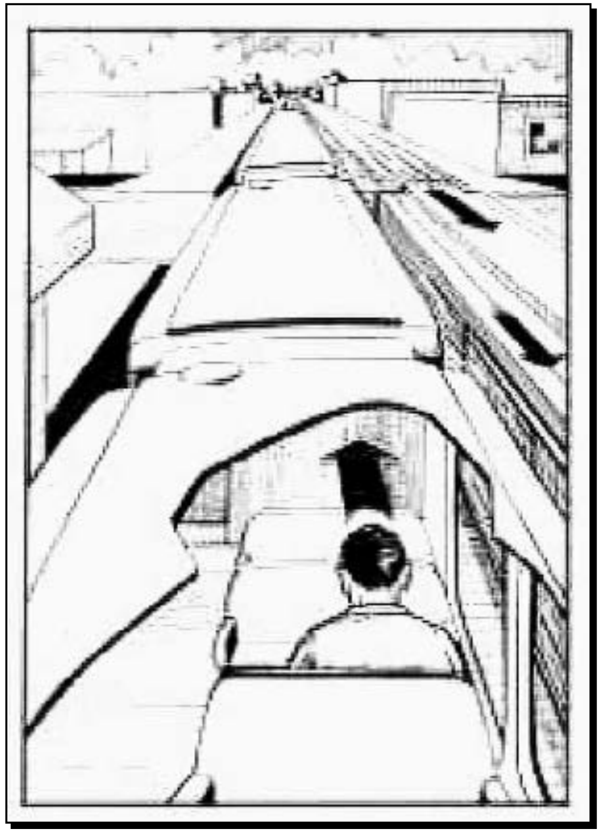
Visual orientation

Linear perspective



Motion parallax

Self-position



Self-motion (vection)

Visual orientation in space

Earth as down

EVA acrophobia

Visual reorientation

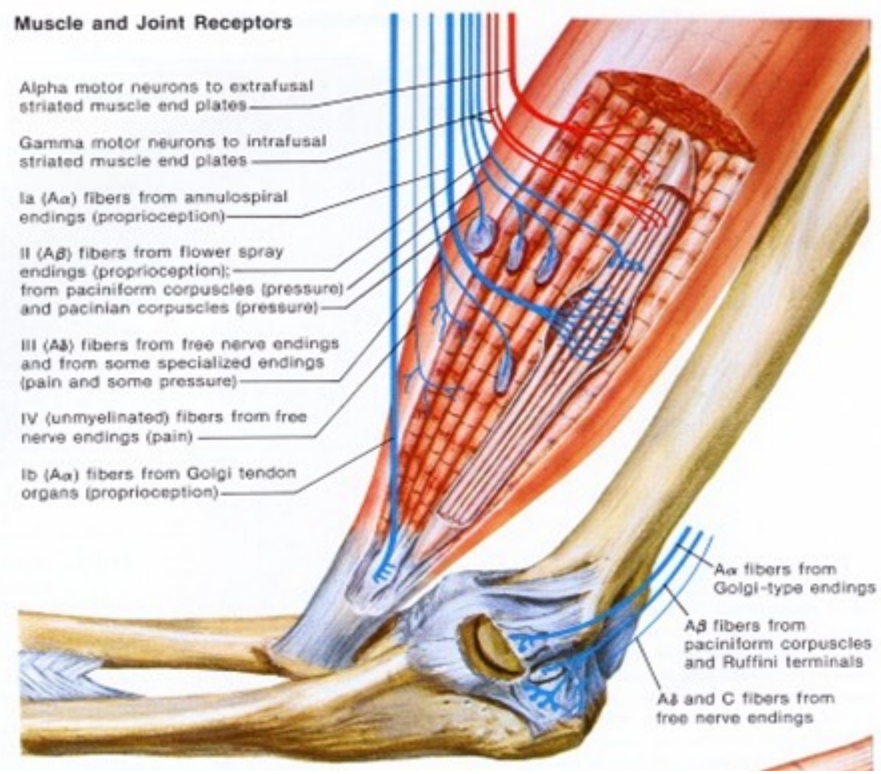
<u>0-G inversion illusion</u> - feeling continuously inverted even in "visually upright" orientation in the cabin, more common during Shuttle inverted attitude launch profile, persists with eyes closed

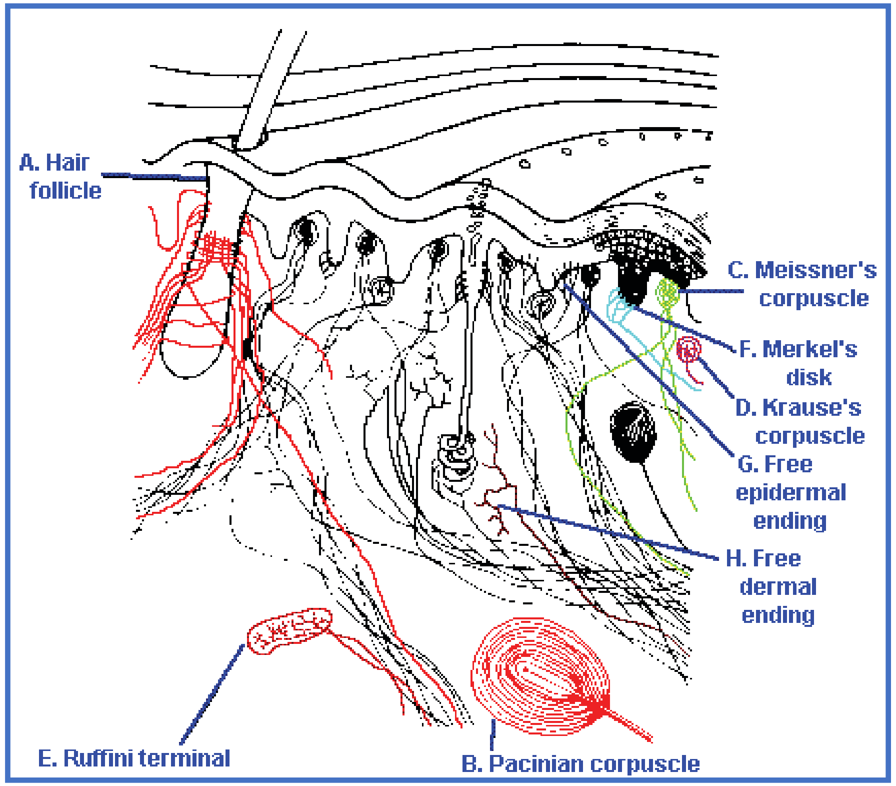
<u>Visual reorientation illusion</u> – change in "down" reference, e.g., when seeing another crewmember floating inverted or viewing the earth, can be provocative, easily reversed

<u>EVA Acrophobia</u> – anecdotal reports of sudden attack of height anxiety, and fear of falling toward Earth during EVAs

<u>3D spatial memory and navigation</u> – developing efficiency can be challenging during early inflight, appears to be retained or easily reacquired with subsequent flights

Somatosensory





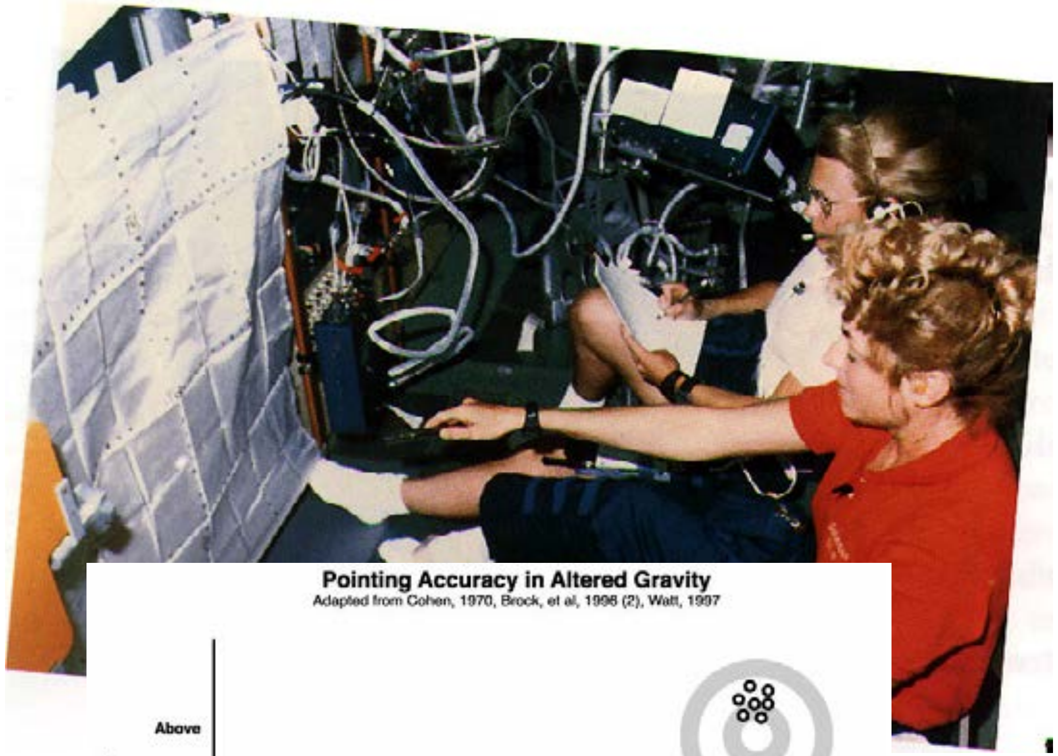
Proprioception

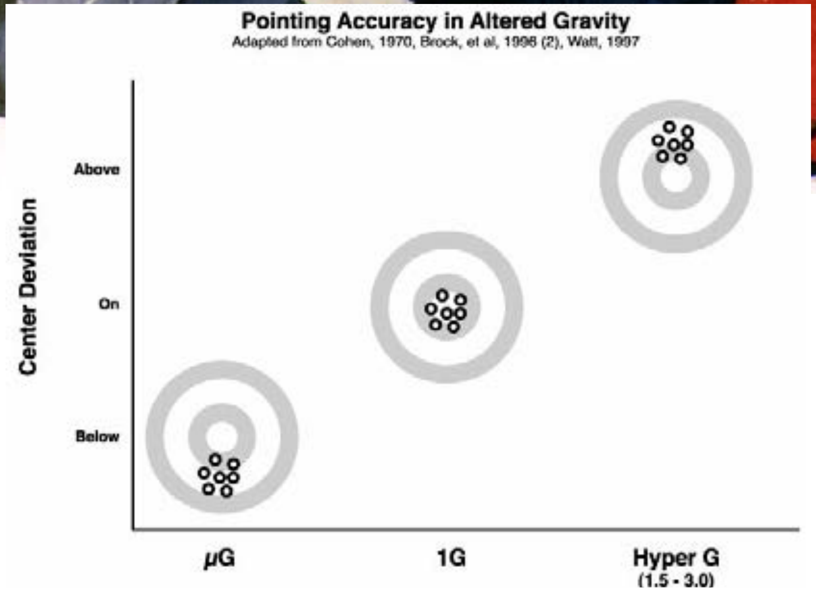
sensations produced by muscle, tendon, and joint receptors responding to orientation or motion of the body or body segments

Haptic Sensation

sensations produced by cutaneous receptors responding to tactile contact with the external world

Somatosensory in space



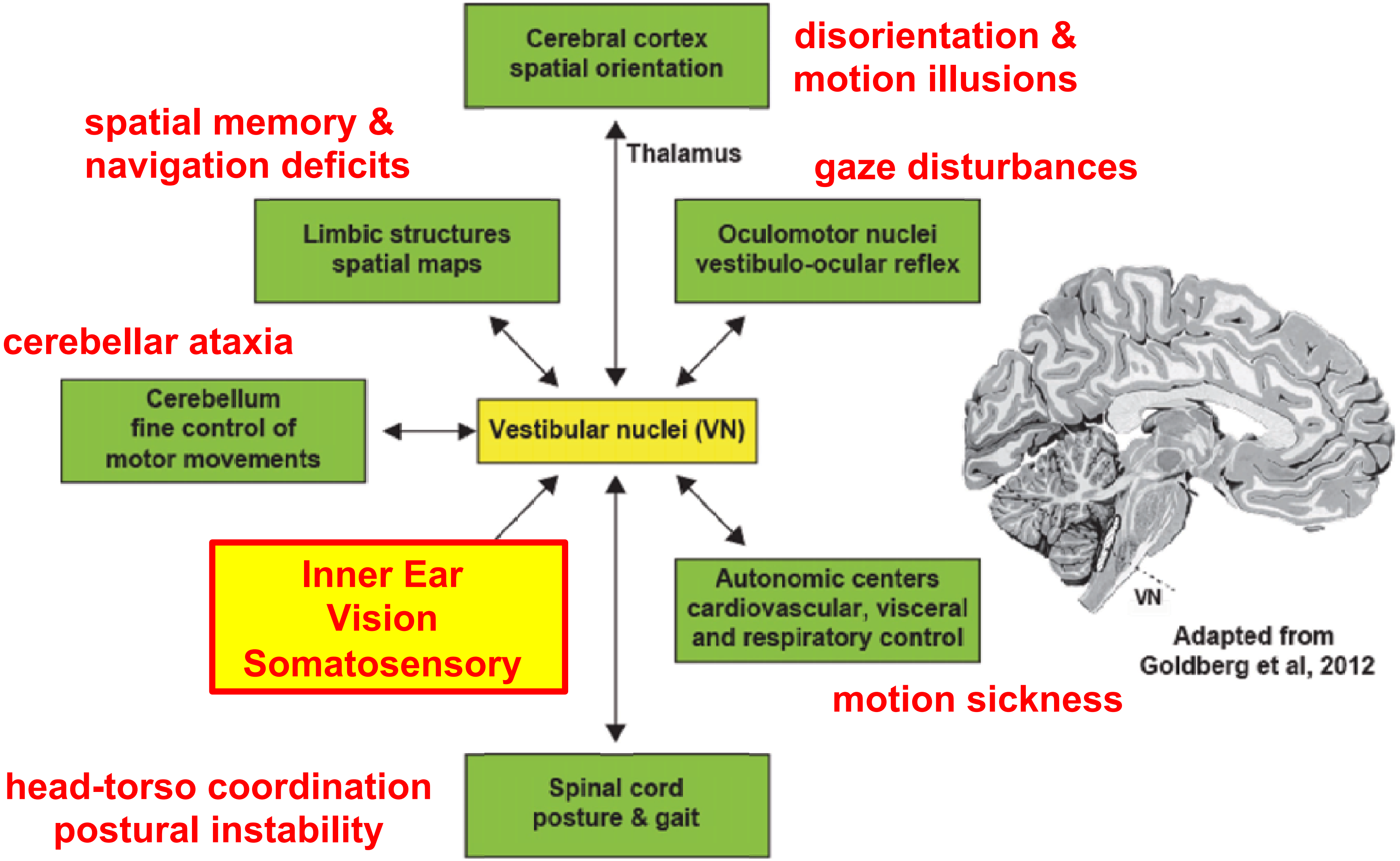


- Altered proprioception associated with unloading leads to impaired judgments of limb position, pointing to memorized target positions and control of hand force, especially in the absence of visual feedback (Gallash et al, 1997; Watt 1997)
- The ability to judge forces needed to push off surfaces to navigate must be refined on orbit (Newman, 2001)
- Crewmembers often report perceived heaviness of their body and limbs during the early postflight period (Ross, 1998)
- Increased skin hypersensitivity at the foot sole appears correlated with reduced postflight postural performance (Lowrey et al, 2014)
- Tactile cues from fixed support can suppress inflight visually-induced vection (Young et al., 1986) and improve post-flight postural performance (Mulavara et al, 2018)

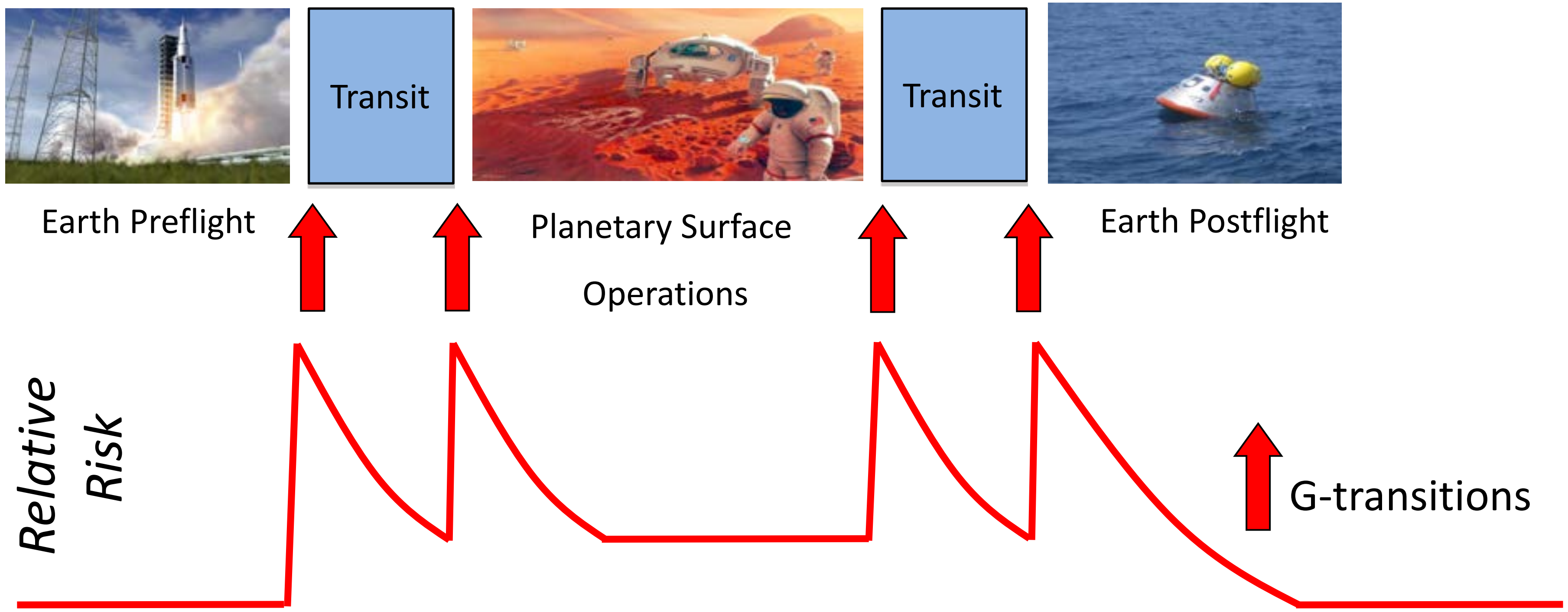
Mechanisms of adaptation

- Gravitational unloading
  - Deconditioning
  - Altered proprioception for mass discrimination and force control
  - Changes in sensor morphology
- Multisensory integration
  - Different patterns of sensory cues, e.g., otolith cues during head tilt
  - Interaction with support surfaces for locomotion and orientation

Outcome measures



Risk greatest at G-transitions



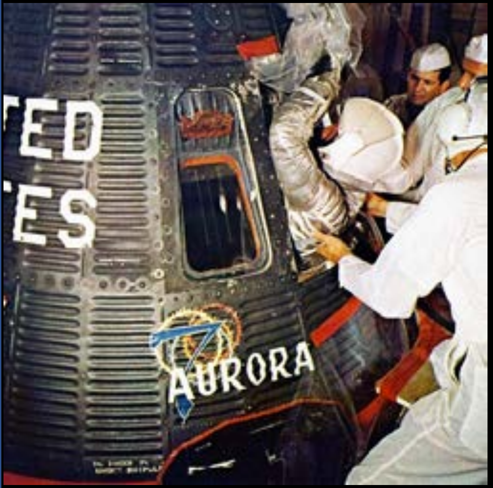
Adaptive changes that optimize sensorimotor function in one gravity environment are maladaptive for transitions to other gravity states

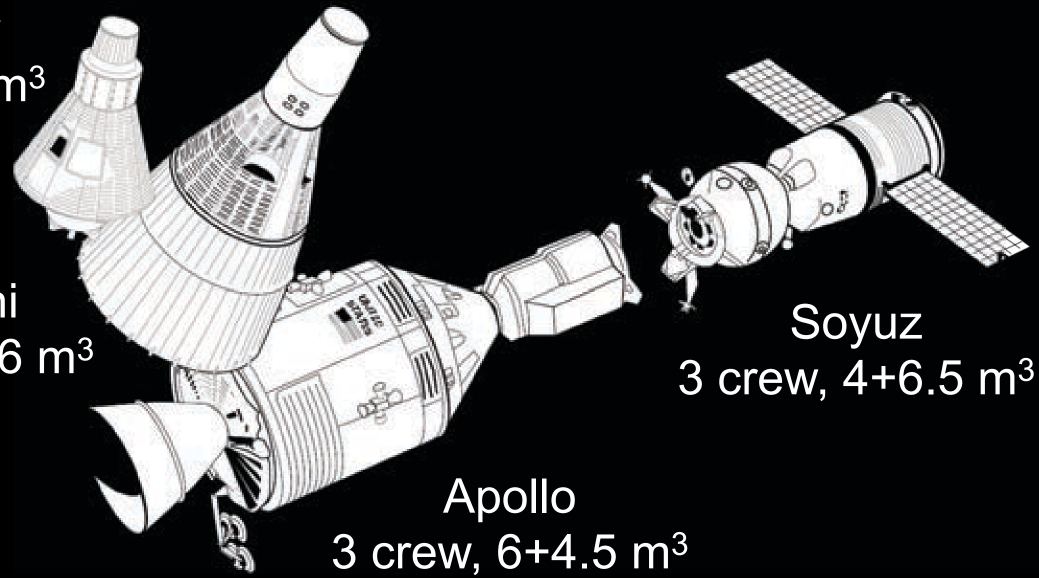
Risk factors

- Individual variability
- Length of flight
- Crew experience
- Use of medication
- Task complexity
- Suit design
- Spacecraft architecture

Space Motion Sickness prevalence

- Prevalence has varied with spacecraft volume:
  - No SMS reported in Mercury or Gemini programs
  - 33% in Apollo (Homick 1975), 54% in Soyuz (Bryanov et al. 1986)
  - 73% in Shuttle (Jennings 1998)
- Decreased prevalence and severity in repeat flyers (Davis et al, 1988)





Mercury
1 crew, 1 m^3

Gemini
2 crew, 1.6 m^3

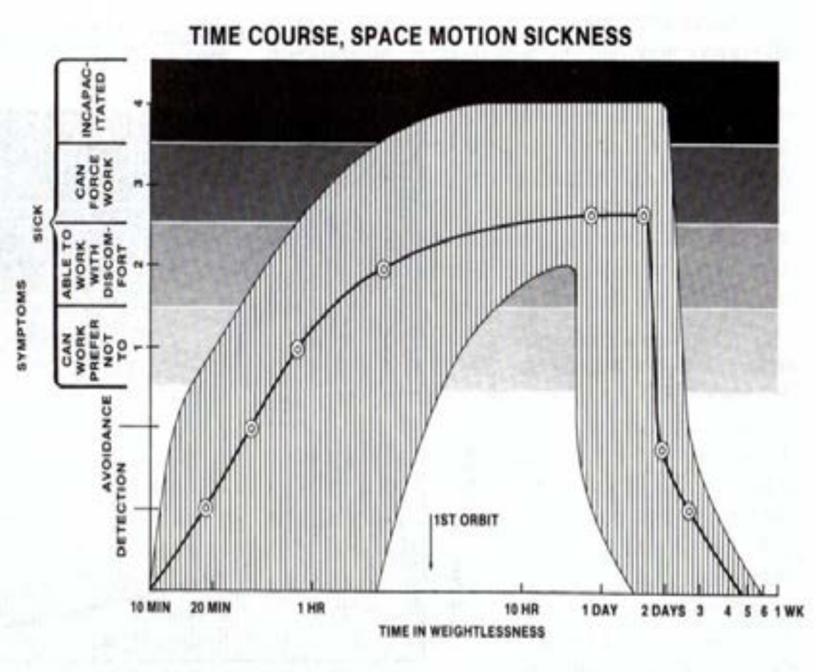
Apollo
3 crew, 6+4.5 m^3

Soyuz
3 crew, 4+6.5 m^3

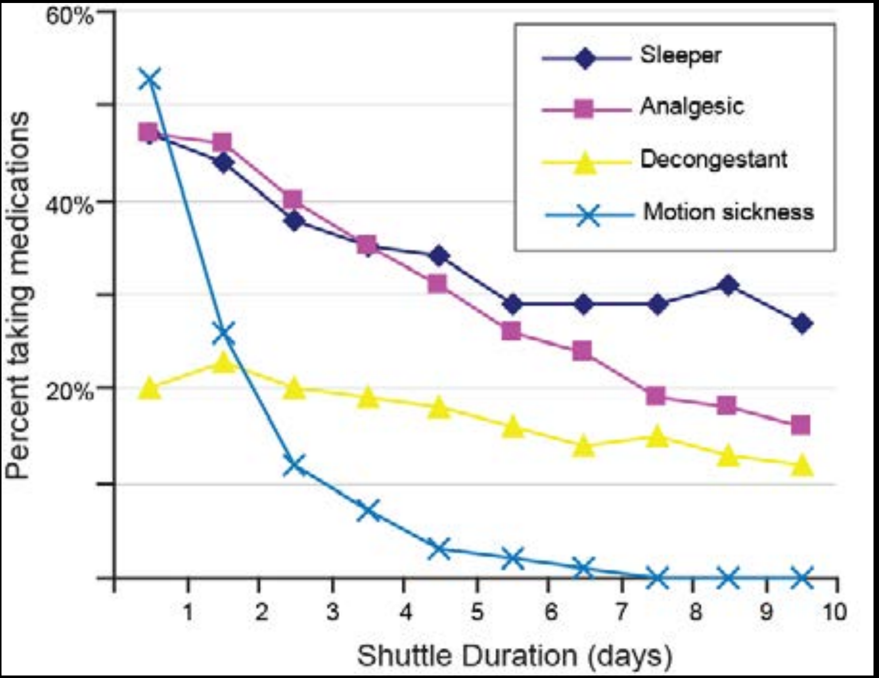
Shuttle
6 crew, 71.5 m^3

Inflight SMS severity & time course

- Symptom severity is variable, with over half categorized as moderate to severe (Jennings 1998)
- Symptoms generally last 2-3 days inflight, although may persist more than 1 week (Reschke et al 2018)
- Critical performance-related procedures such as extra-vehicular activity (EVA) are restricted during the first three days of missions



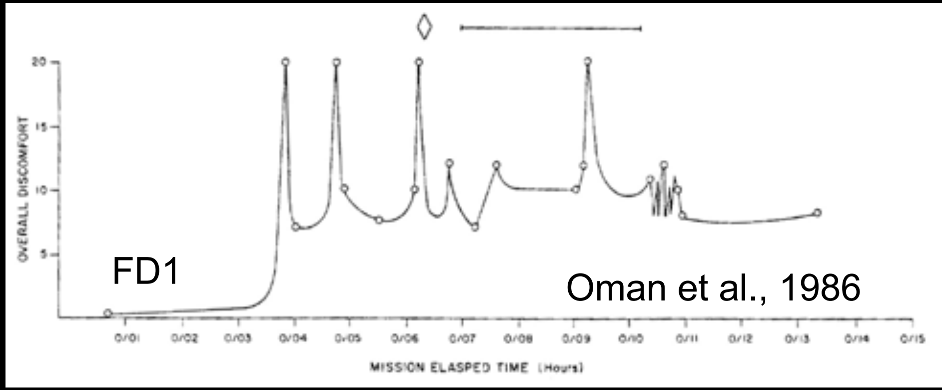
Thornton et al., 1987

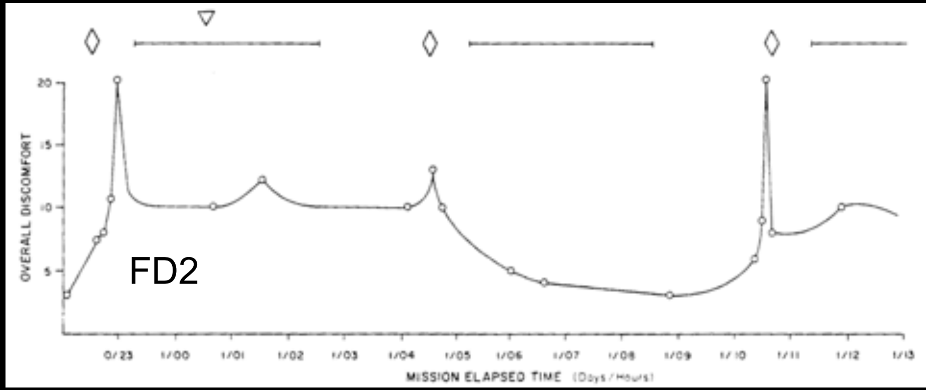


Putcha et al, 1999

Inflight SMS symptoms

- SMS typically is more often associated with stomach awareness, vomiting, headache (due perhaps to headward fluid shifts), impaired concentration (Davis et al. 1988).
- Vomiting can be sudden, infrequent, and often not marked by prodromal nausea.
- Other symptoms can include malaise, anorexia or loss of appetite, lack of initiative, and (for some) increased irritability.
- Fluctuating waves of drowsiness or "sopite syndrome" can mask other symptoms
- **Recommend** training on strategic approaches on how to recognize and manage early symptoms, e.g., recognizing lags in symptom progression, including optimal timing of medication and fluid replacement

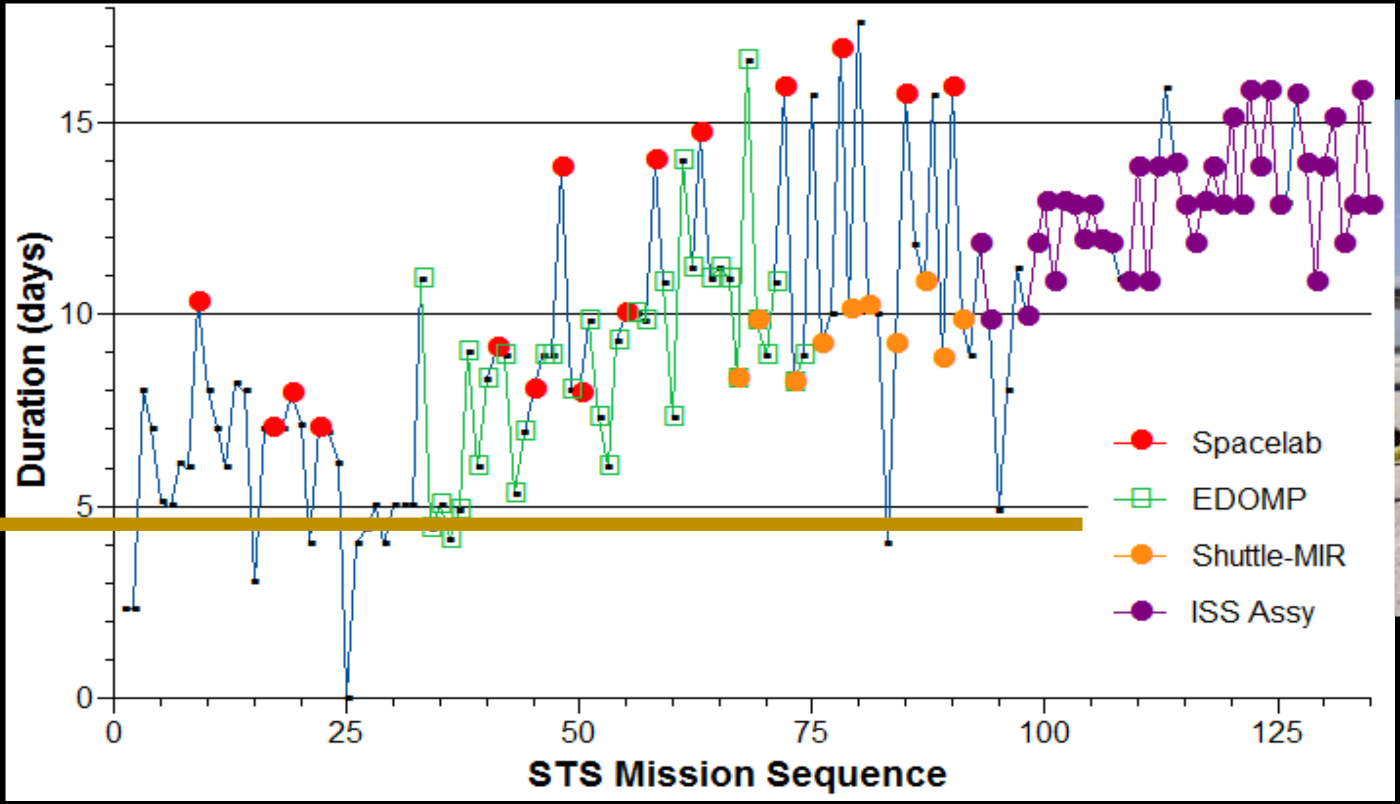




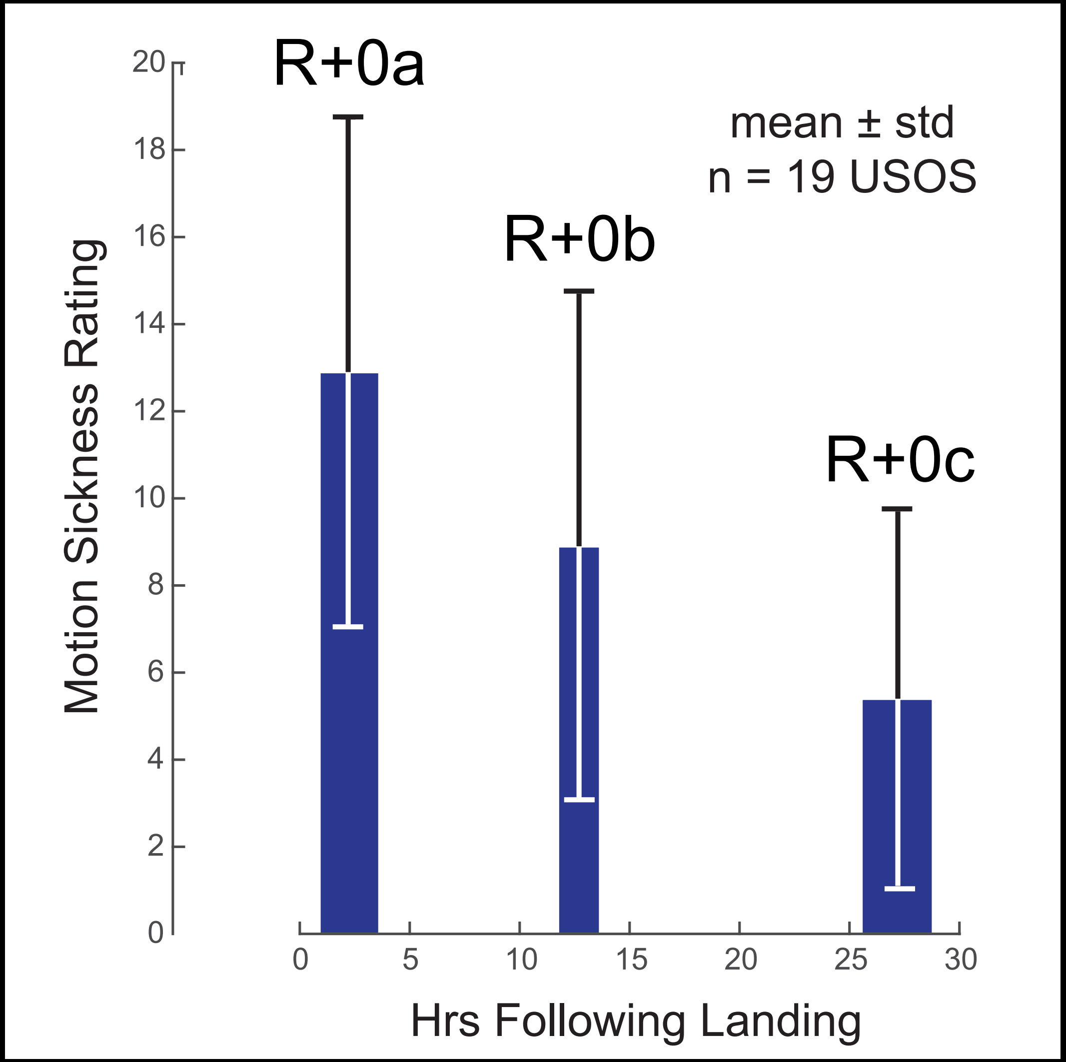
STS reentry motion sickness

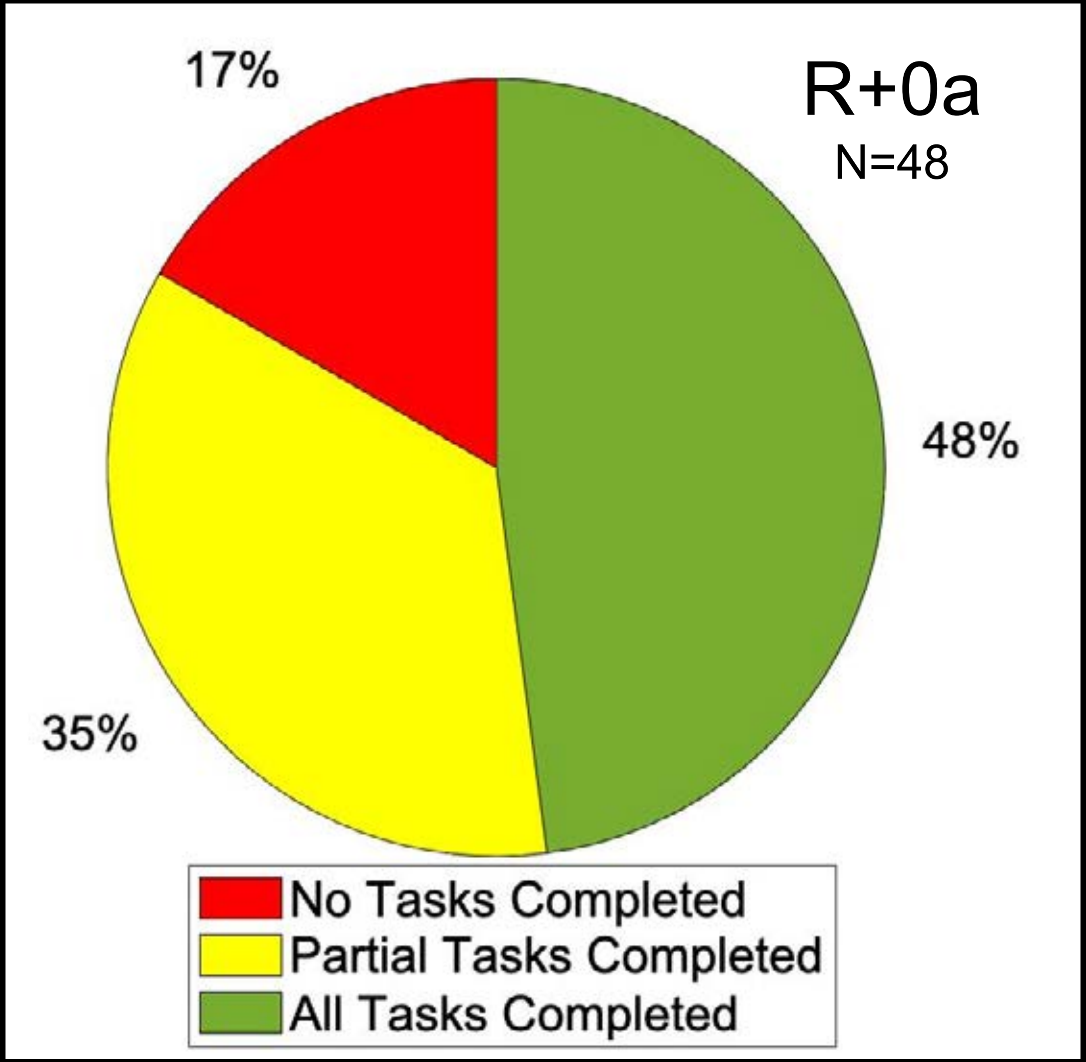
- Prevalence of re-entry nausea was ~15% after Shuttle with majority of crewmembers experiencing clumsiness in movements, difficulty walking and persisting sensation after-effects (Bacal et al. 2003)
- Since post-flight impairment was greater with longer flights only CDRs with prior landing experience were considered for flights of extended duration

Apollo transit durations prior to lunar descent

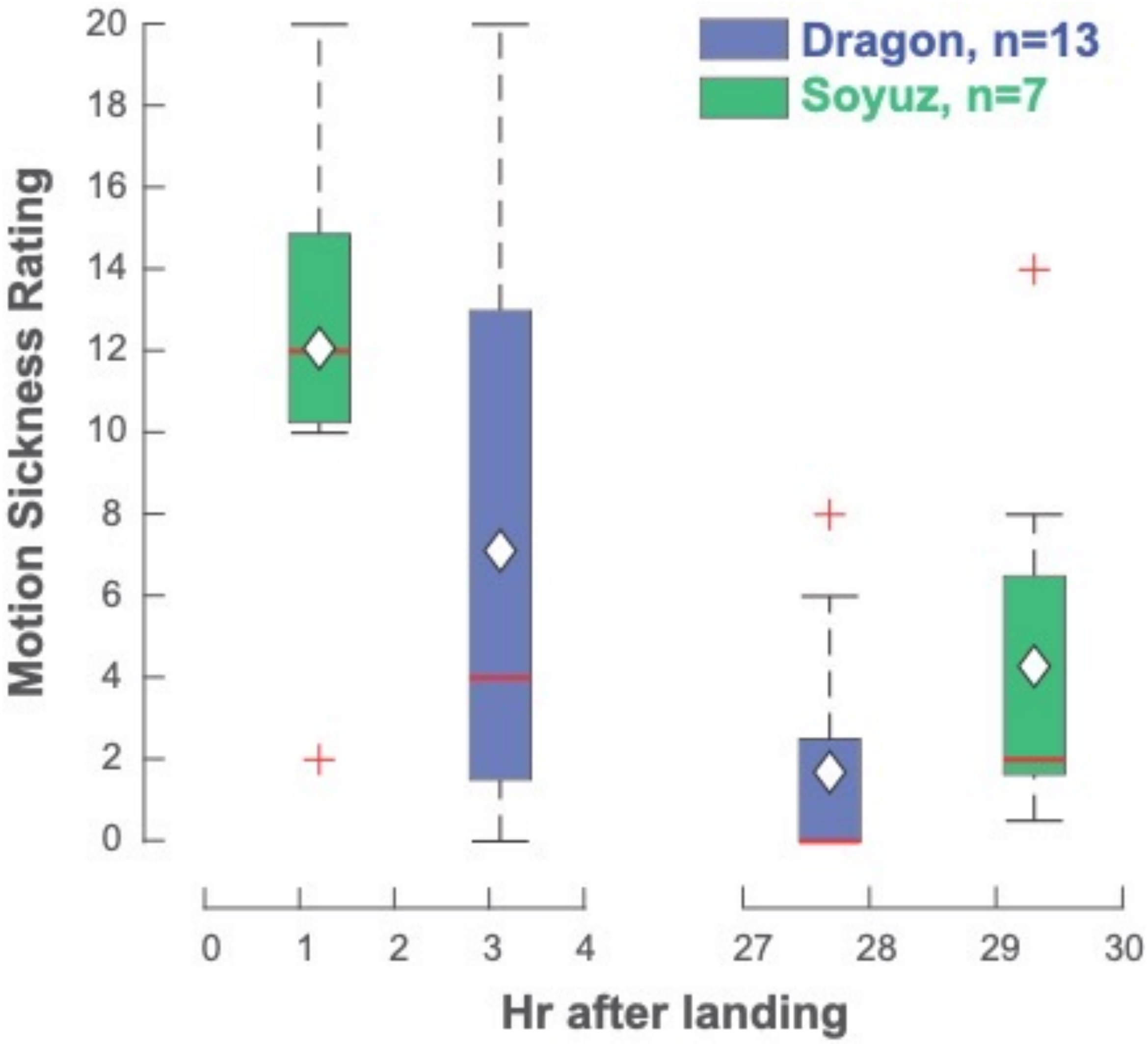


ISS reentry motion sickness



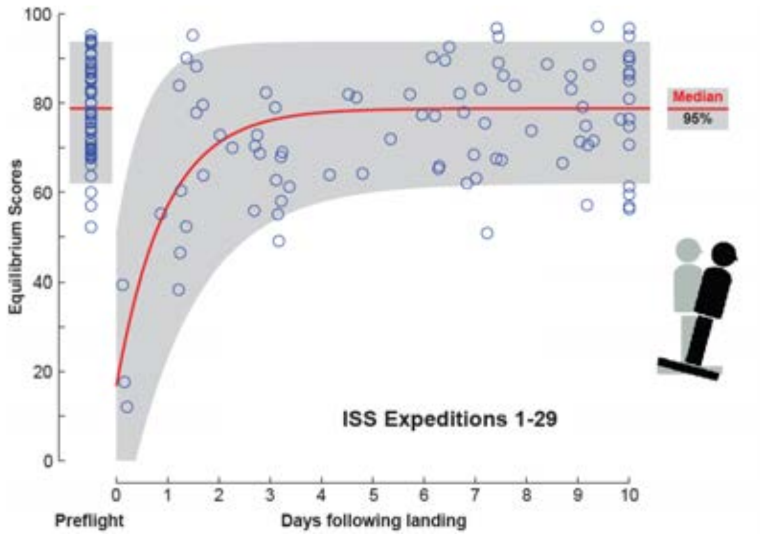


Spaceflight Standard Measures



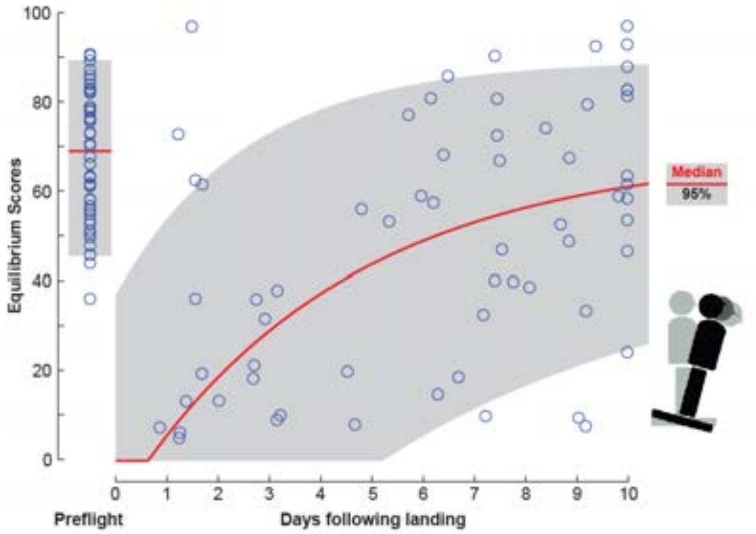
Postflight dynamic posturography

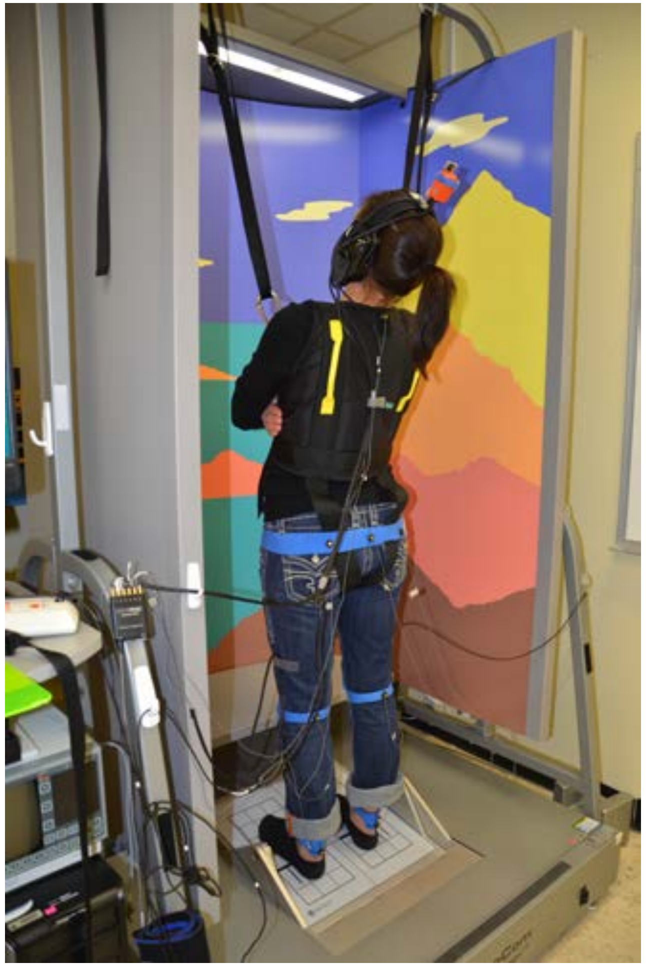
Head Erect



Head Moving

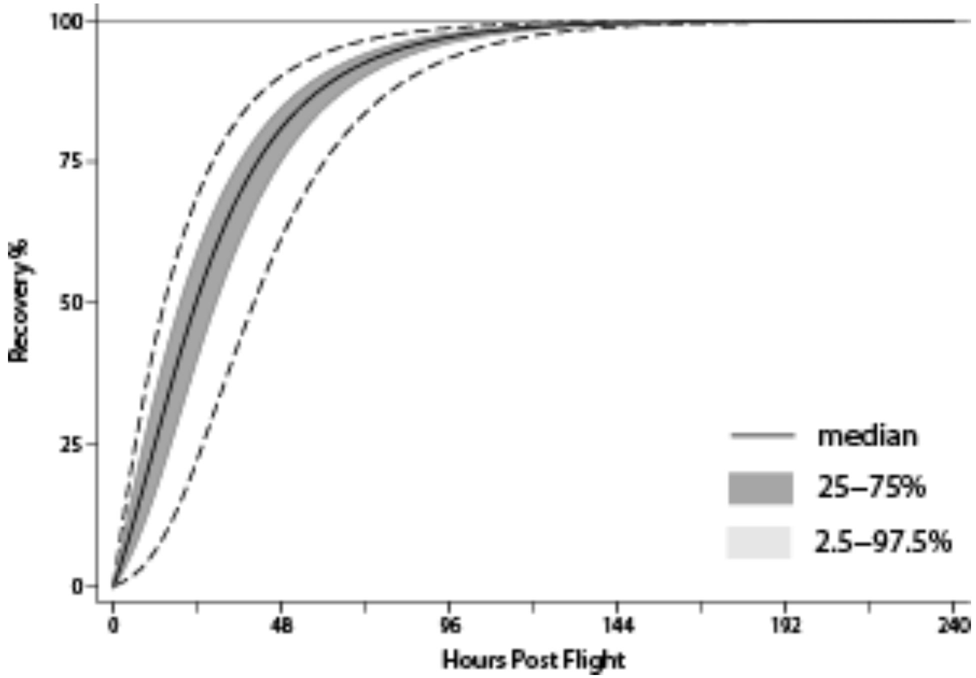
Pitch
0.33 Hz
±20º





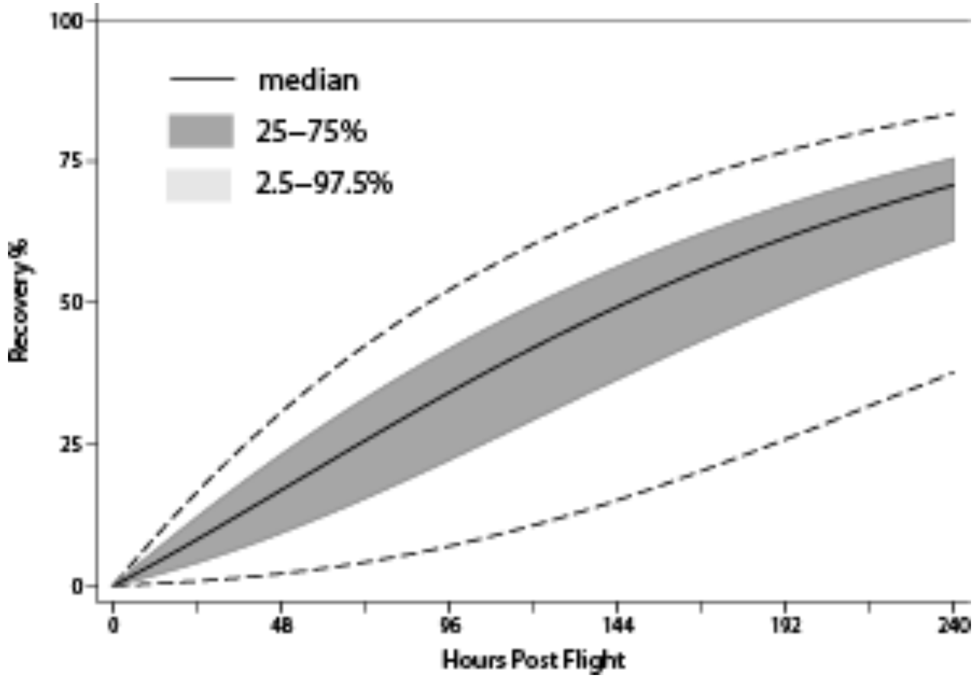
Wood et al., Aviat Space Environ Med (2013)

Short

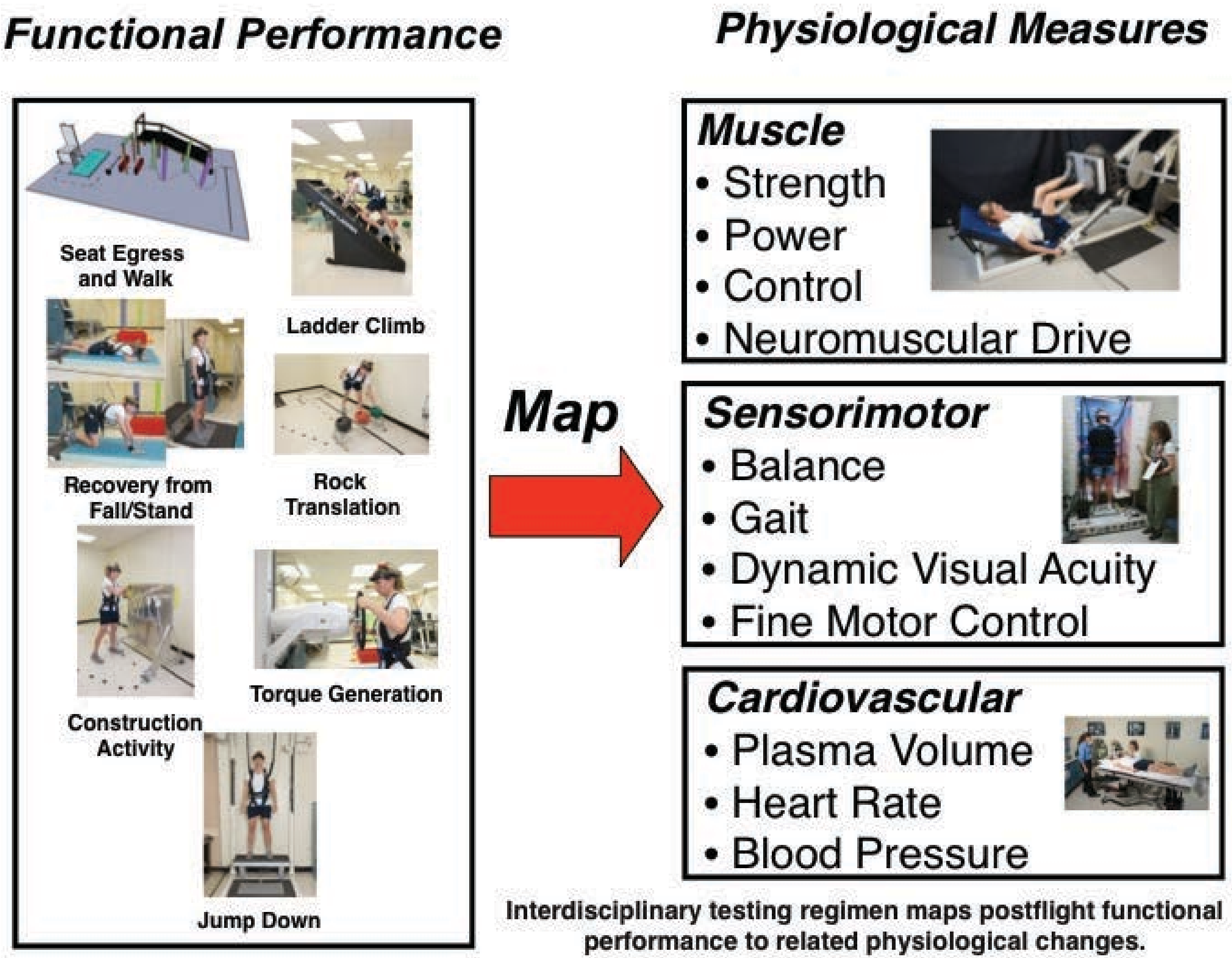


<u>SOT-5M</u>
Eyes Closed,
Unstable support,
Head moving

Long



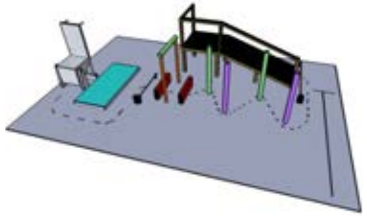
Functional Task Test



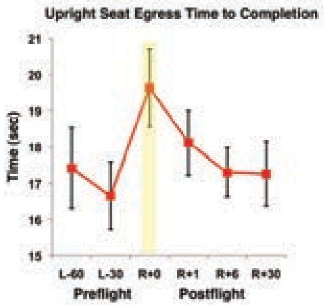
Interdisciplinary testing regimen maps postflight functional performance to related physiological changes.

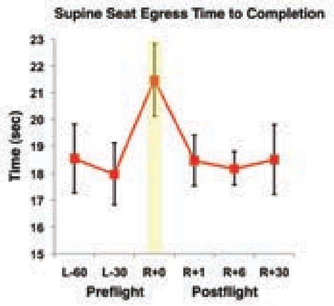
FTT PI: J. Bloomberg

Functional Task Test

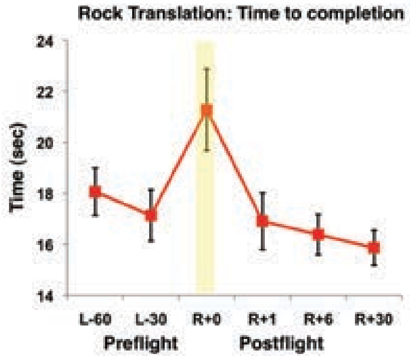


Shuttle n =7

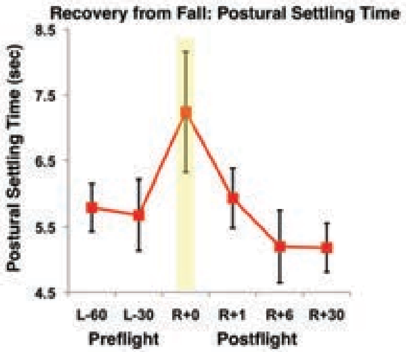




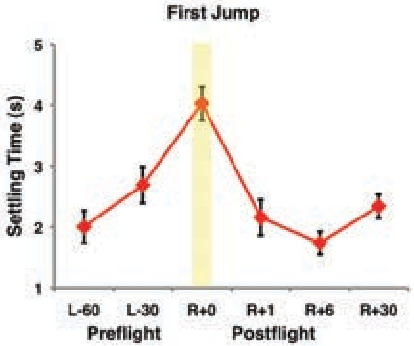
Seat Egress and Walk



Rock Translation



Recovery from Fall/Stand



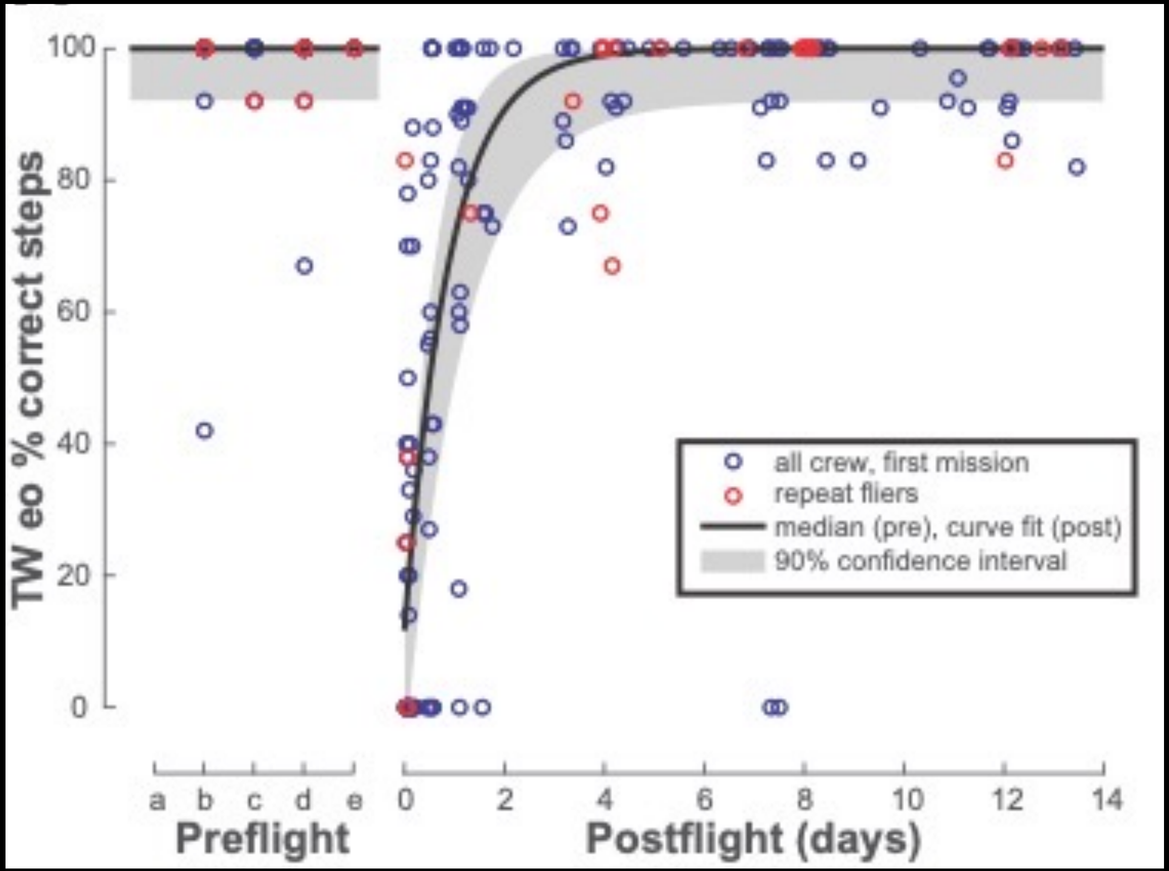
Jump Down

Functional tasks with a postural equilibrium challenge show the greatest change shortly after Shuttle landings (Bloomberg et al, 2012)

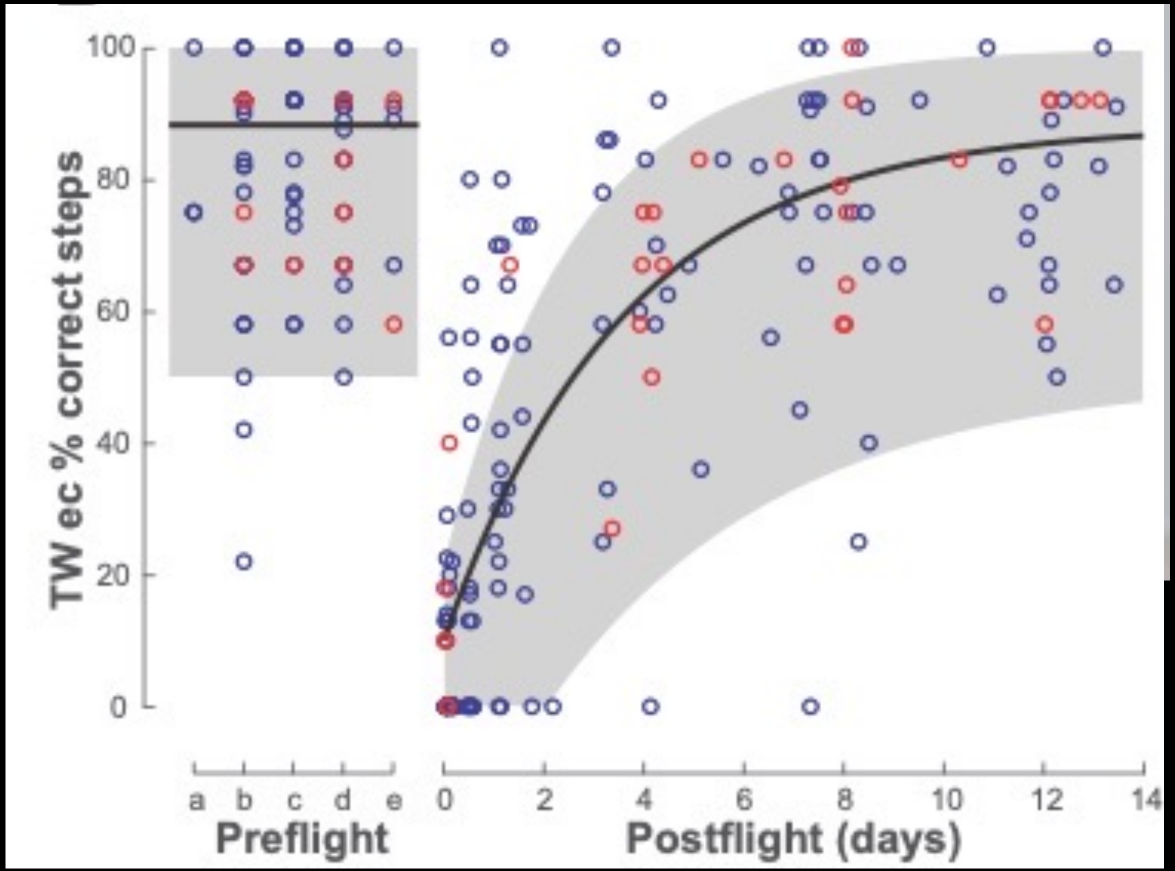
Field Test Objectives

- Characterize functional abilities following long-duration spaceflight as soon as possible after g-transition
- Develop a recovery timeline of functional performance

Tandem walk

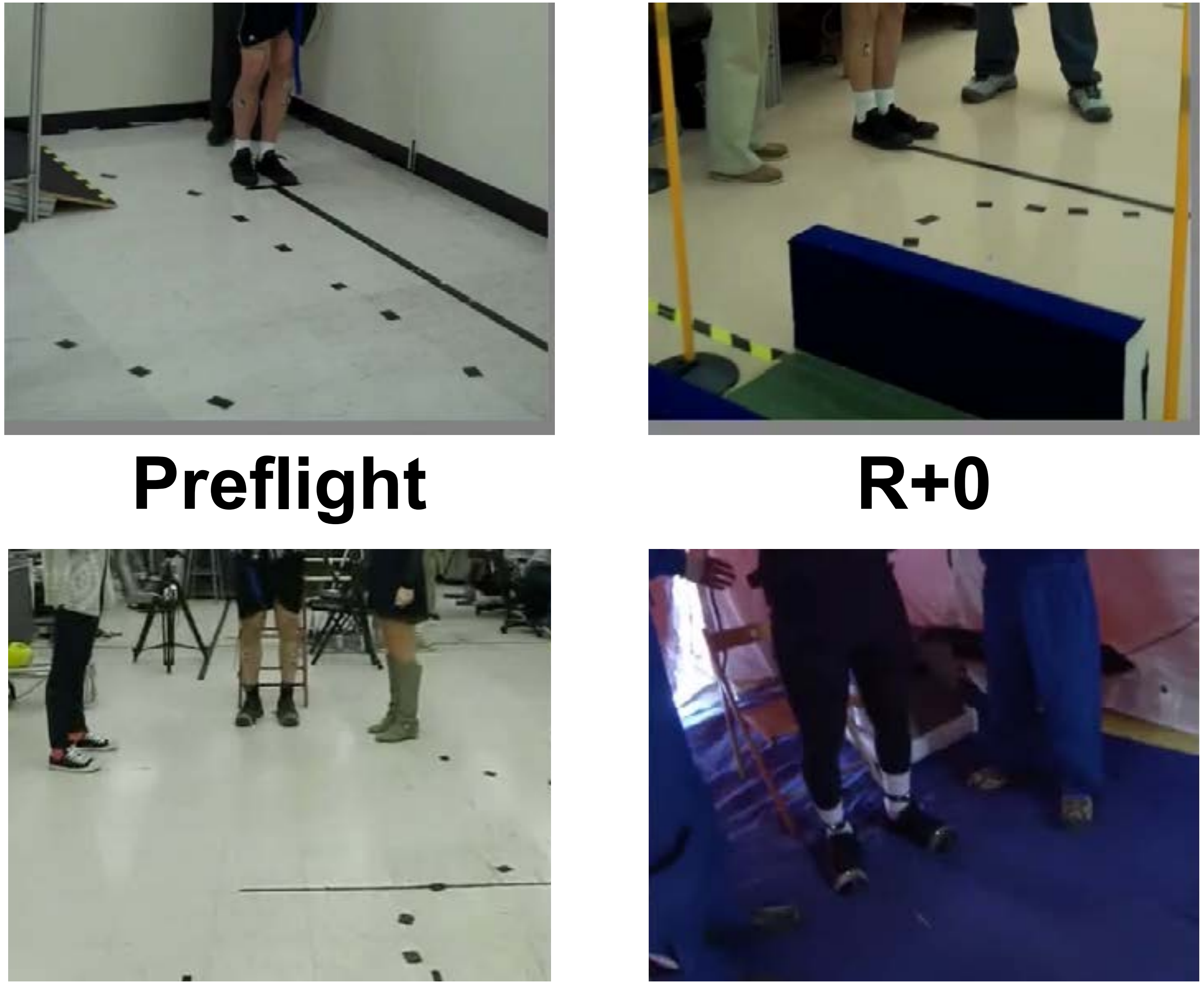


Eyes Open



Eyes Closed

Tandem Walk Eyes Closed



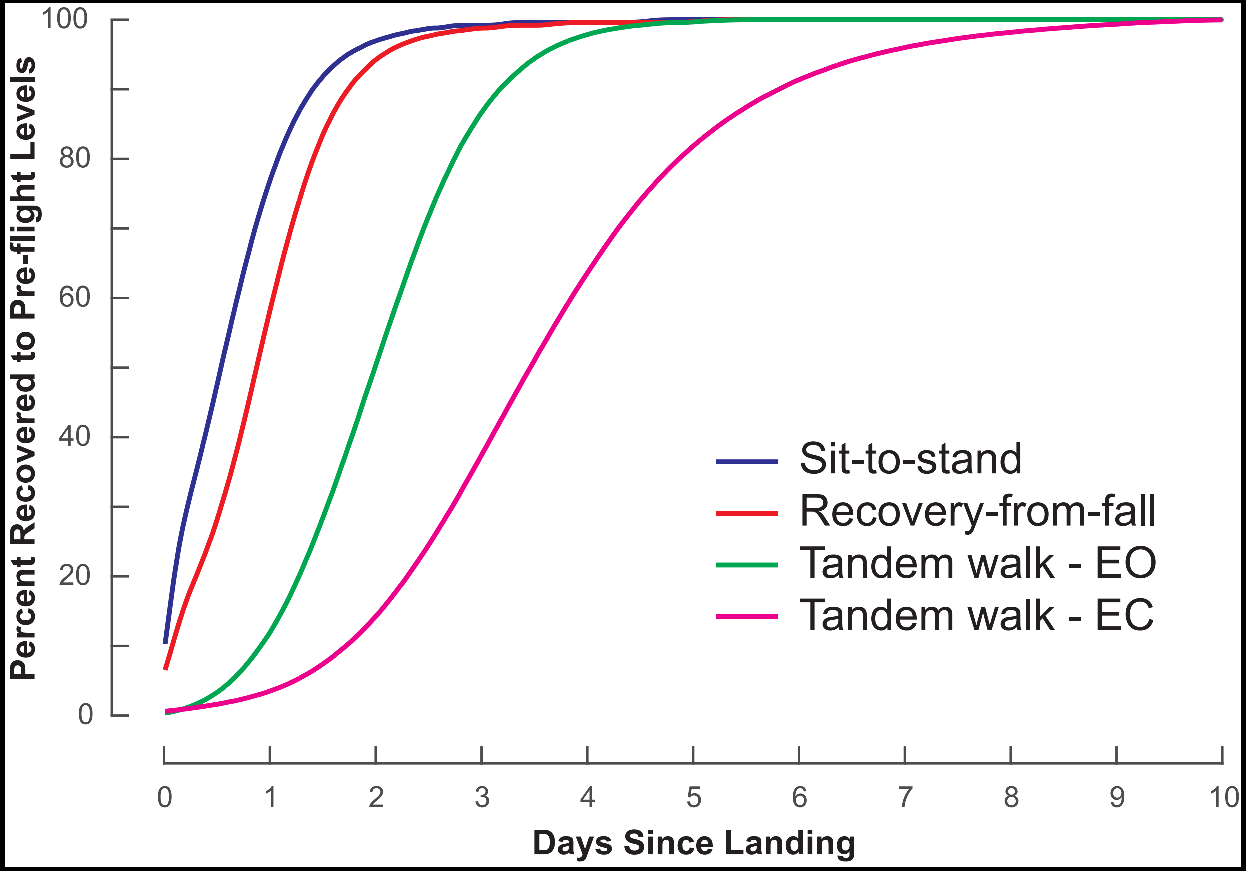
STS - Short

Preflight

R+0

ISS - Long

Recovery to preflight levels



- Sit-to-stand and recovery from fall tasks followed similar recovery trajectories
- In contrast, tandem walking presented a more challenging dynamic gait task requiring a longer timeframe for recovery
- Comparison of eyes open and closed conditions underscore the importance of visual cues

Apollo Landings: Importance of Preflight Training


Lunar Landing
Training Vehicle
EAFB

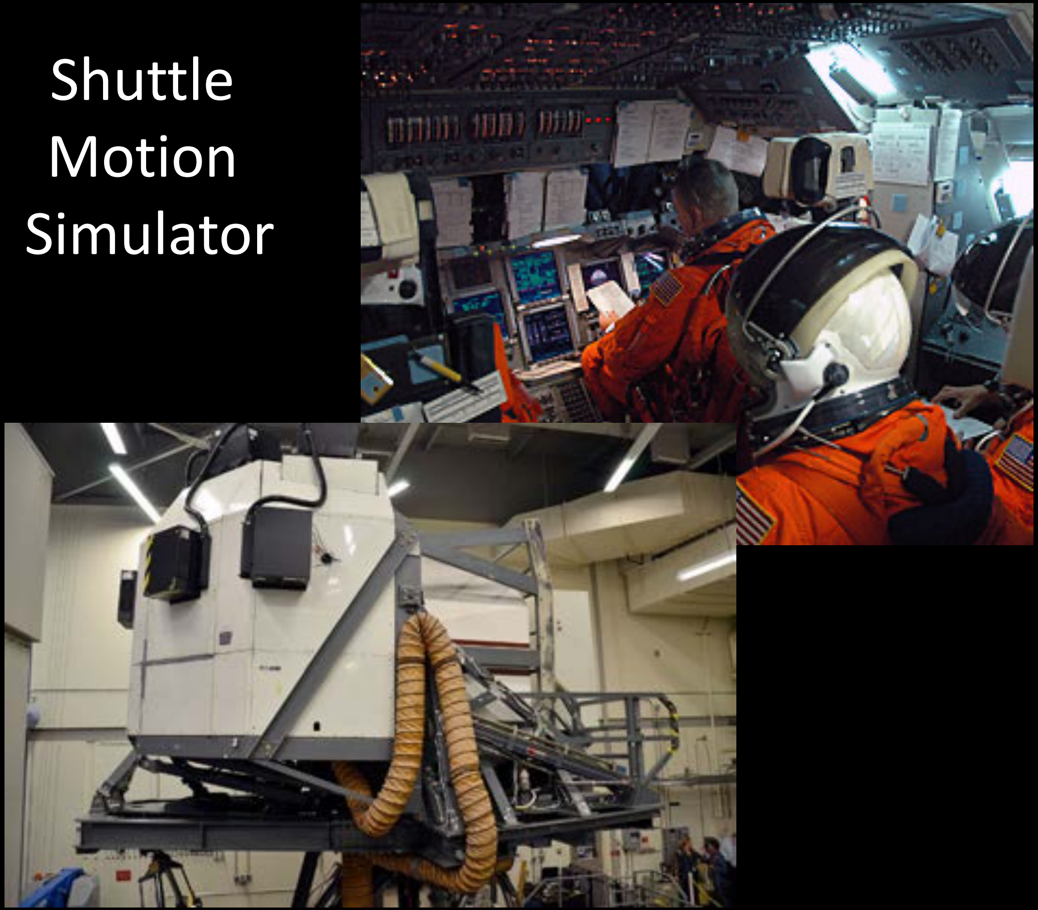

Lunar Landing
Research Facility
Langley


Lunar Module
Simulator
JSC & KSC

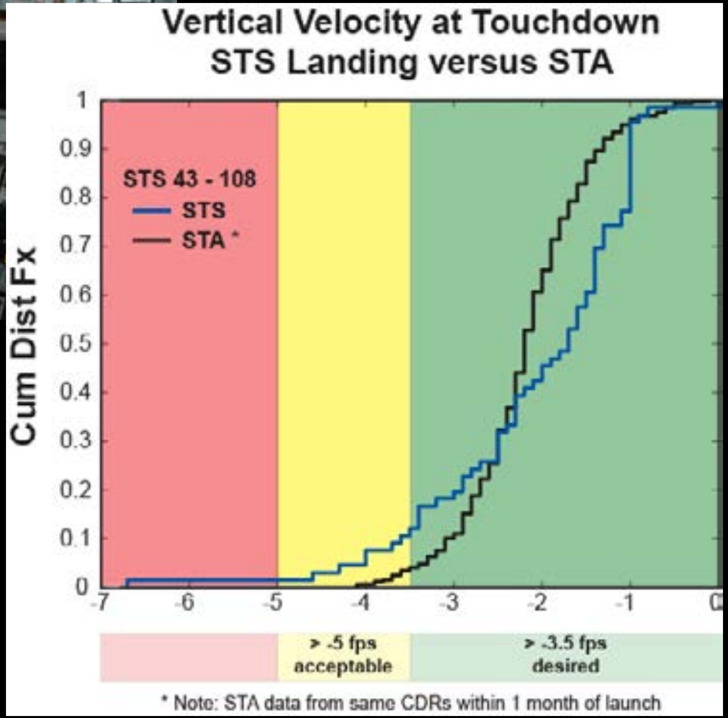
Preflight training was critical for mastery level proficiency and handling of disorientation challenges (e.g., blowing dust and visual illusions)

Shuttle Landings: Importance of Preflight Training

Shuttle Motion Simulator

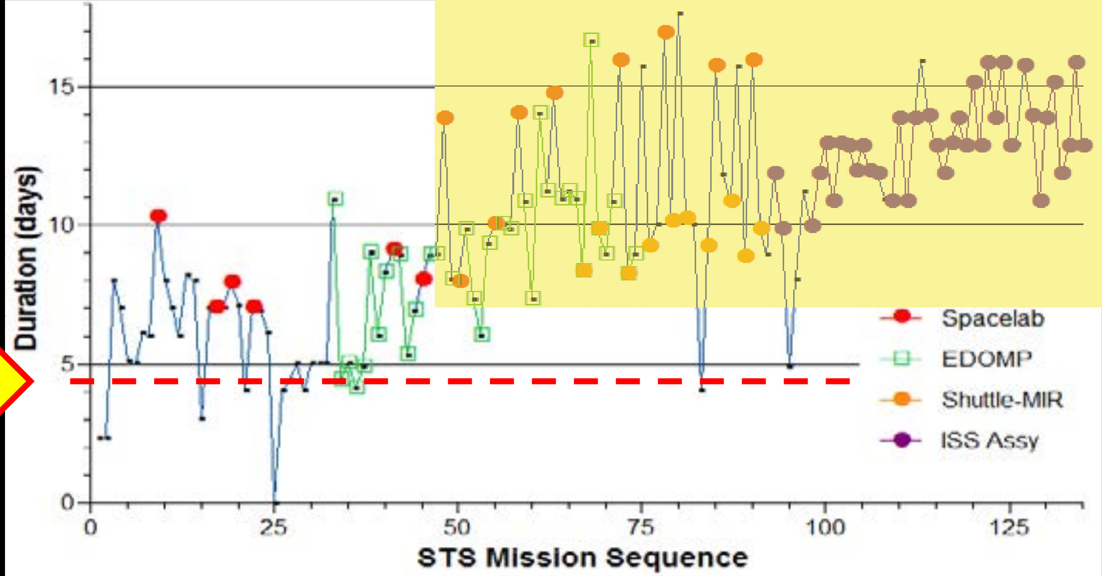


Shuttle Training Aircraft (STA)



Based on NASA lessons learned, a continuum of platforms is required to train the critical skill of adaptability

Rationale for On-board "Just-in-time" trainer

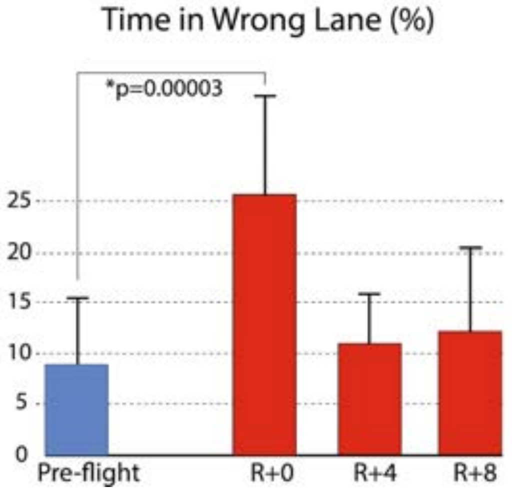


Shuttle on-orbit trainer used for longer duration missions

Apollo transit

- On-board training anecdotally effective:
  - ***CDR1:** helped lower cognitive workload to be able to effectively pilot through disorientation (vertigo)*
  - ***CDR2:** increased awareness of tendency to lag guidance, so I was able to make adjustments in approach during landing*

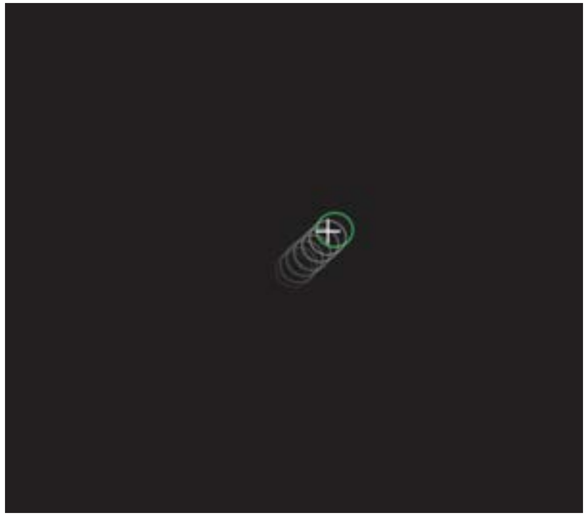
Driving simulation

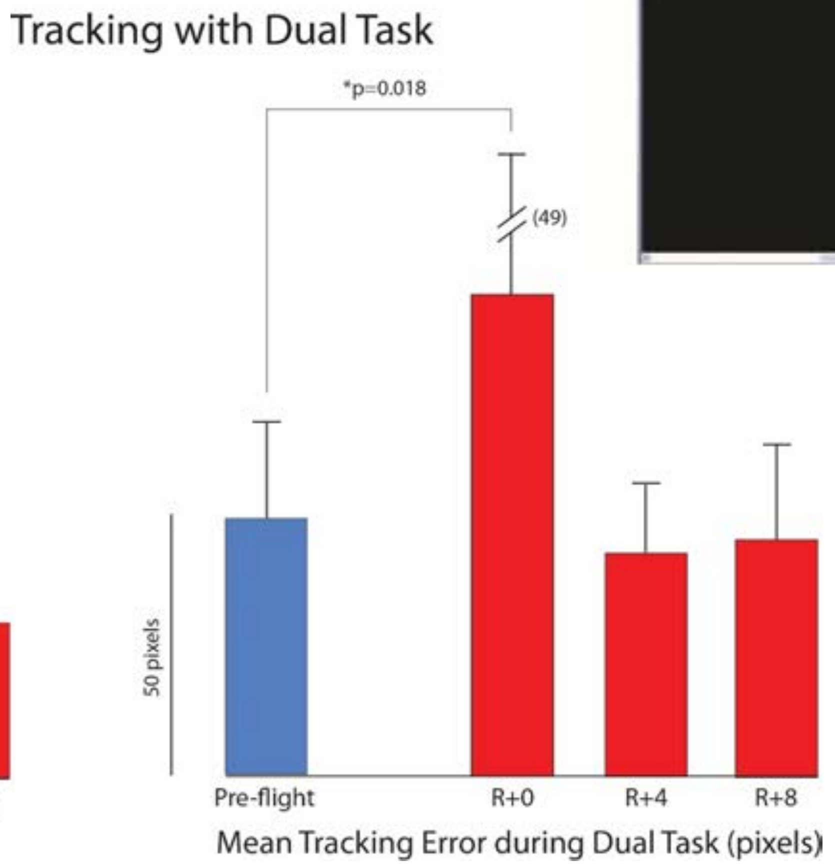


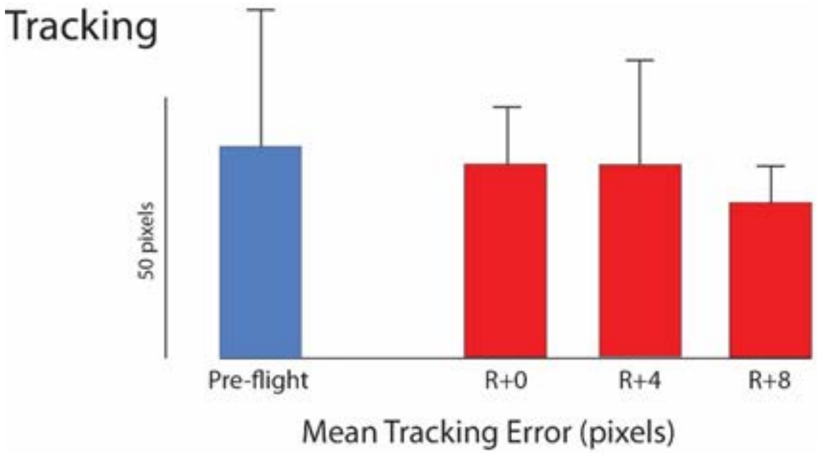
Moore et al., 2019, Sci Rep 9:2677

- ISS crewmembers (n=8) exhibited significant deficits on R+1d in manual dexterity (Pegboard), dual-tasking and tilt motion perception, and a striking degradation in the ability to operate a vehicle
- Similar deficits were not seen in control groups for schedule recency or following 30h sleep restriction
- Limitation: Testing conducted following return to JSC (>R+24 hrs)

Dual task tracking



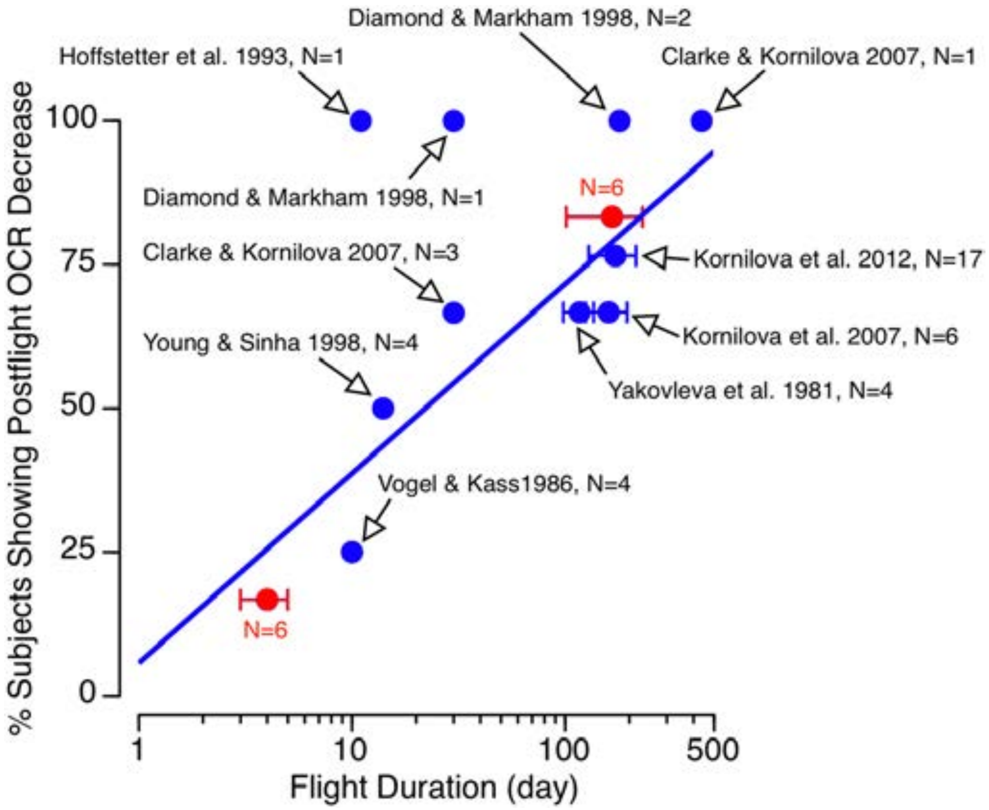




Moore et al., 2019, Sci Rep 9:2677

Vestibulo-ocular reflex

- Clark et al. (2000) reported changes in up/down asymmetry of vertical VOR gain and reductions in torsional VOR gain during active head movements on ISS flights, with some recovery in the later phase
- Reschke et al (2019) reported decreases in post-flight ocular-counterrolling that were dependent on mission duration

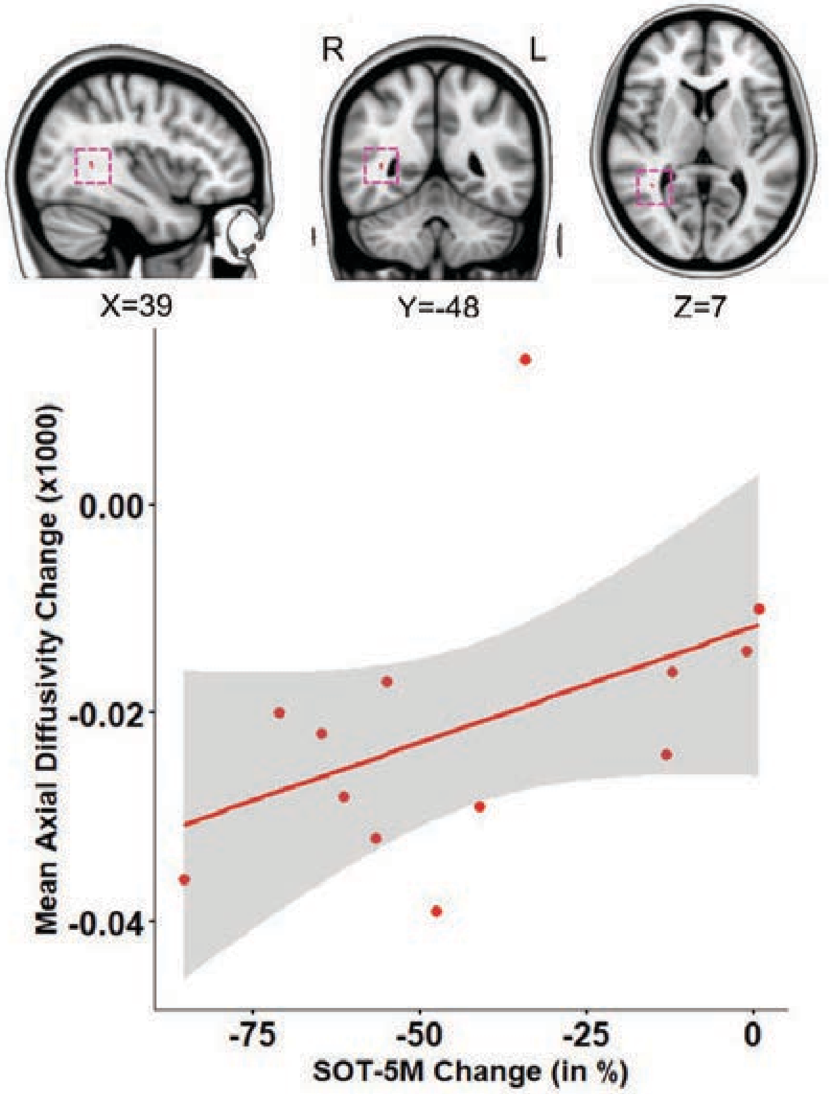


(Reschke et al. 2018, *Sci Report)*

Neuroimaging

- Spaceflight is associated with redistribution of brain extracellular fluids; white matter changes occur throughout the brain and, in some cases, are significantly associated with mission duration and post-flight declines in balance.
- Greater declines in the white matter underlying the vestibular cortex from pre to post flight are associated with larger declines in balance.

PI R. Seidler, Neuromapping



(Lee et al. 2019, *JAMA Neurology)*

Sensorimotor Ground Research Platforms

Laboratory

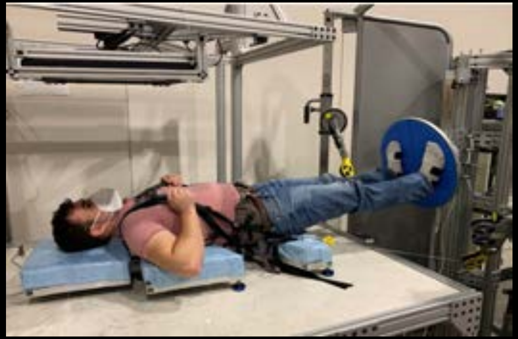
Transient, graded sensory disruption (e.g., Galvanic vestibular stimulation, visual distortion, weighted suit)

Multi-axis motion base / Simulations

Reduced loading

Active Response Gravity Offload System (ARGOS)

Partial g Parabolic Flight



Head-down Bedrest (HDBR)

G-state transition

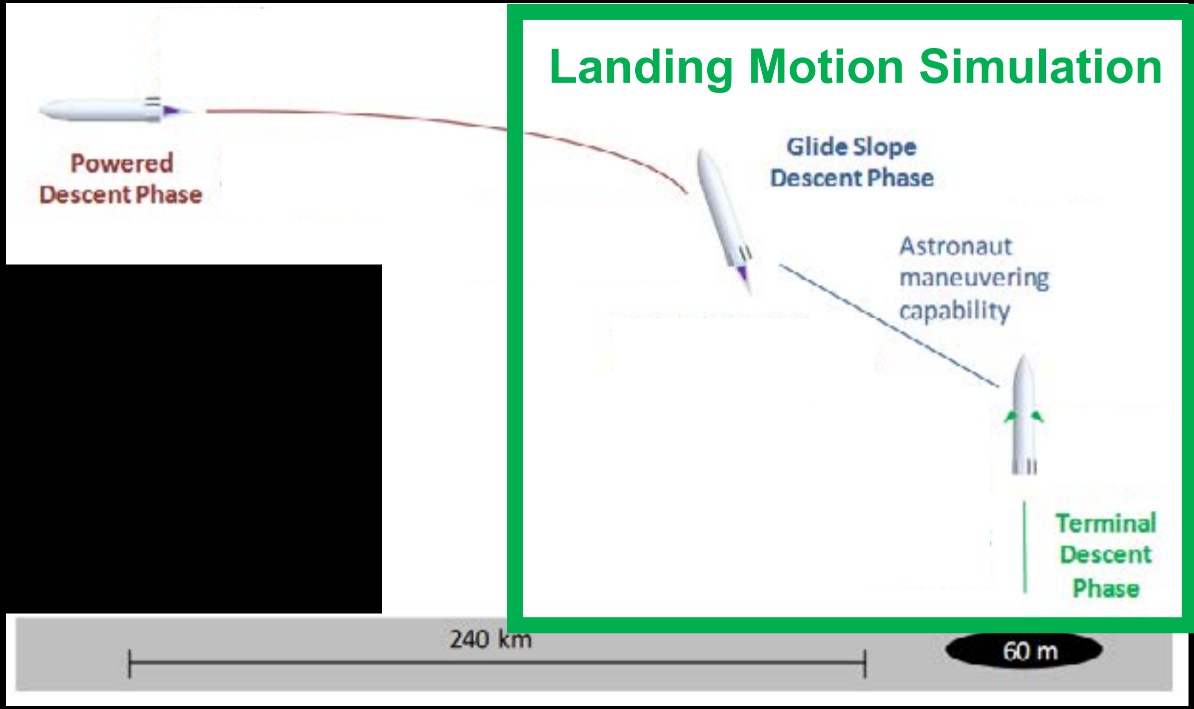
Sustained 3Gx Centrifugation Navy Disorientation Research Device (DRD) - Kraken

Research on Various Flight Phases with Kraken

Onboard Trainer Assess-ments

Kraken G-state Transition Analog

G-transition induced disruption



Landing Motion Simulation

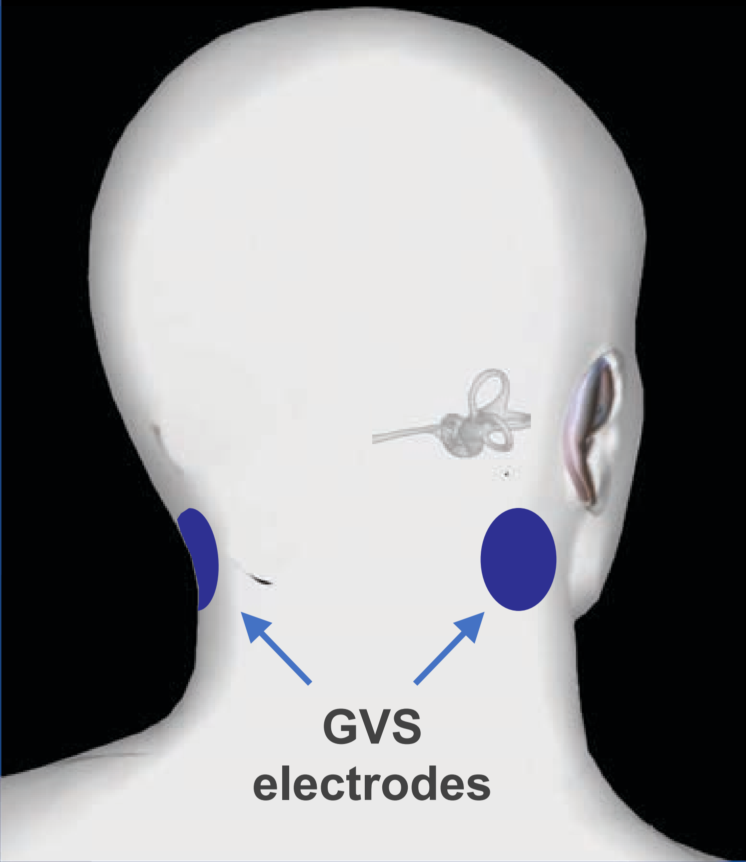
EVA assessments
Self-administered Rehab

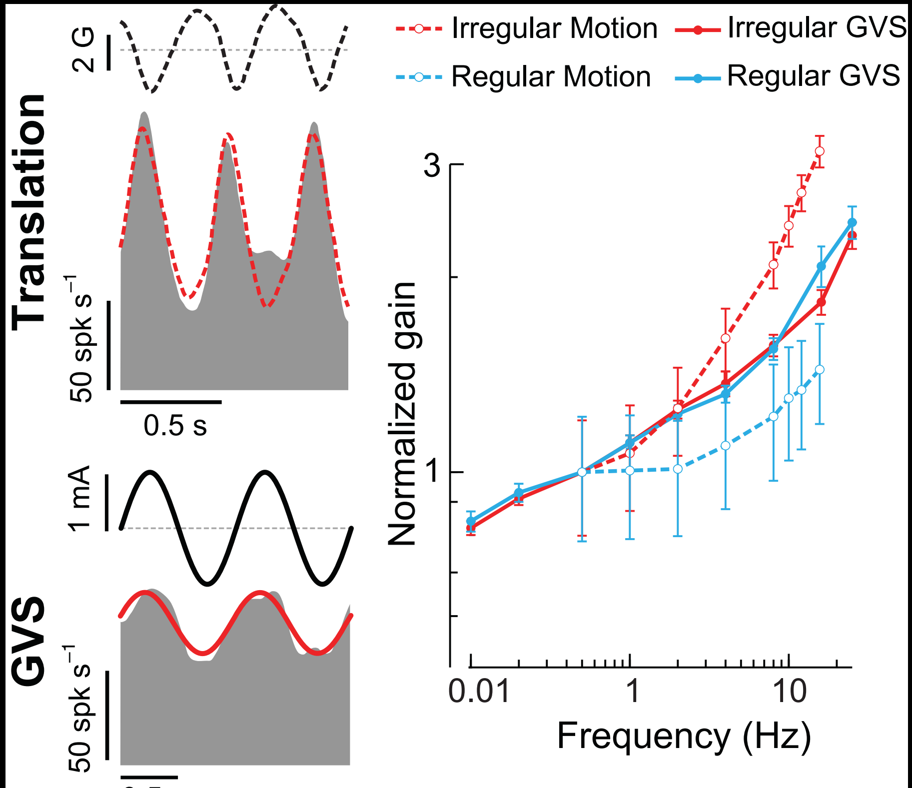
Return to Earth

Capsule Wave Simulation Motion Sickness CMs

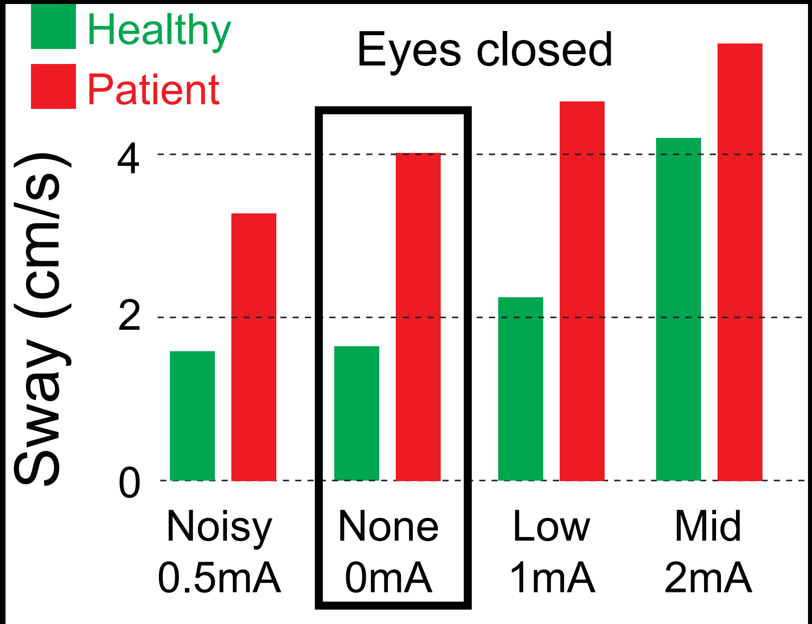
Galvanic Vestibular Stimulation (GVS)

- Galvanic current stimulation (applied using surface electrodes on mastoid) can excite, inhibit, or sensitize neurons thus altering vestibular neural activity
- Low level imperceptible GVS can improve function, while higher levels can result in transient balance disruption and/or spatial disorientation when applied





(from Kwam et al., Nat Comm, 2019)



(from Sprenger et al., J Neurol, 2020)

Portable Spatial Disorientation Trainer

SBIR·STTR America's Seed Fund POWERED BY NASA

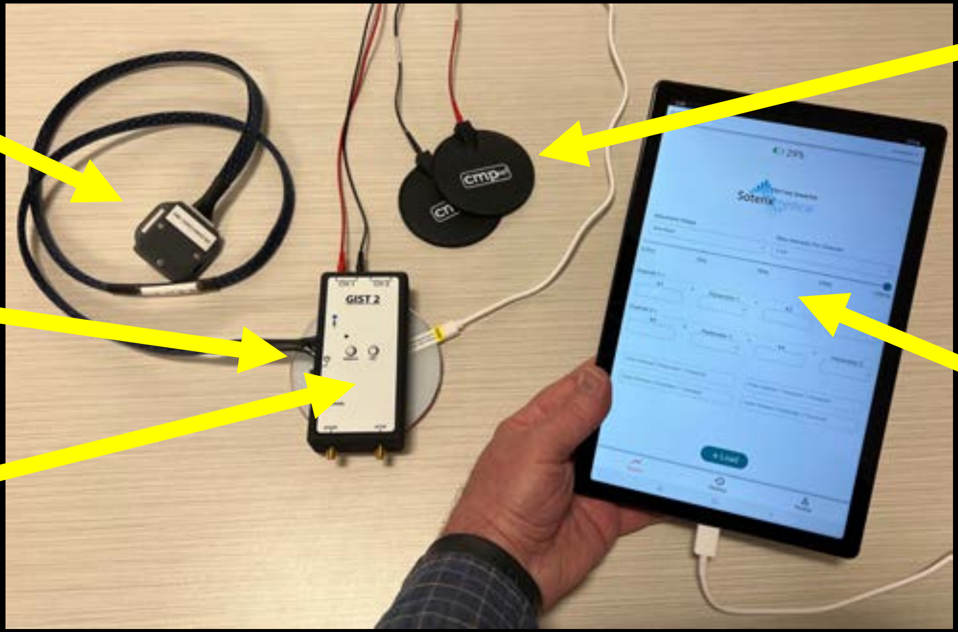
NASA

- Develop a portable head-worn device that can simulate Spatial Disorientation (SD) and enhance training when performing landing and operational tasks
- Galvanic Vestibular Stimulation (GVS), applied using surface electrodes on mastoid alters vestibular neural activity to simulate SD for NASA, military and civilian space programs
- Positive crewmember feedback suggesting 50-90% effective in duplicating post-flight SD
- In addition to NASA award, DARPA chose to fund PII to alternate vendor (Luna Innovations)
- NASA PII award to Soterix Medical; Next Gen features:

Stimulus coupled with head sensor to simulate head-coupled SD

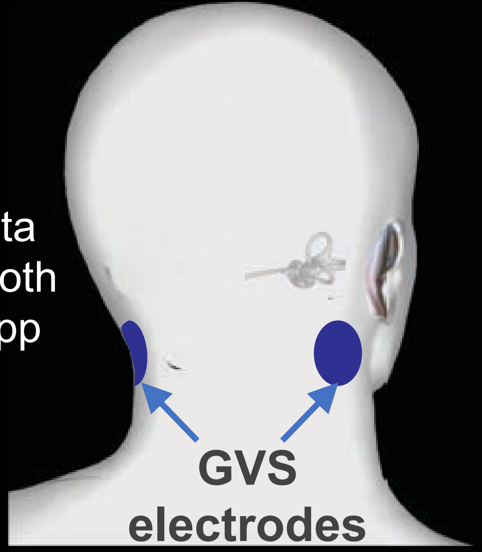
Portable, self-powered stimulator with wireless charging

User-adjustable gain to adjust for individual and task variability



Reconfigurable electrodes with multiple channel capability

Full control with data logger via a Bluetooth connected tablet app

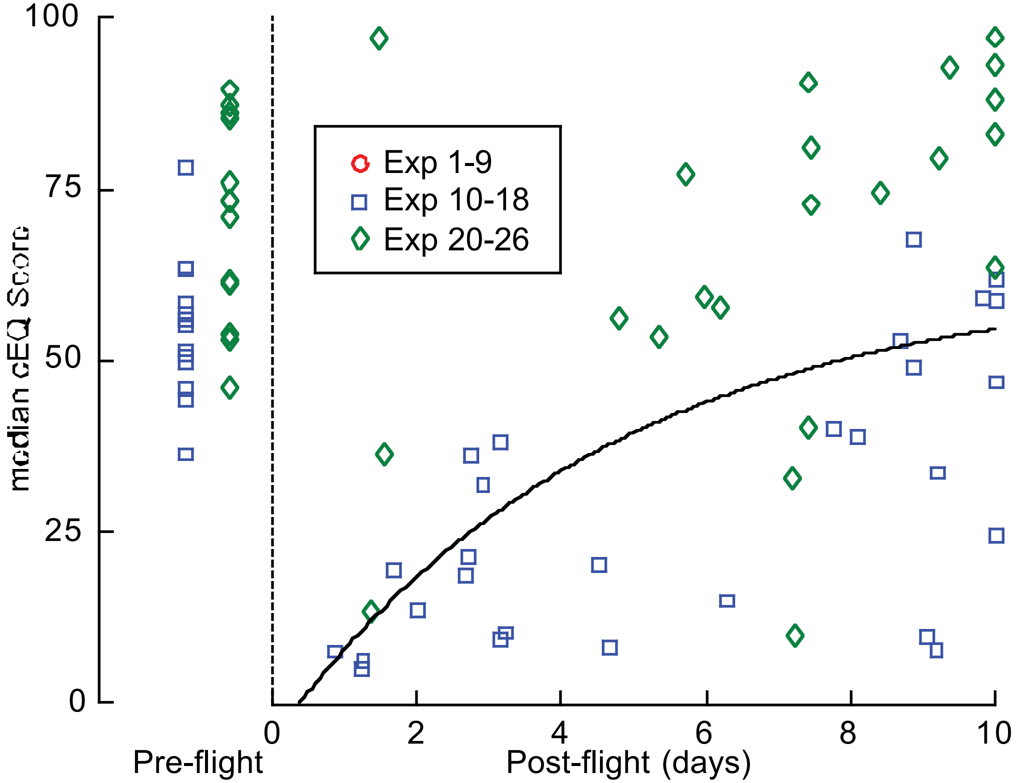


Research on enhancing performance

- Manual crew override: Onboard training, spatial orientation modeling and optimizing display countermeasures
- Sensorimotor assessments for early EVA
- Head and body monitoring for self-administered rehab
- Medications – intranasal scopolamine
- Sensory augmentation and orientation aids (e.g. horizon & vibrotactile)
- Inflight proprioception training

ISS Countermeasures

Head Moving, Eyes Closed, Unstable Support



Interim Resistive Exercise Device

Advanced Resistive Exercise Device

Wood et al., Aviat Space Environ Med (2013)

Post-flight Reconditioning Program

Exercise	Schedule
1 Dynamic Stretch & Warm-up	Every day: R+1-45
2 Aerobic Conditioning	Every day: R+1-45
3 Resistance Exercise	Every other day: R+1-45
4 Mobility, Balance & Proprioception Drills	Every other day: R+1–45
5 Medicine Ball Drills	Every other day, R+1-45
6 Cone and Agility Ladder Drills	Every other day: R+6-45
7 Jumping Drills	Every other day: R+21-45
8 Core Exercise	Every day: R+1-45
9 Static Stretching	Every day: R+1-45

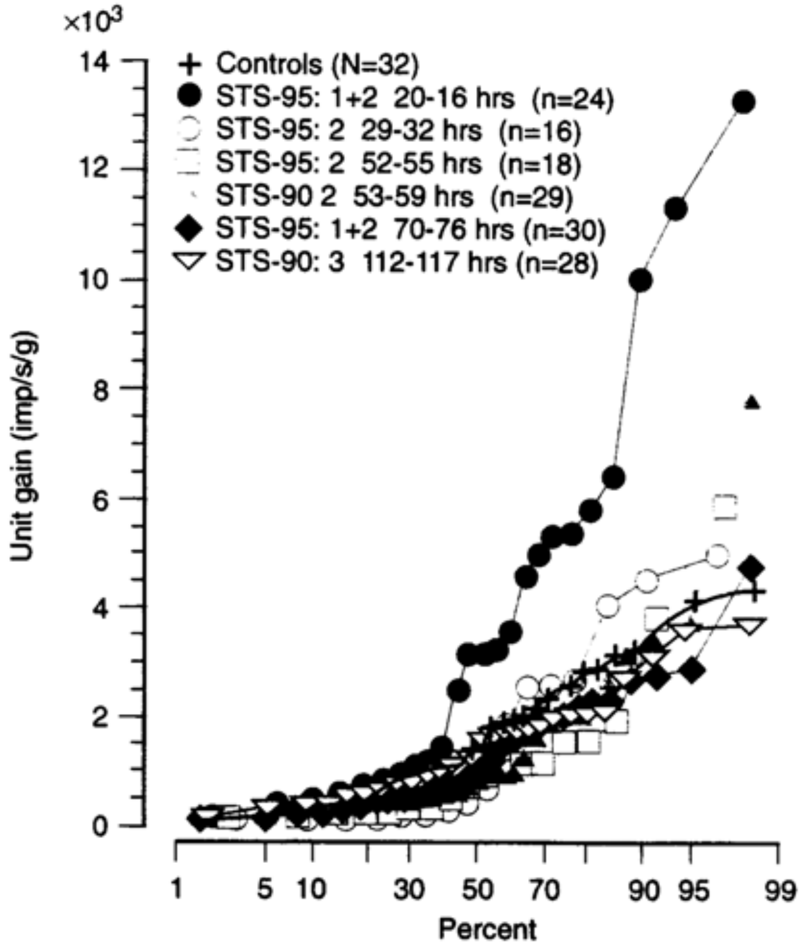
Wood, Loehr & Guilliams, NeuroRehab (2011) 29:185-95

Lessons learned ...

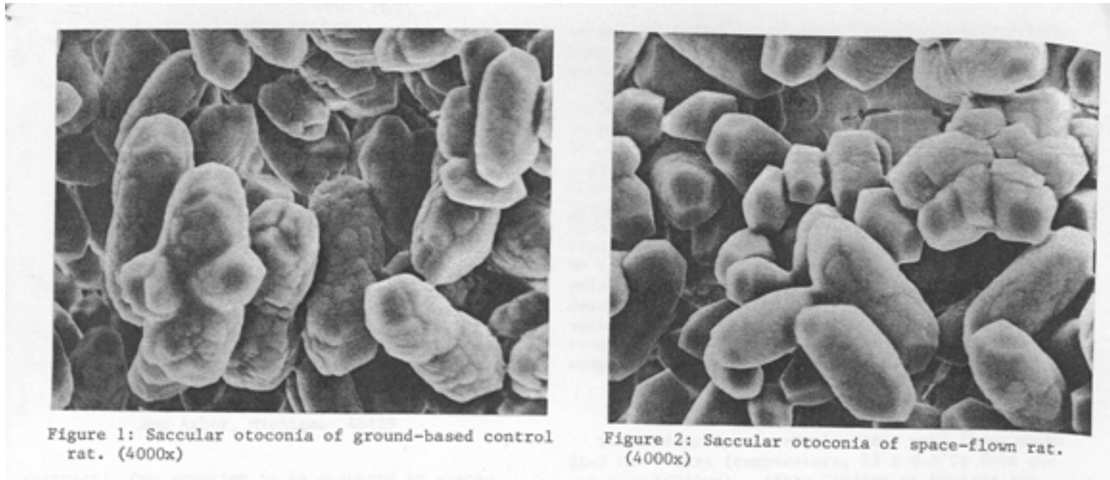
- Returning crewmembers exhibit vestibular/cerebellar and sensorimotor decrements following G-transitions that reflect adaptive responses in central neural pathways
- Large inter-subject variability, also influenced by current countermeasures and amount of active movement
- There is a greater prevalence and severity of sensorimotor deficits with increasing flight duration
- Time course of recovery for a given metric depends on flight duration and task complexity
- Feedback from functional assessments (e.g., posturography) have been helpful in guiding flight surgeons and crew for returning to activities of daily living


EXPLORE
MOON to MARS

Peripheral otolith adaptation



Boyle et al., J Neurophisiol, 2001



Ross et al., Physiologist, 1985