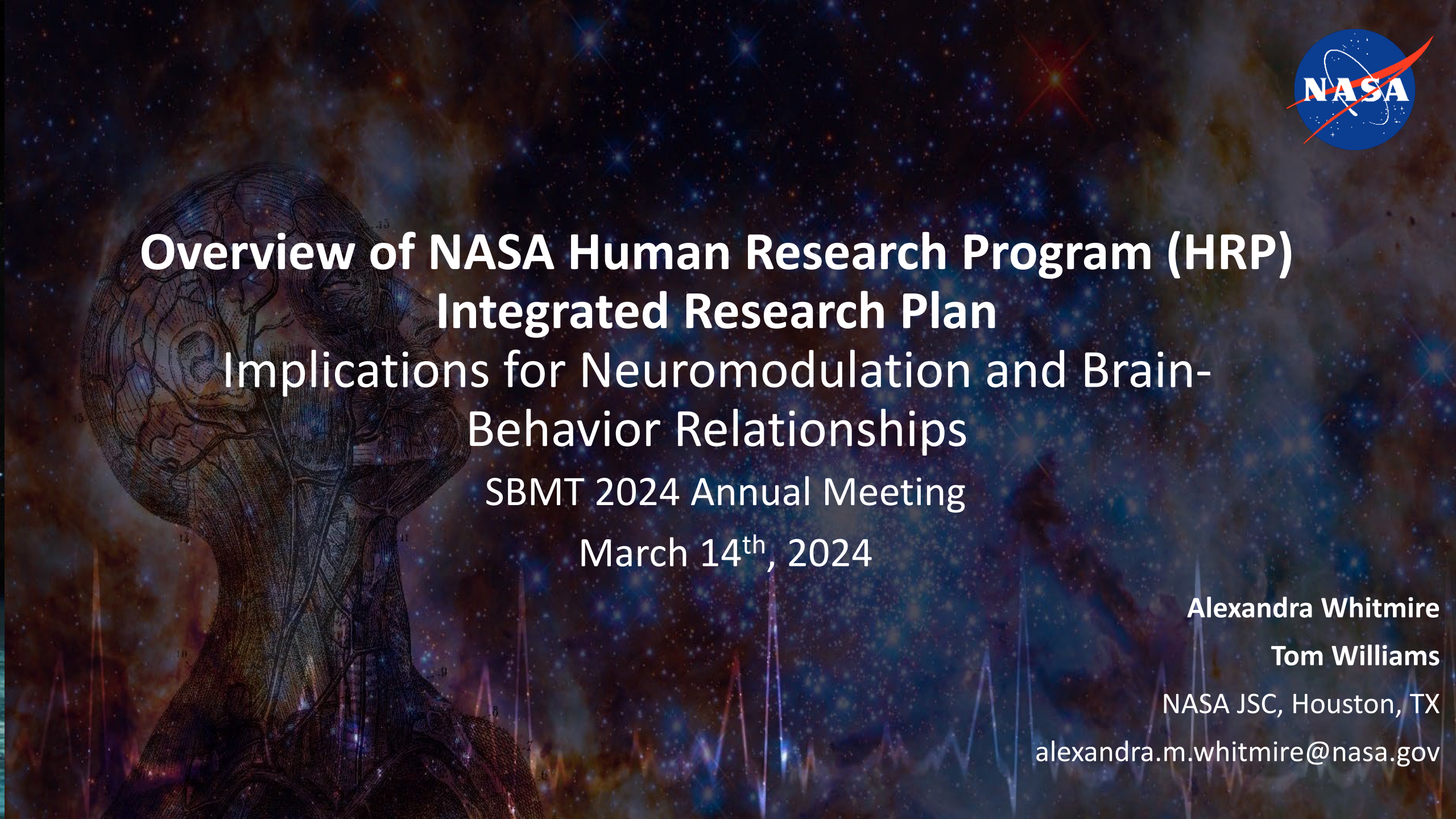


Overview of NASA Human Research Program (HRP) Integrated Research Plan

Implications for Neuromodulation and Brain-Behavior Relationships

SBMT 2024 Annual Meeting

March 14th, 2024

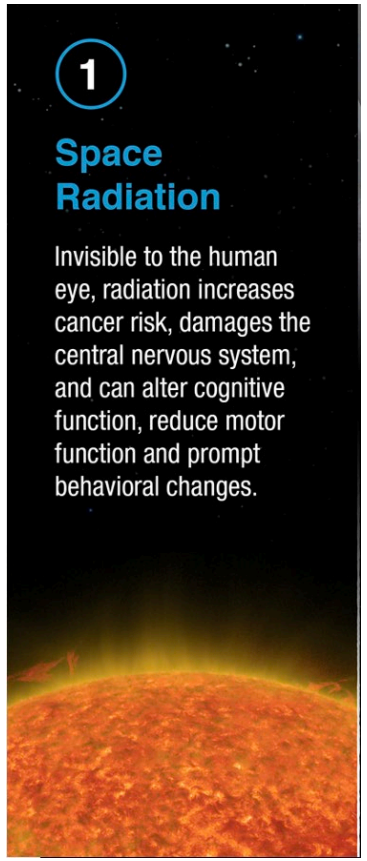
Alexandra Whitmire

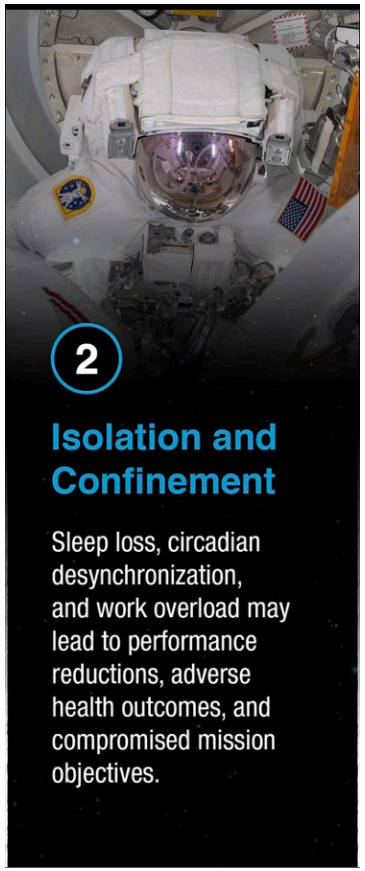
Tom Williams

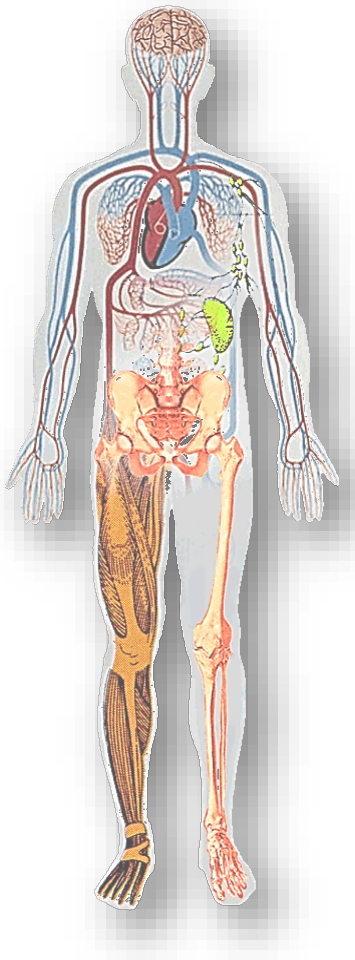
NASA JSC, Houston, TX

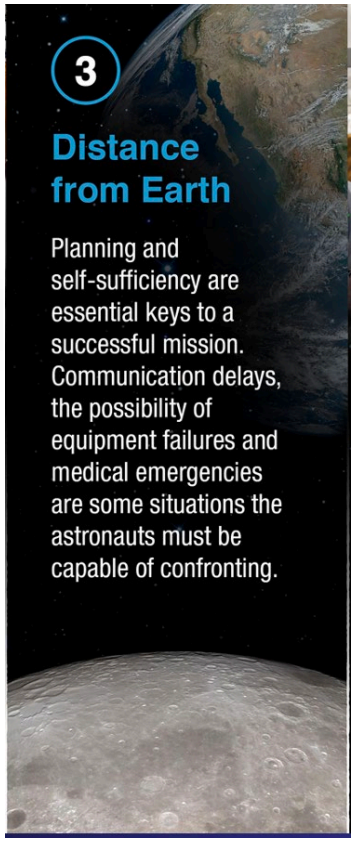
alexandra.m.whitmire@nasa.gov

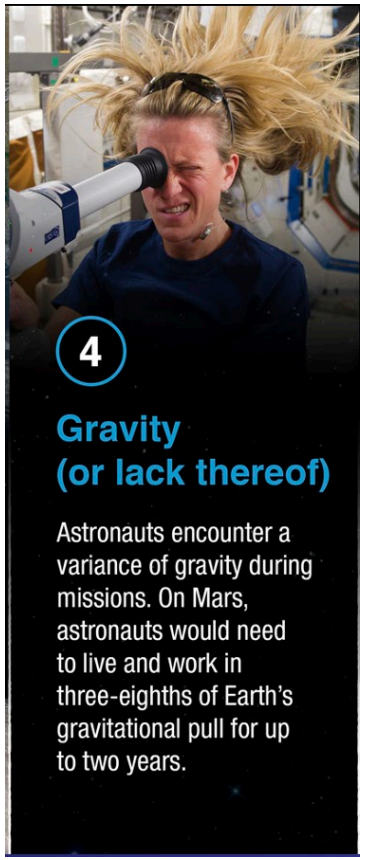
Hazards of Spaceflight

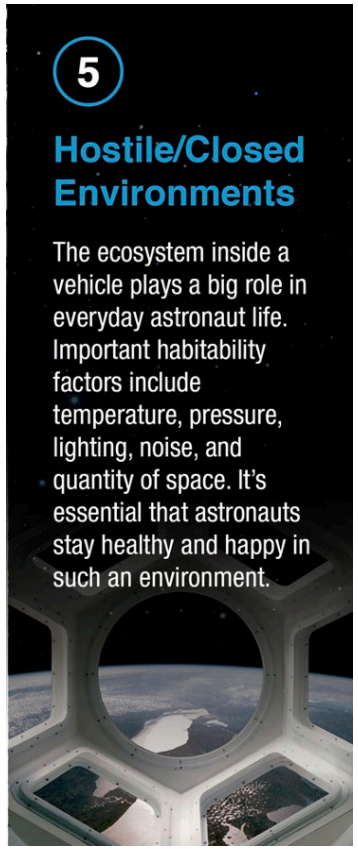










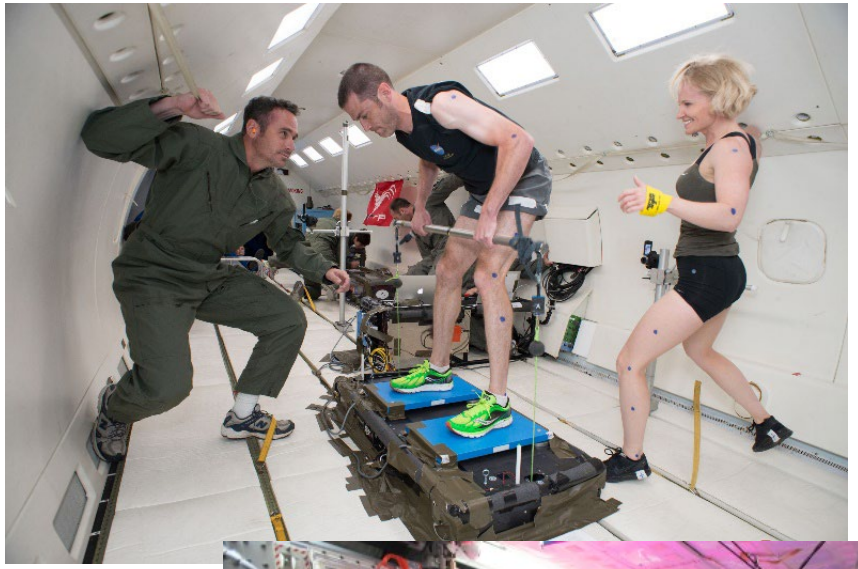


https://www.nasa.gov/hrp/hazards

Characteristics of NASA HRP

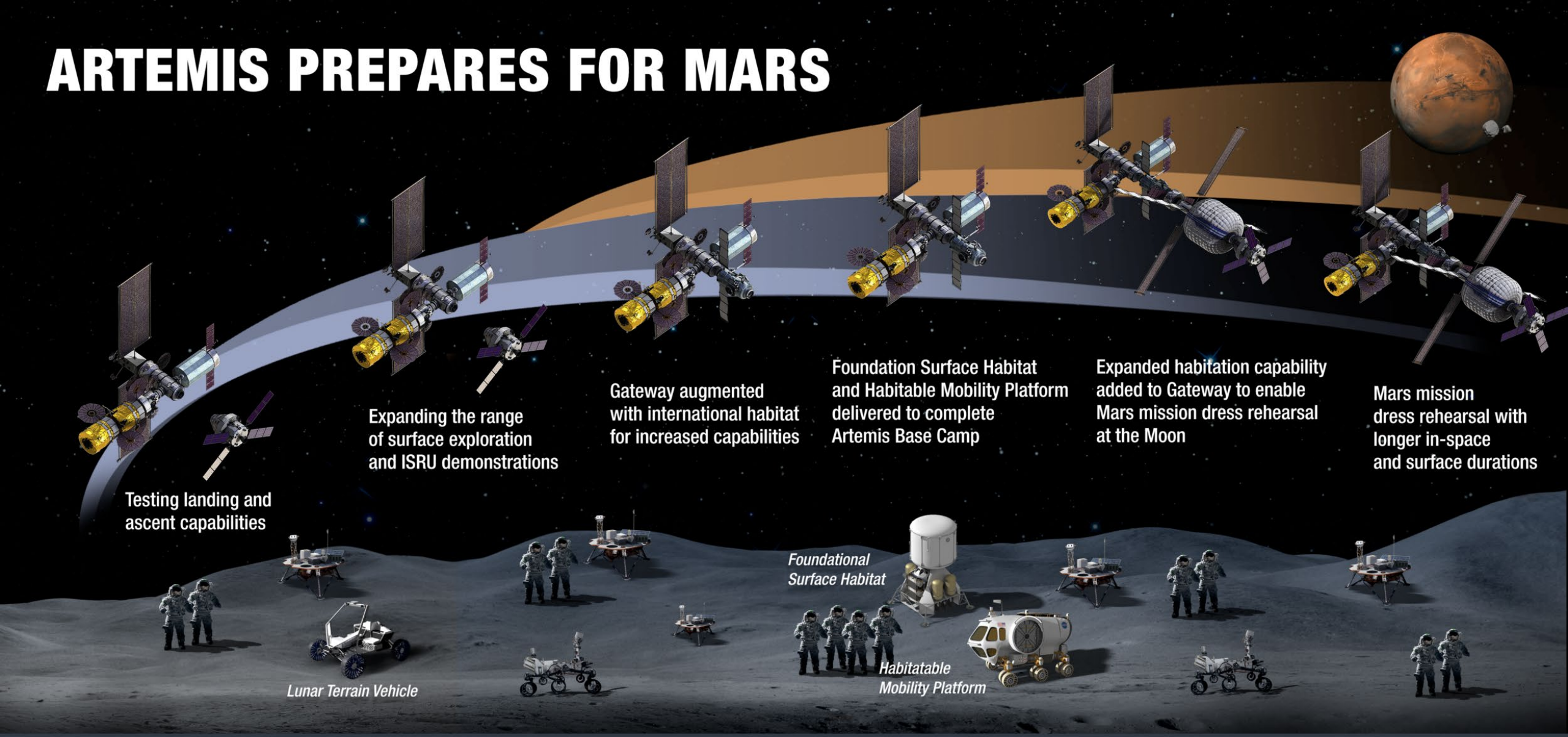
Composed of Five *Elements*

- Space Radiation
  Biological effects of radiation exposure – cancer
- Human Health Countermeasures
  Physiological Changes
- **Human Factors and Behavioral Performance (HFBP)**
  Individual and interpersonal outcomes
  Interfaces between humans, vehicles & habitats
- Exploration Medical Capability
  Medical care for deep-space missions
- Research Operations and Integration
  Infrastructure for flight and analog experiments



https://www.nasa.gov/hrp/hazards

ARTEMIS PREPARES FOR MARS



SUSTAINABLE LUNAR ORBIT STAGING CAPABILITY AND SURFACE EXPLORATION

MULTIPLE SCIENCE AND CARGO PAYLOADS | INTERNATIONAL PARTNERSHIP OPPORTUNITIES | TECHNOLOGY AND OPERATIONS DEMONSTRATIONS FOR MARS

HFBP

Behavioral Medicine

Team Cohesion and Performance

Sleep, Circadian Rhythms, Workload

Human Factors and Human Systems Integration

Injury from Dynamic Loads

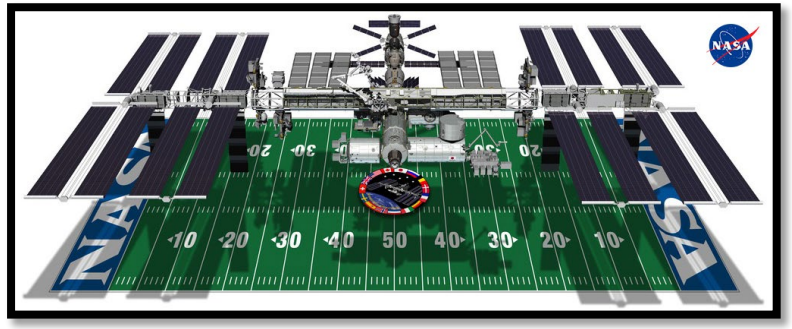
Behavioral Health and Performance

Current Operations

Low Earth Orbit

- Familiar duration and distance
- Real-time communications (ground ops, family, friends)
- Provision of crew care packages
- Evacuation options
- Windows for Earth-viewing
- Exercise variety & long regimens
- Large volume and private quarters
- Mostly six-month duration
- High tempo & shifting operations
- Increasingly mixed crews

ISS



Near Term Exploration Missions

Short Duration Lunar

- Lunar missions around two weeks
- Loss of communication and delayed com (6-14 sec) with ground
- Limited re-supply
- Limited options for evacuation
- Windows for Earth-viewing
- Very limited food and exercise options
- Small volume and lack of privacy
- High-tempo, shifting schedules
- Increasingly autonomous operations, including during emergency

Orion Capsule 316 Ft^3

Gateway Habitat 4415 Ft^3

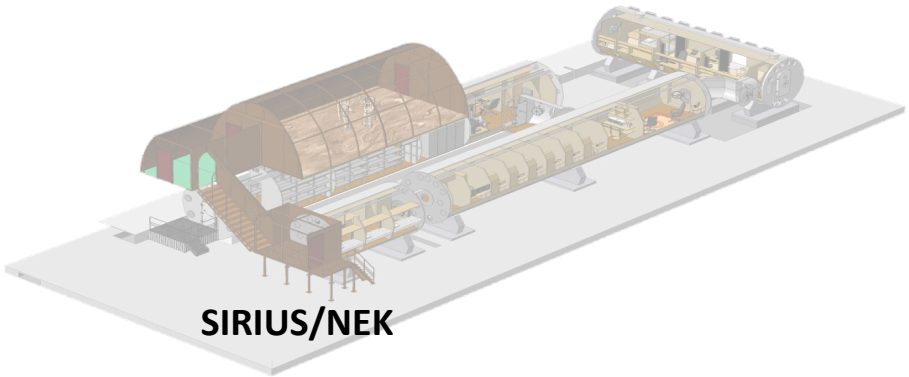
Future Exploration Class Missions

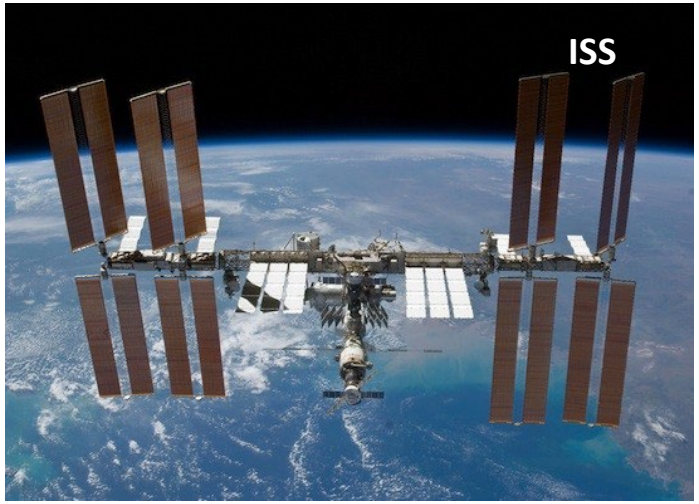
Mars

- Unprecedented duration and distance
- Loss of communication & delayed com (19 minutes) with ground
- No re-supply
- No options for evacuation
- Earth out of view; virtual windows
- Very limited food and exercise options
- Constrained volume & reduced privacy
- Periods of monotony with high-tempo situations; Mars sol
- Highly autonomous operations, including during emergency

Mars

Research Platforms

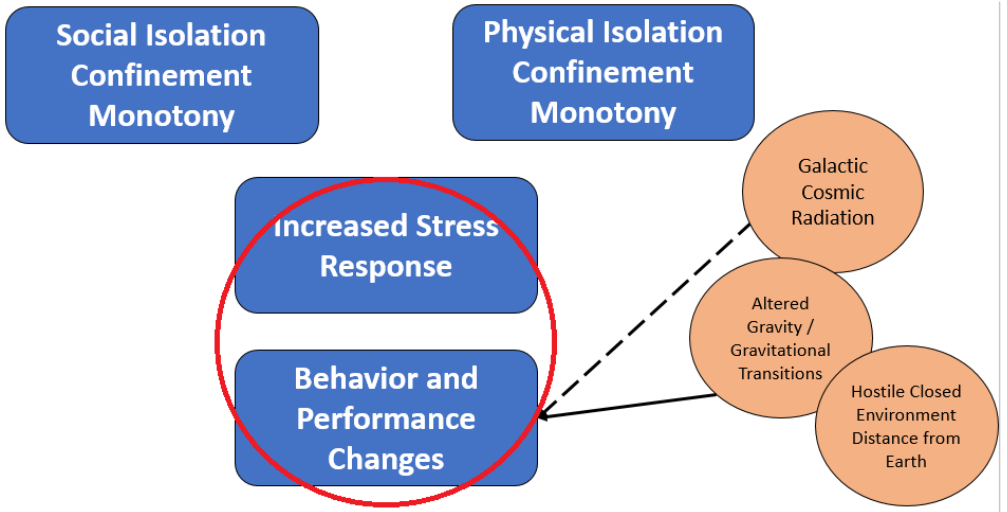




Behavioral Health and Performance Research in Current Spaceflight

High performing crews completing very successful missions

- Average nightly sleep duration just over six hours per night (as measured objectively on ISS up to 2011) *Flynn-Evans et al. (2015)*
- Reaction time measured by Psychomotor Vigilance Task (PVT) related to sleep and fatigue *Dinges et al. (2017)*
- Docking sim performance related to sleep pressure *Petit et al. (2019)*
- Humans are capable of achieving sufficient sleep in space, especially when their schedules afford adequate sleep *Flynn-Evans et al. (2023)*
- Fine motor changes during gravitational transitions *Holden et al. (2019)*
- Research evaluating other aspects of cognitive function suggests minimal changes *Strangman et al. (2015); Tays et al. (2021)*
- Evidence of neurostructural changes; limited functional changes *(Roy-Oreilly et al., 2021)*
- Self-reported stress increases over mission duration for some crew members, particularly during second half of mission *Dinges et al. (2017)*
- Journaling reveals very positive experience overall *Stuster (2010); Stuster (2016)*



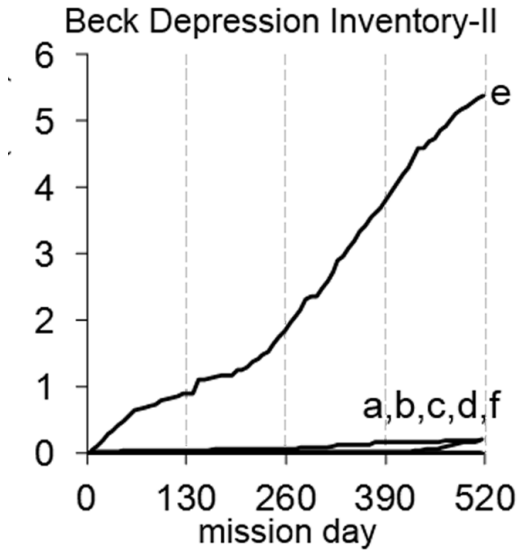
Behavioral Health and Performance Research in Exploration-Like Environments

Successful missions with healthy crew ~ signs of increased risk

- Neurostructural changes following a winter-over in Antarctica
  Stahn et al. (2019)
  - Reductions in hippocampal volume of the dentate gyrus
    - Associated with lower cognitive performance in tests of spatial processing and selective attention (no decreases in performance on other cognitive tests)
    - Associated with reductions in BDNF concentrations

- Behavior and performance changes over mission duration
  - Performance on a spaceflight operational task declined over time (*Stankovic et al., 2022)*
  - Decreases in more conceptual team performance tasks, end of mission compared to early mission *Larson et al. (2020)*
  - 520-day mission NEK: Reduction in activity levels over time *Dinges et al. (2013)*

Behavioral Health and Performance Research in Exploration-Like Environments



Successful missions with healthy crew ~ signs of increased risk

- Declines in emotion recognition, emotion regulation & positive affect
  - Dampening of positive affect and decline in self- regulation (Antarctic Stations) *Alfano et al. (2021)*
  - Slowing in emotion recognition and with bias towards more negative emotion over time (60 days Head-Down Bed-Rest) *Basner et al. (2021)*
  - Inaccuracies in emotion recognition in HERA under acute sleep deprivation *Nasrini et al. (2020)*
- One crew member - depression symptoms increase over time; social isolation *Basner et al. (2014)*

Limitations of Analog Research

- Small n
- Measurement limitations
- Generalizable to exploration?
- Generalizable to astronauts?

Behavioral Health and Performance Research
Predict Vulnerabilities & Resiliencies to Target In-Mission Support

Dinges, Basner, Jones, Stahn, Nindl, Hensch, Roma, Bell – Preliminary Data

ICC – ICARUS (U Penn)

Mission Control at the UPenn Isolation & Confiner Analog Research Unit for Spaceflight **(ICARUS)**.

8-day missions, 4 n per mission; total n=40

ICC – HERA (NASA JSC)

Human Exploration Research Analog **(HERA)**.

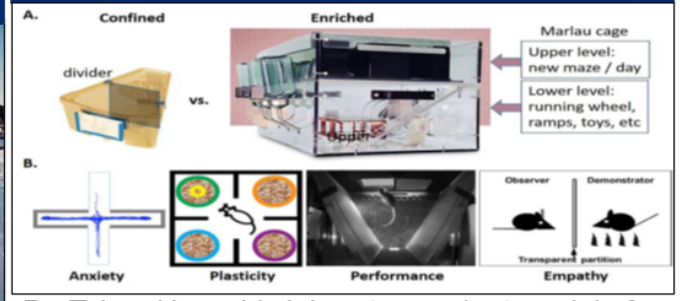
45-day missions, 4 n per mission; total n=32

ICE – Neumayer (Antarctica)

Neumayer III Antarctic station **(Neumayer)**.

14-month missions, total n=18

Animal Model (Harvard)



Dr. Takao Hensch's laboratory rodent model of isolation, confinement, and stress.

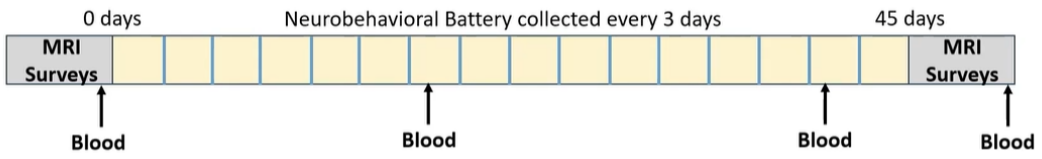
NSCOR Biological Biomarkers
Brain-derived neurotrophic factor (BDNF)
Oxytocin
Cortisol
(Pro/Anti-) Inflammatory Cytokines
Interleukin (IL)-1β
IL-6
IL-10
Tumor necrosis factor (TNF)-a
Insulin-like growth factor (IGF-1)
Vascular endothelial growth factor (VEGF)
Acetylcarnitine (ALCAR)
Ghrelin
Neuropeptide-Y (NPY)
Testosterone
Sex hormone-binding globulin (SHBG)
Dehydroepiandrosterone (DHEA)
Calcium-binding protein spermatid-specific 1 (CABS1)
Melatonin
Isoprostanes (oxidative stress)
Epinephrine and Norepinephrine

Preliminary Results

- Acetylcarnitine (ALCAR)
- Cortisol
- Ghrelin
- Melatonin
- Neuropeptide-Y
- Tumor necrosis factor (TNFa)
- Testosterone
- Vascular endothelial growth factor (VEGF)

In-Mission Resilience Score

HERA



Pre-mission biomarkers predict in-mission resilience

- **Preliminary - both biomarkers and brain structure together**
- **Forward work – inclusion of survey data with biomarkers and neurostructural data**

Behavioral Health and Performance Research Countermeasures for Exploration

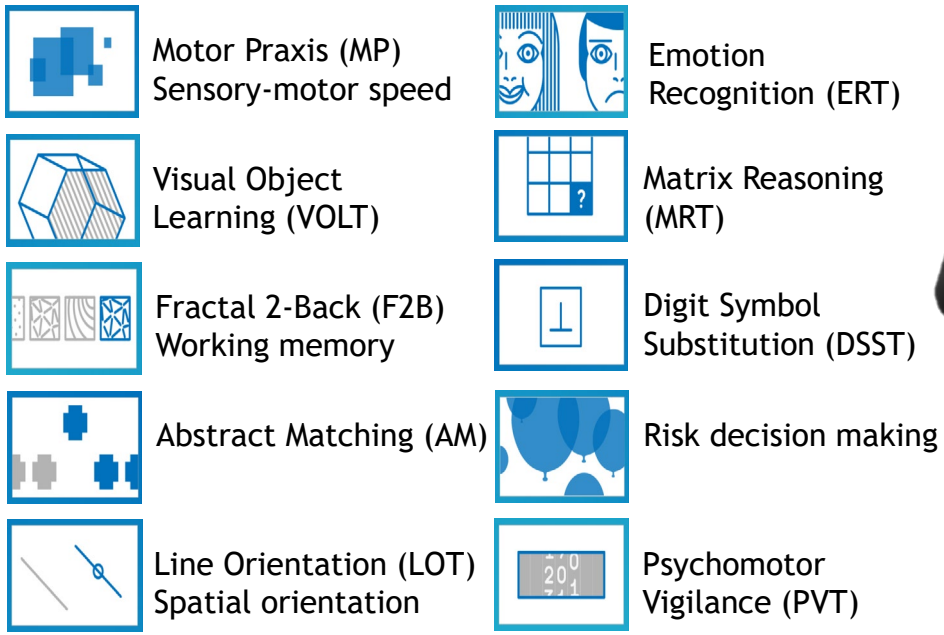
Basner, Stahn – Preliminary Data

Hybrid Training (HT) System combined Virtual Reality technologies with exercise equipment at **Neumayer Station**. The system included:

- Operational performance measures that participants could complete while cycling
- Contact electrodes for logging heart rate as indicator of exercise intensity
- Haptic feedback when increasing work intensity during uphill cycling, storms, or different terrains
- Real-time monitoring of comprehensive metrics for each training session

Methods: 18 participants during two, 12-14 month winter-over missions in Neumayer station were expected to exercise at least 3 times per week for at least 30 minutes per session

Operational Performance measures & includes a brief mood survey



Results: Brain imaging post-mission showed that those who participated in HT did <u>not</u> show decreases in brain volume, compared to those without HT. HT participants also showed changes in BDNF post-mission. Results suggest that Hybrid Training exhibits a **protective effect** on structural brain changes associated with social isolation and confinement, and should be considered as a target-specific neurobehavioral countermeasure

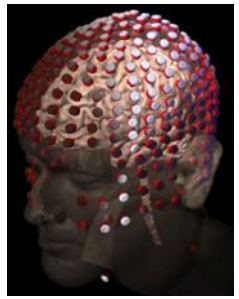
Behavioral Health and Performance Research Countermeasures for Exploration

Strangman, Ikovic

Investigate whether transcranial electrical stimulation has potential to help counteract performance decrements, using a robotic arm procedure (ROBoT-r) as the operationally-relevant outcome measure.

Aims

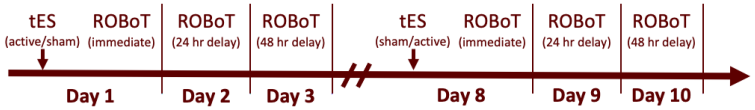
1. Determine if transcranial electrical stimulation (tES) in either of two brain areas effect performance on ROBoT-r using a double-blind crossover design.
2. Quantify the time constant of performance change over 3 days, and the extent of any enhancement for the various aspects of the task.



METHODS

Lab test of n=40 astronaut-like subjects performing ROBoT-r with and without tES using a double-blind crossover design.

- N=20 participants will receive tES over the left anterior insula (as well as sham)
- N=20 participants will receive tES over the right dorsolateral prefrontal cortex (as well as sham)



Analysis includes changes in ROBoT-r performance as a function of:

- tES vs sham stimulation
- Site of tES application (Insula vs dorsolateral prefrontal cortex)
- Time elapsed since stimulation (immediate, 24-hr and 48-hr delay)