Risk of Adverse Cognitive or Behavioral Changes and Psychiatric Disorders Leading to In-mission Health and Performance and Long-term Health Effects (Behavioral Health Risk)
Revision D.1

Human System Risk Board

HSRB CR SA-07566
Approved: 2/13/2025

Risk Custodian Team
S. Dev/SK
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Risk Record

- This revision:
  - Provides updated Likelihood x Consequence (LxC) scores assessed against updated Design Reference Missions (DRMs) and the 5x5 Risk Matrix
  - Additions to Directed Acyclic Graph (DAG)
  - Provides updated ops and long-term health (LTH) evidence from spaceflight and analogs
  - Knowledge gaps for characterization

This information was previously reviewed/dispositioned at:

Meeting	Date	Outcomes/Direction
SMOCB/BRESCB	04/09/24	**Approved**

Contents

1. Risk Title and Risk Statement

- **Risk Title**:
  Risk of Adverse Cognitive or Behavioral Changes and Psychiatric Disorders Leading to In-mission Health and Performance and Long-term Health effects (Behavioral Health Risk)

- **Risk Statement**:
  Given that crews of future exploration missions will be exposed to extended durations of isolation and confinement, great distance from Earth, and protracted exposures to radiation and altered gravity, a possibility exists that these singular or combined hazards could lead to (a) adverse cognitive or behavioral changes affecting crew health and performance during the mission; (b) development of psychiatric disorders if adverse behavioral health changes are undetected or inadequately mitigated; and (c) long-term health consequences, including late-emerging cognitive and behavioral changes.

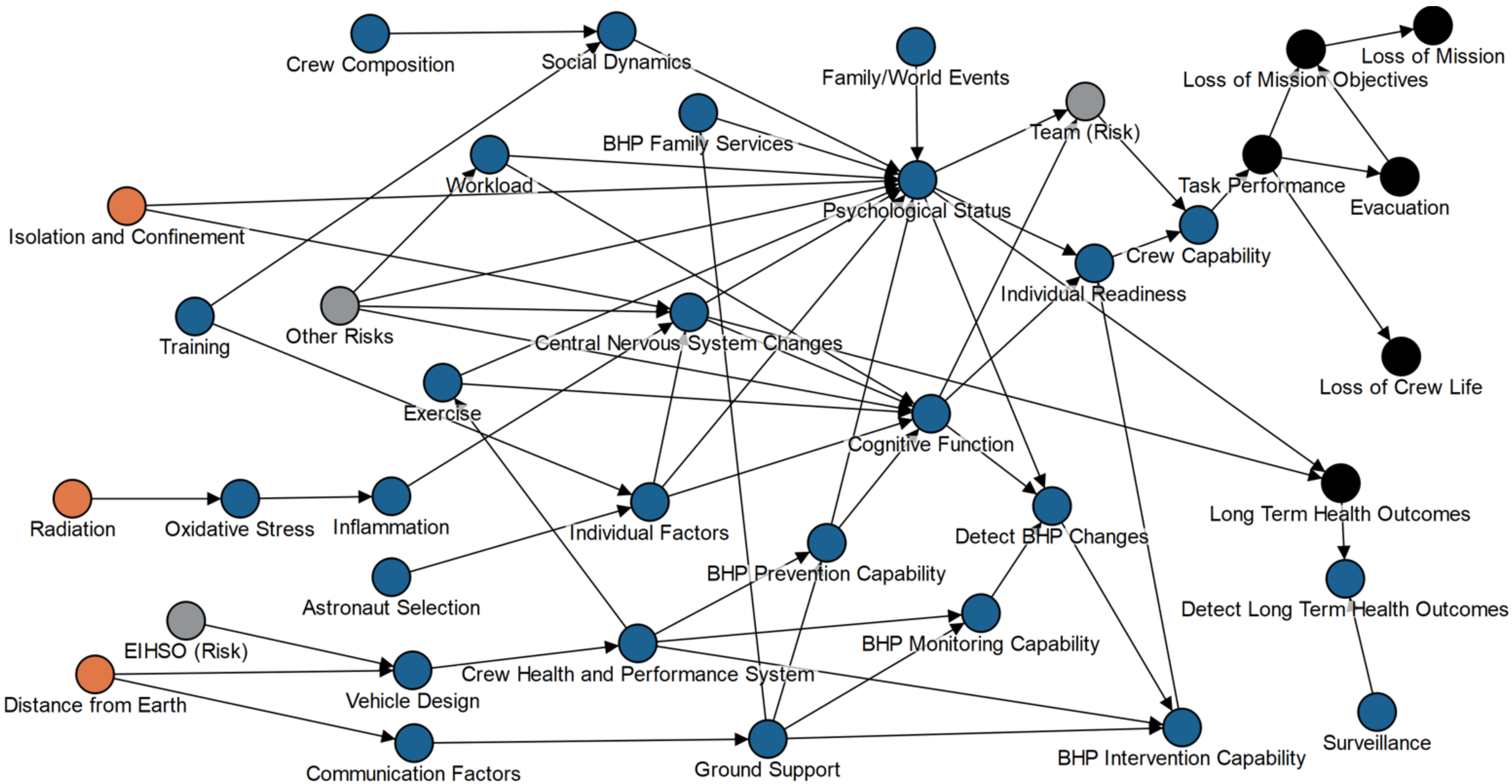
2. Risk History

Item	Date	Outcome/Status
HSRB Risk Presentation	02/13/2025	**Decisional** – CR SA-07566 HSRB DAGtionary Updates and DAG Corrections; CR approved with modifications. Rev D.1
HSRB Risk Presentation	07/25/2024	**Decisional** - CR SA-06808 Updates to the Behavioral Health Risk (Rev D). Approved with modifications.
HSRB Risk Presentation	04/11/2024	**Informational** – CR Kickoff SA-06808 Updates to the BMed Risk
HSRB Risk Presentation	05/13/2022	**Decisional** – CR SA-05096 HSRB Directed Acyclic Graphs Errata Changes; CR Approved out of board, Rev C.1
HSRB Risk Presentation	12/17/2020	**Decisional** - CR approved with modifications (Risk Rev C)
Risk Evaluated via CR	8/31/2020	CR Evaluation period ended
HSRB Risk Presentation	8/30/2020	**Informational** – CR Kickoff
Risk Evaluated via CR	10/06/2015	**Decisional** – CR approved as written (Risk Rev B)
Action Item Closure	06/01/2015	**Decisional** – Corrected 2x2 color from yellow to green for DSS (LTH) (Risk Rev A.1)
HSRB Risk Presentation	12/17/2014	**Decisional** – CR approved with modifications. Approved risk baseline (Risk Rev A)
Risk Evaluated via CR	11/26/2014	**Decisional** – To update the risk
HSRB Risk Presentation	11/19/2014	**Informational** – Evaluate previous content, assess, and disposition risk based on new process
Risk Evaluated via CR	09/02/2009	**Decisional** – Proposed to baseline risk content. Approved as written on 09/24/2009 (Baseline)
HSRB Risk Presentation	08/18/2009	Informational - Content reviewed.

3. Executive Summary

- Updated evidence from spaceflight and from studies in conditions analogous to spaceflight indicates subclinical changes occur in psychological and cognitive measures, however, data is required to characterize meaningful change and operational outcomes, and further research is required to strengthen the evidence base for this risk.
- Risk title and statement have been altered to reflect subclinical changes in behavioral medicine outcomes.
- The Extravehicular Activity (EVA) Risk has been added to the DAG.
- Negligeable additional evidence is available for LTH effects; i.e., to date, scant evidence exists of an increased prevalence of neurodegenerative disease in low Earth orbit (LEO), and the evidence base is weak for lunar and Mars DRMs.
- The following gaps have been identified for further characterization: communication delays during lunar missions (leading to an LxC and color change), high tempo EVAs, pain, and radiation exposure.
- An update has been provided on countermeasures (CM): current CMs appear to be effective for LEO, however these measures are used during real time communication, and it remains to be determined if current CM technology can be adapted to future DRMs.
- Crewmember selection procedures reduce risk
- The behavioral medicine risk is complex and influenced by several other risks.

4. Directed Acyclic Graph - DAG



Directed Acyclic Graph (Narrative)

The Behavioral Risk is centered around two nodes: **Psychological Status** and **Cognitive Function**.

- **Psychological Status** refers to the mood and the psychological state of the crewmember at any given time during a mission. These factors can directly affect **Crew Capability** by decreasing an individual's readiness for **Task Performance** if the crewmembers are distracted, preoccupied, dysregulated, unmotivated, fatigued, or uncooperative. This also affects the **Team (Risk).** The equilibrium that is present in **Psychological Status** for an individual astronaut is affected by
  - **Family/World Events,** which can occur while an astronaut is on a long mission. These can include deaths and loss that provoke grief and affect mood and motivation.
  - **Social Dynamics** with the rest of the crewmembers are dependent on **Crew Composition**. NASA typically does not select crews for their compatibility, however, this may be required for longer duration exploration missions.
  - **Central Nervous System (CNS) Changes** that can occur as a result of **Isolation and Confinement** or can occur because of **Other Risks** including **Medical (Risk), Pharm (Risk), Food and Nutrition (Risk), Sensorimotor (Risk), Spaceflight Associated Neuro-ocular Syndrome (SANS Risk), Sleep (Risk), CO_2 (Risk), Hypoxia (Risk), Immune (Risk), and Extravehicular Activities (EVA Risk)**. CNS changes can also be affected by **Oxidative Stress/Inflammation** as a result of **Radiation** exposure and other causes.
  - **Workload** can affect mood and psychological state. Workload is impacted by operational tempo in the context of performing EVAs, science tasks, maintenance tasks, and public outreach.
  - **Individual Factors,** including **Age**, **Sex**, **Genetic Predispositions**, and others, affect the resilience of individual astronauts and the magnitude of impacts to **Psychological Status**.

- **Cognitive Function** refers to the astronaut's attributes such as planning, reasoning/decision-making, attention, memory, cognitive speed, and other thought processes, which can be affected by a variety of factors in the spaceflight environment. Disruption in **Cognitive Function** can also directly affect **Crew Capability** and decrease readiness for **Task Performance** required for a variety of mission objectives. This can affect the **Team (Risk)** by requiring other team members to compensate for the individual's deficits. The equilibrium that is present in **Cognitive Function** for an individual astronaut is affected by
  - **CNS Changes,** as described above.
  - **Workload,** which can affect ability to focus and general cognitive function. Workload is impacted by operational tempo in the context of EVAs (EVA Risk), science tasks, maintenance tasks, and public outreach through cognitive and physical fatigue (Medical Risk and Sleep Risk).
  - **Individual Factors,** including **Age, Sex, Genetic Predispositions,** and others, affect the resilience of individual astronauts and the magnitude of impacts to **Cognitive Function**.

- CMs to mitigate issues with **Psychological Status** and **Cognitive Function** can be administered before flight or during the mission and in some cases must be included in **Vehicle Design** allocations and the **Crew Health and Performance System** to reduce risk. These CMs include

  - **Selection** of crewmembers who are resilient to decrements in **Psychological Status** and **Cognitive Function**.
  - **Training,** which historically has been provided before flight and enables crewmembers to develop individual resilience as well as team cohesion. This may need to be included during flight as well during future missions.
  - **Exercise,** which has a strong connection with mood and motivation of the crewmember and affects both **Psychological Status** and **Cognitive Function** in positive ways.
  - **Behavioral Health and Performance (BHP) Prevention Capability**, which could include **Exercise**, however other preventive measures are performed including care packages, family conferences, private psychological conferences (PPC), and more.
  - BHP Monitoring Capability to enable the crew to identify when their **Psychological Status** or **Cognitive Function** changes**,** and to determine appropriate times to implement **BHP Intervention Capability**. This includes regular assessments of **Cognitive Function** and evaluations during private medical conferences as well as PPCs.
  - **BHP Intervention Capability,** which includes clinically indicated PPCs, private family conferences, ground-based family support services intervention by other crewmembers, and other BHP interventions that may include medications if warranted.

- Most of the current CMs are dependent on real-time communication and resupply. As **Communication Factors** change with **Distance from Earth**, access to **Ground Support** that enables successful **BHP Monitoring Capability** and **BHP Intervention Capability** becomes strained or non-existent.

- Both CNS Changes and **Psychological Status** of an individual astronaut throughout a mission can cause **Long-Term Health Outcomes**. Post-flight and post-career **Surveillance** can **Detect Long-Term Health Outcomes** of interest and better characterize the long-term risk to astronauts.

5. Risk Summary

Risk Title: Risk of Adverse Cognitive or Behavioral Changes and Psychiatric Disorders Leading to In-mission Health and Performance and Long-term Health effects
Risk Custodian Team: Sheena Dev, James Picano, Devan Petersen

Risk Statement: Given that crews of future exploration missions will be exposed to extended durations of isolation and confinement, greater distances from Earth, as well as increased exposures to radiation and altered gravity, there is a possibility that these singular or combined hazards could lead to (a) adverse cognitive or behavioral changes affecting crew health and performance during the mission; (b) development of psychiatric disorders if adverse behavioral health changes are undetected or inadequately mitigated; and (c) long-term health consequences, including late-emerging cognitive and behavioral changes.

Primary Hazard: Isolation and Confinement

Secondary Hazard(s): Hostile Closed Environment, Distance from Earth, Radiation, Altered Gravity

Countermeasures: ***Monitoring:*** private psychological conferences (PPC) and cognitive monitoring (for Long-duration space exploration (LDSE)), unobtrusive monitoring* ***Prevention:*** Preflight: selection and training (LDSE); Inflight: operational psychology services (care packages, family conferences, etc.), exercise, and habitat and systems designs (for beyond LEO), nutrition and supplements*, task and decision support (HSIA)* ***Intervention:*** PPC and pharmaceuticals (LDSE)

Contributing Factors: Mission duration (>6 months), workload, personality (for LDSE), Sleep, Team dynamics, family and psychosocial stressors (e.g., illness or death of loved one, world events, etc.), individual factors (e.g., age, sex, genetic predispositions), habitat design and systems (e.g., atmosphere*, food acceptability*, habitable volume*, privacy*, lighting, etc.), deficient sensory stimulation*, medical conditions, medication side effects, pain, dangerous operational environment

State of Knowledge: Sub-diagnostic behavioral health conditions were anecdotally reported on several long-duration missions. Inflight symptoms have never reached diagnostic threshold despite related instances of lost mission objectives or early return. Estimated incidence of behavioral health symptoms on the International Space Station (ISS) is 0.62 person-year, although this is likely an underestimate. Incidence of psychiatric disorders in Antarctic studies is ≥ 4.5%; an increase in behavioral health symptoms over time with a preliminary non-linear increased incidence past 5–6 months has been established in experiments conducted in analogs of spaceflight. Alterations in the morphology and function of the brain have been identified in astronauts who have participated in long-duration missions on the ISS , although cognitive performance or long-term health implications of these changes are unknown. Biomarker data obtained from long-duration ground analogs of spaceflight reveal declines in a key neurotrophin linked to reductions in brain volume. A case report and anecdotal evidence indicates inconsistent, mild cognitive decrements in LEO. Clinically meaningful cognitive decrements after flight is hypothesized to relate to physiological adaptation and persisted at least 6 months after landing in a single case study; lifetime course and prevalence are unknowns. Animal research suggests possible short-term cognitive decrements due to radiation exposure with uncertain human translatability. Limited study of adult atomic bomb survivors indicates no likelihood of excess neurodegenerative disease. Adult cranial radiotherapy survivors show clinically meaningful cognitive decrements from high-dose terrestrial radiation and some evidence of likelihood of excess neurodegenerative disease. Emerging evidence from terrestrial epidemiological studies of multiple U.S. cohorts with occupational radiation exposure now show excess relative risk for Parkinson's Disease mortality. Minimal evidence exists of excess neurodegenerative diseases in astronauts who have participated in short-duration LEO missions, however, the likelihood for long-duration and DRMs beyond LEO is unknown. The most current countermeasures have limited feasibility beyond LEO, increasing risk.

L x C Drivers Summary: *Ops LxC: Sub diagnostic conditions.* LTH LxC: *Neuropsychological conditions and psychiatric disorders.*
Ops Likelihood per DRM: LEO-long duration: >1.0% likelihood. Reduced likelihood for <30 days. **Lunar Orbital:** similar likelihood as LEO; possibility of increased likelihood due to smaller habitat volume, smaller crew size, limited food system, no or limited resupply. **Lunar Orbital + Surface:** similar to Lunar Orbital, but possibility of increased probability of temporary decrements due to reduced habitability, higher EVA workload, and radiation exposure. **Mars (both):** Increased probability due to duration, distance from Earth, limited communication, no resupply, radiation exposure, no currently validated countermeasures for asynchronous connection to home and BHP monitoring and intervention.
Ops Consequence per DRM: All short DRMs: Assumed lower consequence during most short missions. **Long LEO and Lunar Orbital:** Effective mitigation requires crew time and resources. **Lunar Orbital + Surface:** Assumed higher consequence for early Artemis due to reduced habitability. **Mars (both):** Increased opportunity for exacerbation due to duration and limited prevention and intervention due to communication delay with mission control and no evacuation or early return capability.
LTH Likelihood per DRM: All Short DRMs: lower likelihood of cognitive decrements due to shorter exposures to hazards. Unknown likelihood of behavioral health disorders. **Long LEO:** Single case study finding of cognitive decrements after flight that are assumed reversible and related to physiological state; unknown prevalence and course. Brain morphology alterations have uncertain relevance but drive concern. **Lunar Orbital** and **Lunar Orbital + Surface:** Unknown prevalence of cognitive and psychological disorders. **Mars:** Unknown late-emerging neurodegenerative disease outcomes (possibly including permanent disability).
LTH Consequence per DRM: Psychiatric disorders assumed to be outpatient treatable with moderate impact to quality of life. Unknown late-emerging neurodegenerative disease outcomes (possibility including permanent disability).

Risk Disposition Rationale Summary per DRM: Ops: Monitor for sub diagnostic conditions due to lower likelihood for short LEO and short Lunar Orbital DRMs. Short lunar orbital + surface mission characteristics differ enough from prior missions to create uncertainty (e.g., probable communication delays with mission control and high tempo EVAs). Mitigation required for all long DRMs using crew time and resources at a minimum. Subclinical conditions have threatened or contributed to loss of mission objectives in the past and are more likely to emerge with longer durations and with inadequate mitigation capabilities due to communication delay with mission control. **LTH**: monitor for psychiatric and neuropsychological conditions after flight and lifetime surveillance after short and long DRMs. Single case study finding of cognitive decrements after flight requires characterization due to uncharacterized behavioral health outcomes with distance from Earth, operational performance demands upon planetary surface landing, and uncharacterized neurocognitive outcomes outside LEO. Mars planetary requires mitigation and close cognitive monitoring through post-landing recovery. Lifetime surveillance thereafter.

DRM Categories	Mission Type and Duration	LxC Ops	Risk Disposition Ops	LxC LTH	Risk Disposition LTH
Low Earth Orbit	Short (<30 days)	4x1	Accepted with Monitoring	1x3	Accepted with Monitoring
	Long (30 days to 1 year)	5x2	Requires Mitigation	2x3	Accepted with Monitoring
Lunar Orbital	Short (<30 days)	4x2	Requires Characterization	1x3	Accepted with Monitoring
	Long (30 days to 1 year)	5x2	Requires Mitigation	2x3	Requires Characterization
Lunar Orbital + Surface	Short (<30 days)	4x2	Requires Characterization	1x3	Accepted with Monitoring
	Long (30 days to 1 year)	5x2	Requires Mitigation	2x3	Requires Characterization
Mars	Preparatory (<1 year)	5x3	Requires Mitigation	2x3	Requires Characterization
	Planetary (730-1224 days)	5x3	Requires Mitigation	2x5	Requires Mitigation

*** Countermeasures or contributing factors that are not yet proven**

6. LxC Quick look

Previous (Converted to 5x5, February 2023)

DRM Categories	Mission Type and Duration	LxC Ops	Risk Disposition Ops	LxC LTH	Risk Disposition LTH
Low Earth Orbit	Short (<30 days)	4x1	Accepted with Monitoring	1x3	Accepted with Monitoring
	Long (30d - 1 year)	5x2	Requires Mitigation	2x3	Accepted with Monitoring
Lunar Orbital	Short (<30 days)	4x1	Accepted with Monitoring	1x3	Accepted with Monitoring
	Long (30d - 1 year)	5x2	Requires Mitigation	2x3	Requires Characterization
Lunar Orbital + Surface	Short (<30 days)	4x2	Requires Characterization	1x3	Accepted with Monitoring
	Long (30d - 1 year)	5x2	Requires Mitigation	2x3	Requires Characterization
Mars	Preparatory (<1 year)	5x3	Requires Mitigation	2x3	Requires Characterization
	Planetary (1 -3 years)	5x3	Requires Mitigation	2x5	Requires Mitigation

Current (July 2024)

DRM Categories	Mission Type and Duration	LxC Ops	Risk Disposition Ops	LxC LTH	Risk Disposition LTH
Low Earth Orbit	Short (<30 days)	4x1	Accepted with Monitoring	1x3	Accepted with Monitoring
	Long (30d - 1 year)	5x2	Requires Mitigation	2x3	Accepted with Monitoring
Lunar Orbital	Short (<30 days)	4x2	Requires Characterization	1x3	Accepted with Monitoring
	Long (30d - 1 year)	5x2	Requires Mitigation	2x3	Requires Characterization
Lunar Orbital + Surface	Short (<30 days)	4x2	Requires Characterization	1x3	Accepted with Monitoring
	Long (30d - 1 year)	5x2	Requires Mitigation	2x3	Requires Characterization
Mars	Preparatory (<1 year)	5x3	Requires Mitigation	2x3	Requires Characterization
	Planetary (1 -3 years)	5x3	Requires Mitigation	2x5	Requires Mitigation

7. Assumptions

All LxC assessments:

- Assume that NASA Standards 3001 have been met
- CMs equivalent to those used currently on the ISS are in use
- Based on the HSRB LxC Matrix and the HSRB DRM Categories
- Additional assumptions are documented below

DRM Categories	Mission Type and Duration	Assumptions
Low Earth Orbit (LEO)	Short (<30 days)	
	Long (30 d-1 yr.)	
Lunar Orbital	Short (<30 days)	Communication delay is significant enough to impact real time communication with mission control (2.5 to 10s one way)
	Long (30 d-1 yr.)	Communication delay is significant enough to impact real time communication with mission control (2.5 to 10s one way)
Lunar Orbital + Surface	Short (<30 days)	Communication delay is significant enough to impact real time communication with mission control (2.5 to 10s one way)
	Long (30 d-1 yr.)	Communication delay is significant enough to impact real time communication with mission control (2.5 to 10s one way)
Mars	Preparatory (<1 year)	Communication delay is significant enough to impact real time communication with mission control (up to 20 mins round trip) Significant crew independence from ground support
	Planetary 1 – 3 yrs.)	Communication delay is significant enough to impact real time communication with mission control (up to 20 mins round trip) Significant crew independence from ground support

* Countermeasures or contributing factors that are not yet proven

- Crew size does not undermine team functioning (Team Risk) or resource allocation

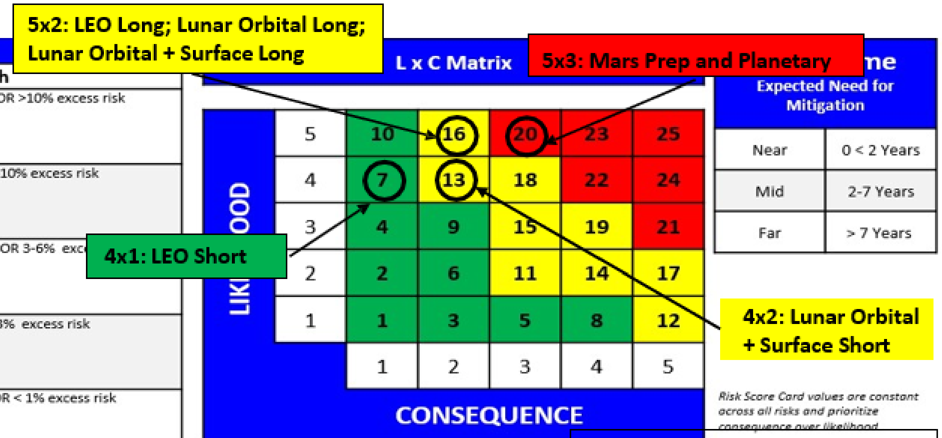
Current countermeasures in use:

- ***Monitoring:*** private psychological conferences (PPC) and cognitive monitoring (for long-duration space exploration [LDSE]), unobtrusive monitoring*
- ***Prevention:*** Before flight: crewmember selection and training (LDSE); After flight: operational psychology services (care packages, family conferences, etc.), exercise, and habitat and systems designs (for beyond LEO), nutrition and supplements*, task and decision support (HSIA)*
- ***Intervention:*** PPC and pharmaceuticals (LDSE)

8. HSRB Risk Likelihood x Consequence Matrix

Operations

LIKELIHOOD RATING	In-Mission	Flight Recertification	Long Term Health
5 Very High	More likely to happen than not during the mission or probability (P) >10%	Very likely to happen. Controls are insufficient or P> 10%	Likelihood is very high OR >10% excess risk
4 High	Likelihood is during the mission or 1%<P≤10%	Likely to happen. Controls have significant limitations or uncertainties or 1%<P≤ 10%	Likelihood is high OR 6-10% excess risk
3 Moderate	May happen during the mission or 0.1%<P≤1%	Not likely to happen. Controls exist with some limitations or uncertainties or 0.1%<P≤1%	Likelihood is moderate OR 3-6% exc
2 Low	Unlikely to happen during the mission or .01%<P≤0.1%	Not expected to happen. Controls have minor limitations or uncertainties or 0.01%<P≤0.1%	Likelihood is low OR 1-3% excess risk
1 Very Low	Nearly certain to not occur in-mission or P≤0.01%	Extremely remote possibility that it will happen. Strong controls in place or P≤0.01%	Likelihood is very low OR < 1% excess risk



CONSEQUENCES		1	2	3	4	5
IN MISSION	Crew Health Impact	Temporary discomfort	Minor injury/illness that can be dealt with by crew without ground support, minor crew discomfort	Significant injury/illness or incapacitation that requires diagnosis and/or treatment support from ground, may affect personal safety	Critical injury/illness of one crew member requiring extended medical intervention and support, may result in temporary disability	Death or permanently disabling injury/illness affecting one or more crewmember (LOCL/LOC)
	OR					
	Mission Objectives Impact	Insignificant impact to crew performance and operations – no additional resources required	Minor impact to crew performance and operations – requires additional resources (time, consumables)	Significant reduction in crew performance, threatens loss of a mission objective	Severe reduction of crew performance that results in loss of multiple mission objectives	Loss of mission due to crew performance reductions or loss of crew
FLIGHT RECERT	Crew Flight Recertification Status	Immediate flight recertification status	with limited intervention	Flight recertification status within 1 year with nominal intervention or restricted flight status	Flight recertification status requires extended medical intervention and takes > 1 year	Unable to be Recertified for Flight Status, premature career end
LONG TERM HEALTH	Health Outcomes	Career related short term self-resolving medical conditions	Career related medical conditions manageable with outpatient medical treatments	Treatable career related medical condition that requires hospitalization for management	Chronic career related medical condition requiring intermittent hospitalization or nursing care	Career related premature death or permanent disability requiring institutionalization
	OR					
	Quality of Life	No impact on quality of life OR independence in activities of daily living	Minor, short-term impact on quality of life OR rare support required for activities of daily living	Moderate long-term impact on quality of life OR may require some time-limited support for activities of daily living	Major long-term impact on quality of life OR requires intermittent support for activities of daily living	Chronic debilitating impact on quality of life OR requires continuous support for activities of daily living

Assumptions for Long Term Health Risk Matrix:

- *Long Term Health extends from the end of the post mission time period and covers an astronaut's lifetime.*
- *Conditions considered within the LTH Risk Matrix are those that 1) are related to the astronaut career, 2) are beyond those expected as part of natural aging, and 3) include acute, chronic and latent conditions.*
- *Quality of Life is defined as impact on day-to-day physical and mental functional capability and/or lifetime loss of years*

Long-Term Health

LIKELIHOOD RATING	In-Mission	Flight Recertification	Long Term Health
5 Very High	More likely to happen than not during the mission or probability (P) >10%	Very likely to happen. Controls are insufficient or P> 10%	Likelihood is very high OR >10% excess risk
4 High	Likelihood is high during the mission or 1%<P≤10%	Likely to happen. Controls have significant limitations or uncertainties or 1%<P≤ 10%	Likelihood is high OR 6-10% excess risk
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L x C Matrix

LIKELIHOOD					
5	10	16	20	23	25
4	7	13	18	22	24
3	4	9	15	19	21
2	2	6	11	14	17
1	1	3	5	8	12
	1	2	3	4	5
	CONSEQUENCE				

2x3 LEO long; Lunar Orbital long; Lunar Orbital + Surface Long; Mars Prep

2x5 Mars Planetary

1x3 LEO short, Lunar Orbital short; Lunar Orbital + Surface short

Time frame Expected Need for Mitigation	
Near	0 < 2 Years
Mid	2-7 Years
Far	> 7 Years

Risk Score Card values are constant across all risks and prioritize consequence over likelihood.

CONSEQUENCES		1	2		4	5
IN MISSION	Crew Health Impact	Temporary discomfort	Minor injury/illness that can be dealt with by crew without ground support, minor crew discomfort	Significant injury/illness or incapacitation that requires diagnosis and/or treatment support from ground, may affect personal safety	Critical injury/illness of one crew member requiring extended medical intervention and support, may result in temporary disability	Death or permanently disabling injury/illness affecting one or more crewmember (LOCL/LOC)
	OR					
	Mission Objectives Impact	Insignificant impact to crew performance and operations – no additional resources required	Minor impact to crew performance and operations – requires additional resources (time, consumables)	Significant reduction in crew performance, threatens loss of a mission objective	Severe reduction of crew performance that results in loss of multiple mission objectives	Loss of mission due to crew performance reductions or loss of crew
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Assumptions for Long Term Health Risk Matrix:

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- *Conditions considered within the LTH Risk Matrix are those that 1) are related to the astronaut career, 2) are beyond those expected as part of natural aging, and 3) include acute, chronic and latent conditions.*
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Risk Postures – 2020 update

Basis of Likelihood Estimates

- Which threshold?
  - Sub-clinical signs and symptoms of behavioral and cognitive changes (Long-Term Surveillance of Astronaut Health [LSAH] Data Request ID: #10912)
    - Consequence level = 1–3
      - Requires crew time and resources to mitigate during mid-duration (6 months) LEO (consequence level 2)
      - Has threatened or contributed to lost mission objectives in more austere conditions (consequence level 3)
      - Estimate for Mars is (consequence level 3)
        - Current mitigation is dependent on communication and resupply capabilities
    - ISS incidence: 0.62 per person-year
      - Consequence level is unknown; assumed closer to 2
  - Disorders (Integrated Medical Model [IMM])
    - Consequence level = 4
      - Requires extended medical intervention and support
    - 0 inflight – threshold overestimates observed incidence AND consequence
    - Incidence estimates are based on terrestrial population studies

- **Sub-clinical signs and symptoms of behavioral and cognitive changes (LSAH Data Request ID: #10912)**
  - Likelihoods considered:
    - P[at least 1 event]
    - P[X events] ≥ 0.01%

Likelihood	
5	P<10%
4	1%<P≤10%
3	0.1%<P≤1%
2	0.01%<P≤0.1%
1	<0.01%

	Minimum (3 crew, 14 days)	(6 crew, 30 days)	(4 crew, 6 months)	Maximum (6 crew, 1 year)
LEO and Lunar (consequence 1-2)	4 x 1 6.824% P[1 event] ≥0.01%	5 x 1-2 26.29% P[2 event] ≥0.01%	5 x 2 71.06% P[4 events] ≥0.01%	5 x 2 97.58% P[9 events] ≥0.01%

	Minimum (4 crew, 6 months)	(6 crew, 1 year)	(4 crew, 730 days)	Maximum (6 crew, 1224 days)
Mars (consequence 3)	5 x 3 71.06% P[4 events] ≥0.01%	5 x 3 97.57% P[9 events] ≥0.01%	5 x 3 99.30% P[11 events] ≥0.01%	5 x 3 99.30% P[21 events] ≥0.01%

9. Risk Postures

Low Earth Orbit (< 30 Days)
Operations

4x1	Accepted with Monitoring

- **LxC Drivers for Likelihood:** 6.82% (14-day; 3-person crew; P[1 event] ≥ 0.01%) – 26.29% (30-day, 6-person crew; P[2 events] ≥ 0.01%) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). Short-duration, large habitat volume, habitability CMs, BHP prevention CMs, resupply, and ample real-time communication bandwidth reduce the likelihood.

- **LxC Drivers for Consequence:** To date, most signs and symptoms of behavioral and cognitive changes during short-duration missions have had minor impacts to crew health and performance. Only mild and/or transient cognitive decrements have been reported anecdotally or observed to date. Effective mitigation requires nominal crew time during short-duration missions (e.g., appropriate rest).

- **Rationale for Risk Disposition:** Monitor for sub-diagnostic (e.g., signs and symptoms) behavioral and cognitive changes during short-duration missions which have currently effective mitigation due to crewmember selection, BHP CMs and interventions, and standards.

- **DRM Specific Assumptions:** N/A

- **DRM Specific Evidence/Level of Evidence:** 2-Moderate

Low Earth Orbit (< 30 Days)
Long-Term Health

1x3	Accepted with Monitoring

- **LxC Drivers for Likelihood:** Estimated to be very low excess risk. The prevalence of psychiatric disorders in astronauts is unknown. Minimal evidence of increased prevalence of neurodegenerative disease in astronauts who fly short-duration LEO missions. Assumes mitigation resulting from crewmember selection and BHP operations, and family support services for reintegration.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorders due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have a moderate impact on quality of life during the course of the condition.

- **Rationale for Risk Disposition:** Monitor for psychiatric and cognitive changes and implement intervention as needed. Limited data with which to base disposition drives uncertainty.

- **DRM Specific Assumptions**: N/A

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Low Earth Orbit (30 d – 1 yr)
Operations

5x2	Requires Mitigation

- **LxC Drivers for Likelihood:** 60.54% (6-month; 3-person crew; P[4 events] ≥ 0.01%) – 97.58% (1-year; 6-person crew; P[9 events] ≥ 0.01%) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). Short-duration, large habitat volume, habitability CMs, BHP prevention CMs, resupply, and ample real-time communication bandwidth decrease the likelihood of non-bereavement conditions. The minimal incidence estimate of bereavement is 1.61 per-mission on ISS.

- **LxC Drivers for Consequence:** Effective mitigation currently requires crew time and resources. As mission duration increases, chances increase that signs or symptoms of behavioral and cognitive changes become more than transient. Bereavement is not caused by spaceflight but can worsen during longer-duration isolation and confinement. Lost mission objectives and early return have occurred in more austere habitability conditions and with fewer crewmember selection and training CMs.

- **Rationale for Risk Disposition:** Even with crewmember selection and training, effective mitigation requires BHP CMs and interventions during the mission.

- **DRM Specific Assumptions:** N/A

- **DRM Specific Evidence/Level of Evidence:** 2-Moderate

Low Earth Orbit (30 d – 1 yr)
Long-Term Health

2x3	Accepted with Monitoring

- **LxC Drivers for Likelihood:** Excess risk is estimated to be a low. The prevalence of psychiatric disorders in astronauts is unknown. The prevalence of long-term or late-emerging cognitive changes in crewmembers of long-duration missions in LEO is unknown. Assumes mitigation from crewmember selection and BHP Operations, and family support services for reintegration. The impact of elevated radiation exposure is unknown.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorders due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have a moderate impact on quality of life during the course of the condition. Temporary cognitive decrements after landing related to physiological readaptation to 1G is uncertain (evidence from single case study only). Emerging evidence from terrestrial epidemiological studies of multiple U.S. cohorts with occupational radiation exposure now show excess relative risk for Parkinson's Disease mortality.

- **Rationale for Risk Disposition:** Monitor for behavioral and cognitive changes to intervene as needed before diagnostic threshold is reached. Monitor cognitive function before return-to-flight. Requires characterization due to limited data on which to base the disposition, especially 1-year missions. Requires characterization of late-emerging changes or conditions (e.g., conditions that have an expected onset later in life).

- **DRM Specific Assumptions:** N/A

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Lunar Orbital (< 30 Days)
Operations

4x2	Requires Characterization

- **LxC Drivers for Likelihood:** 6.82% (14-day; 3-person crew; P[1 event] ≥ 0.01%) – 26.29% (30-day, 6-person crew; P[2 events] ≥ 0.01%) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). P[1 event] > 0.01%. The short duration reduces likelihood. Communication delays with ground support impact BHP prevention and monitoring, small habitat volume, and fewer habitability CMs and resupply, and disrupted sleep increase likelihood.

- **LxC Drivers for Consequence:** To date, most signs and symptoms of behavioral and cognitive changes during short-duration missions have had minor impacts to crew health and performance. Only mild and/or transient cognitive decrements have been anecdotally reported or observed to date. Communication delays impacting current CMs will at minimum require additional crew time and have unknown impacts to the behavioral health. Effective mitigation requires nominal crew time standards during short-duration missions (e.g., appropriate rest).

- **Rationale for Risk Disposition:** Monitor for sub-diagnostic (e.g., signs and symptoms) behavioral and cognitive changes during these short-duration missions with greater vehicle austerity. Monitor cognitive performance due to uncertainty associated with exploration atmosphere and sleep/fatigue contributing factors in greater vehicle austerity. Impacts of communication delays are unknown. No validated inflight prevention and monitoring approaches have been developed for asynchronous or delayed communications with mission control.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way**).**

- **DRM Specific Evidence/Level of Evidence:** 2-Moderate

Lunar Orbital (< 30 Days)
Long-Term Health

1x3	Accepted with Monitoring

- **LxC Drivers for Likelihood:** Excess risk is estimated to be very low. The prevalence of psychiatric disorders in astronauts is unknown. Minimal evidence exists of excess prevalence of neurodegenerative disease during short-duration missions in LEO. Assumes mitigation from crewmember selection and BHP operations, and family support services for reintegration.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorders due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have moderate impact on quality of life during the course of the condition.

- **Rationale for Risk Disposition:** Monitor for psychiatric and cognitive changes to implement intervention as needed. Limited data with which to base disposition drives uncertainty. Monitor to characterize uncertainties regarding the effects of exploration atmosphere.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way**).**

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Lunar Orbital (30 d – 1 yr)
Operations

5x2	Requires Mitigation

- **LxC Drivers for Likelihood:** 60.54% (6-month; 3-person crew; P[4 events] ≥ 0.01%) – 97.58% (1-year; 6-person crew; P[9 events] ≥ 0.01%) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). The minimal incidence estimate of bereavement is 1.61 per-mission on the ISS. Communication delays, small habitat volume, fewer habitability CMs and resupply, and disrupted sleep will likely increase the likelihood, but the amount of the increase is unknown. The impact of elevated radiation exposure is unknown.

- **LxC Drivers for Consequence:** Effective mitigation currently requires crew time and resources. As the mission duration increases, the chances increase that signs or symptoms of behavioral and cognitive changes become more than transient and delayed communication limits current BHP inflight prevention, monitoring, and intervention approaches. Bereavement is not caused by spaceflight but can be worsened in longer-duration isolation and confinement. Lost mission objectives and early return have occurred in more austere habitability conditions and with fewer crewmember selection and training CMs.

- **Rationale for Risk Disposition:** Even with crewmember selection and training, effective mitigation requires BHP inflight CMs, interventions, and standards. No validated inflight prevention and monitoring approaches have been developed for asynchronous or delayed communications. Lost mission objectives and early return have occurred in more austere habitability conditions with fewer CMs.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way**)**.

- **DRM Specific Evidence/Level of Evidence:** 2-Moderate

Lunar Orbital (30 d – 1 yr)
Long-Term Health

2x3	Requires Characterization

- **LxC Drivers for Likelihood:** Excess risk is estimated to be low. Prevalence of psychiatric disorders in astronauts is unknown. The prevalence of long-term or late-emerging cognitive changes in crewmembers of long-duration LEO missions is unknown. The impact of elevated radiation exposure is unknown. Assumes mitigation from crewmember selection, BHP operations, and family support services for reintegration.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorders due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have moderate impact on quality of life during the course of the condition. A temporary cognitive decrement after landing related to physiological readaptation to 1G is uncertain (evidence from single case study only). Emerging evidence from terrestrial epidemiological studies of multiple U.S. cohorts with occupational radiation exposure now show excess relative risk for Parkinson’s Disease mortality.

- **Rationale for Risk Disposition:** Monitor for behavioral and cognitive changes to intervene as needed before diagnostic threshold is reached. Monitor cognitive functions before return-to-flight. Requires characterization due to limited data on which to base the disposition, especially for 1-year missions. Requires characterization of late-emerging changes or conditions (e.g., conditions that have an expected onset later in life).

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way**).**

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Lunar Orbital + Surface(< 30 Days) Operations

4x2	Requires Characterization

- **LxC Drivers for Likelihood:** 6.82% (14-day; 3-person crew; P[1 event] ≥ 0.01%) – 26.29% (30-day, 6-person crew; P[2 events] ≥ 0.01%) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). The short duration of the mission decreases the likelihood. Communication delays impacting BHP prevention and monitoring, small habitat volume, fewer habitability CMs and resupply, EVA tempo, and disrupted sleep may increase likelihood.

- **LxC Drivers for Consequence:** To date, most signs and symptoms of behavioral and cognitive changes during short-duration missions have had minor impacts to crew health and performance. Only mild and/or transient cognitive decrements have been reported anecdotally or observed to date. However, changes affecting the human landing system could induce cognitive changes of higher consequence during the early Artemis missions, requiring crew time and resources to mitigate. Reductions in CMs and habitability requirements (e.g., food and hydration, sleep and fatigue mitigation capabilities, exercise capabilities) add additional risk to the astronauts that can be expressed as cognitive decrements. Uncertainties driving further concern for cognitive performance include the atmosphere of the human landing system and EVA pace and workload. Greater chances of loss of a mission objectives exist during a short-duration mission.

- **Rationale for Risk Disposition:** The consequences of changes in behavioral and cognitive performance are uncertain given the greater austerity of mission parameters (e.g., reduced volume and habitability, privacy, and sleep CMs, increased surface workload, unknown cognitive performance associated with exploration atmosphere, limited food system, and limited hydration), which pushes additional mission risk onto the human that can be expressed as cognitive decrements. Impacts of communication delays not known. No validated inflight prevention and monitoring approaches have been developed for asynchronous or delayed communications.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way).

- **DRM Specific Evidence/Level of Evidence:** 2-Moderate

Lunar Orbital + Surface (< 30 Days) Long-Term Health

1x3	Accepted with Monitoring

- **LxC Drivers for Likelihood:** Excess risk is estimated to be very low. Prevalence of psychiatric disorders in astronauts is unknown. Minimal evidence of excess prevalence of neurodegenerative disease during short-duration missions in LEO. Assumes mitigation from crewmember selection, BHP Operations, and family support services for reintegration.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorder due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have a moderate impact on quality of life during the course of the condition.

- **Rationale for Risk Disposition:** Monitor for psychiatric and cognitive changes to implement intervention as needed. Limited data with which to base disposition drives uncertainty. Monitor to characterize uncertainties regarding exploration atmosphere.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way).
-

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Lunar Orbital + Surface (< 30 d – 1 yr) Operations

5x2	Requires Characterization

- **LxC Drivers for Likelihood:** 60.54% (6-month; 3-person crew; P[4 events] ≥ 0.01%) – 97.58% (1-year; 6-person crew; P[9 events] ≥ 0.01%) of subclinical signs or symptoms behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). Minimal incidence estimate of bereavement is 1.61 per-mission on ISS. Communication delays, small habitat volume, fewer habitability CMs and resupply, EVA tempo, and disrupted sleep will likely increase likelihood by an unknown amount.

- **LxC Drivers for Consequence:** Effective mitigation currently requires crew time and resources. As duration increases, chances increase that signs or symptoms of behavioral and cognitive changes become more than transient, and delayed communication limits current BHP inflight prevention, monitoring, and intervention approaches. Bereavement is not caused by spaceflight but can be worsened in longer-duration isolation and confinement. Lost mission objectives and early return have occurred in more austere habitability conditions and with fewer crewmember selection and training CMs.

- **Rationale for Risk Disposition:** Even with crewmember selection and training, effective mitigation requires BHP inflight CMs, interventions, and standards. No validated inflight prevention and monitoring approaches have been developed for asynchronous or delayed communications. Lost mission objectives and early return have occurred in more austere habitability conditions with fewer CMs.

- **DRM Specific Assumptions:** Commination delay is significant enough to impact real time communication with mission control (2.5-10s one way).

- **DRM Specific Evidence/Level of Evidence:** 2-Moderate

Lunar Orbital + Surface (< 30 d – 1 yr) Long-Term Health

2x3	Requires Characterization

- **LxC Drivers for Likelihood:** Excess risk is estimated to be low. The prevalence of psychiatric disorders in astronauts is unknown. The prevalence of long-term or late-emerging cognitive conditions in crewmembers of long-duration missions in LEO is unknown. The impact of elevated radiation exposure is unknown. Assumes mitigation from crewmember selection, BHP operations, and family support services for reintegration.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorders due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have a moderate impact on quality of life during the course of the condition. A temporary cognitive decrement after landing related to physiological readaptation to 1G is uncertain (evidence from single case study only).

❖ **Rationale for Risk Disposition:** Monitor cognitive changes to intervene as needed before diagnostic threshold is reached. Monitor cognitive functions before return-to-flight. Requires characterization due to limited data on which to base the disposition, especially for 1-year missions. Requires characterization of late-emerging changes or conditions (e.g., conditions that have an expected onset later in life).

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (2.5-10s one way).

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Mars Preparatory (<1 yr.)

5x3	Mitigation

Operations

- **LxC Drivers for Likelihood:** 71.06% (6-month; 4-person crew) – 97.58% (1-year; 6-person crew) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). Communication delays that impact BHP prevention and monitoring, small habitat volume, fewer habitability CMs, no resupply, increased exposure to radiation, and disrupted sleep increase likelihood by an unknown amount.

- **LxC Drivers for Consequence:** Concern exists that increased duration and/or severity of symptoms of behavioral and cognitive changes due to no evacuation or early return capability, limited hybrid-autonomous CMs, and no hybrid-autonomous treatment capabilities will impact crew health and performance. Bereavement can be worsened by longer-duration isolation and confinement and distance from Earth, which also threatens loss of mission objectives.

- **Rationale for Risk Disposition:** Even with crewmember selection and training, effective mitigation requires BHP inflight CMs and interventions. No validated inflight prevention and monitoring approaches have been developed for asynchronous or delayed communications. Lost mission objectives and early return have occurred in more austere conditions with fewer CMs. Mitigation is necessary to prevent worsening of signs and symptoms of behavioral and cognitive changes due to no evacuation/early return capability.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (up to 20 mins one way); Significant crew independence from ground support.

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Mars Preparatory (<1 yr.)
Long-Term Health

2x3	Requires Characterization

- **LxC Drivers for Likelihood:** Excess risk is estimated to be low for long-duration missions in LEO. The prevalence of psychiatric disorders in astronauts is unknown. The prevalence of long-term or late-emerging cognitive conditions in crewmembers of long-duration missions in LEO is unknown. The impact of elevated radiation exposure is unknown. Assumes mitigation from crewmember selection, BHP operations, and family support services for reintegration.

- **LxC Drivers for Consequence:** It is assumed that psychiatric disorders due to reintegration adjustment will be treatable on outpatient basis with eventual return to baseline and will have moderate impact on quality of life during the course of the condition. A temporary cognitive decrement after landing related to physiological readaptation to 1G is uncertain (evidence from single case study only). Emerging evidence from terrestrial epidemiological studies of multiple U.S. cohorts with occupational radiation exposure now show excess relative risk for Parkinson's Disease mortality.

- **Rationale for Risk Disposition:** Monitor for behavioral and cognitive conditions to intervene as needed before diagnostic threshold is reached. Monitor cognitive function before return-to-flight. Requires characterization due to limited data on which to base the disposition, especially for 1-year missions. Requires characterization of late-emerging changes or conditions (e.g., conditions that have an expected onset later in life).

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (up to 20 mins one way); Significant crew independence from ground support.

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Mars Planetary (730-1224 d)
Operations

5x3	Requires Mitigation

- **LxC Drivers for Likelihood:** 99.30% (730-days; 4-person crew) – 99.99% (1224-days; 6-person crew) of subclinical signs or symptoms of behavioral and cognitive changes sufficient to be noted in inflight medical records (Antonsen et al., 2017; LSAH data request #10912). Communication delays impacting BHP prevention and monitoring, small habitat volume, fewer habitability CMs, no resupply, EVA tempo, increased exposure to radiation, and disrupted sleep increase the likelihood by an unknown amount. Long-duration coupled with distance from Earth increases likelihood of repeated or persistent signs and symptoms of behavioral and cognitive changes, however, the quantity of the changes is unknown.

- **LxC Drivers for Consequence:** An increased possibility exists that signs and symptoms of behavioral and cognitive changes will persist (vs. transient) and/or will be more severe, which would normally indicate support is required from ground personnel before these behaviors threaten a mission objective. Limited hybrid-autonomous CMs and no hybrid-autonomous treatment capability exist currently, which increases consequence. No evacuation/early return capability for worst-case mitigation exists. Evidence of post-landing cognitive operational performance decrements requires further characterization to assess potential impacts to planetary surface operations. Bereavement can be worsened by longer-duration isolation and confinement and distance from Earth.

- **Rationale for Risk Disposition:** Even with crewmember selection and training, effective mitigation requires BHP inflight CMs and interventions developed for asynchronous communications. Lost mission objectives and early return have occurred in more austere habitability conditions with fewer CMs.

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (up to 20 mins one way); Significant crew independence from ground support.

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

Mars Planetary (730-1224 d)
Long-Term Health

2x5	Requires Mitigation

- **LxC Drivers for Likelihood:** Excess risk is estimated to be low. Radiotherapy cancer survivors indicate 1.63-1.91% excess risk of dementia and translatability to spaceflight is unknown. The prevalence of long-term psychiatric disorders in astronauts is unknown. The prevalence of long-term or late-emerging cognitive conditions in crewmembers of long-duration missions outside of LEO is unknown. Assumes mitigation from crewmember selection, BHP operations, and family support services for reintegration. The impact of elevated radiation exposure is unknown.

- **LxC Drivers for Consequence:** Psychiatric disorders due to reintegration adjustment and/or late-emerging neurodegenerative disease are unknown. It is assumed that psychiatric disorders will be outpatient treatable to return to baseline and will have a moderate impact on quality of life and flight status. (evidence from a single case study only). Impacts of elevated radiation exposure are unknown. Cognitive disorder or neurodegenerative disease outcomes (possibly including permanent disability) are unknown. Emerging evidence from terrestrial epidemiological studies of multiple U.S. cohorts with occupational radiation exposure now show excess relative risk for Parkinson's Disease mortality.

- **Rationale for Risk Disposition:** Reintegration behavioral health support and cognitive monitoring is indicated given that the long duration and the physiological adaptation to 1G is likely to impact behavioral health and cognition during the return-to-flight period. Unknown excess likelihood or consequence of cognitive conditions or neurodegeneration on which to base disposition. Requires characterization of late-emerging changes or conditions (e.g., conditions that have an expected onset later in life).

- **DRM Specific Assumptions:** Communication delay is significant enough to impact real time communication with mission control (up to 20 mins one way); Significant crew independence from ground support.

- **DRM Specific Evidence/Level of Evidence:** 3-Weak

10. Overall Assessment of the Evidence

- ❖ Updated evidence from flight studies and ground studies conducted in conditions analogous to spaceflight strengthen the evidence base for LEO and lunar DRMs
  - Changes in cognitive performance are associated with spaceflight hazards and stressors: sleep restriction, sustained and acute altered gravity, nutrition.
  - Crewmembers experienced elevations in self-reported mood and affect.
  - Operational impacts of observed changes in behavioral health outcomes are unknown.

- Likelihood estimates have a high degree of uncertainty.

❖ No evidence exists of increased neurodegenerative disease in the limited datasets available for LEO DRMs
- Remains unknown for lunar and Mars DRM

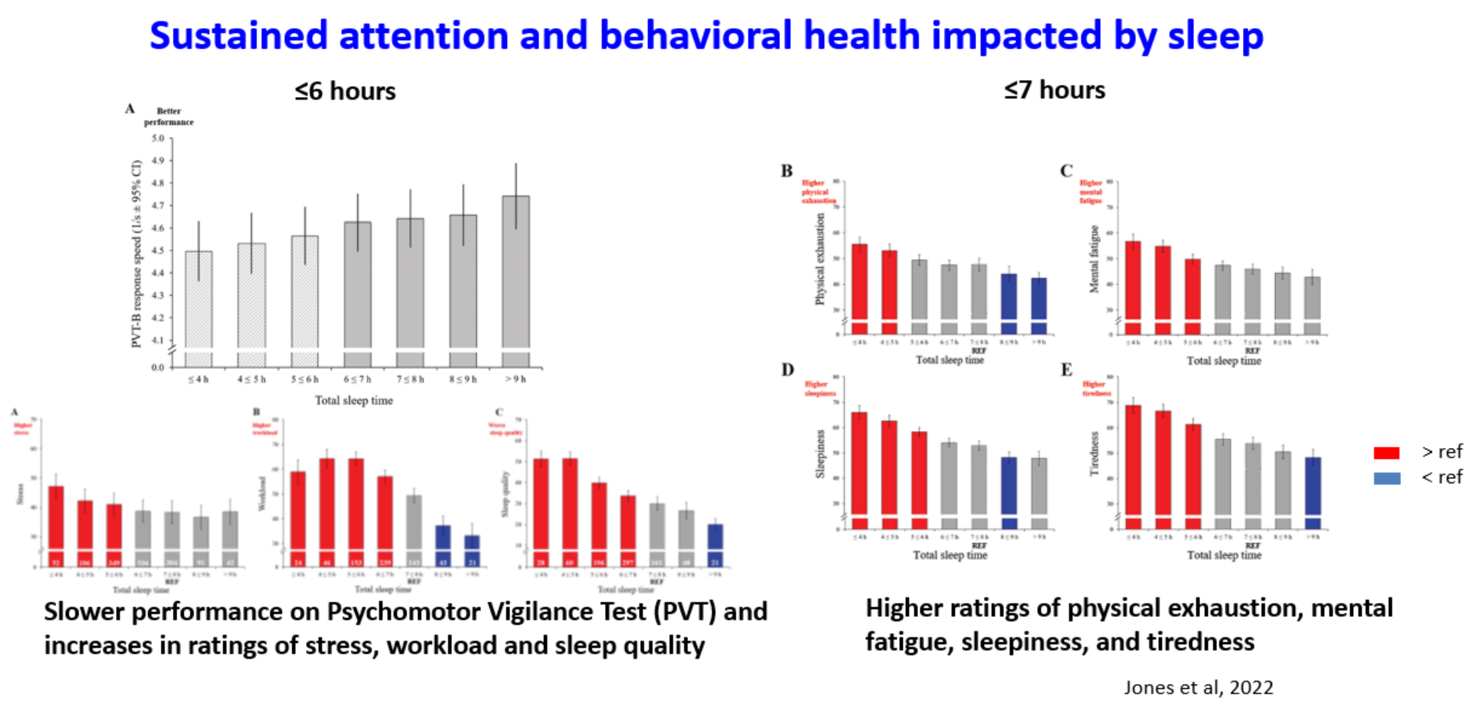
❖ New characterization gaps for risk drivers
- Expected lunar communication delays that lead to a LxC and color change for lunar orbital short duration
- High tempo EVAs
- Pain

❖ Impact of radiation exposure is unknown
- Animal studies indicate that radiation exposure equivalent to Lunar DRMs effect cognition.
- Elucidation on how animal studies may be used to inform human risk is required.

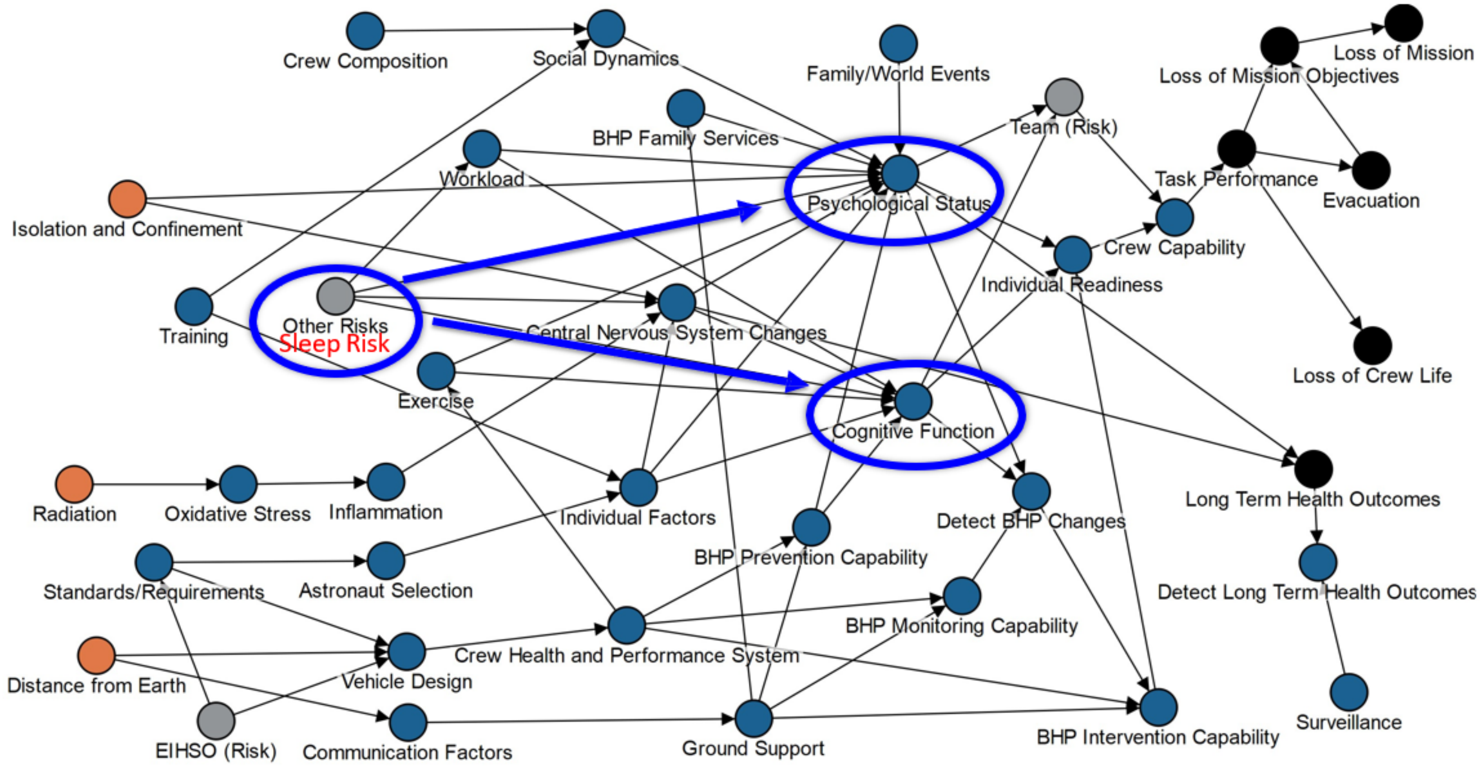
11. State of Knowledge

11.1 State of Knowledge – New Evidence (Rev D)

11.1.1 Spaceflight Evidence



DAG – Sleep impacts behavioral health



Inflight occurrences of subclinical signs and symptoms of depression and anxiety

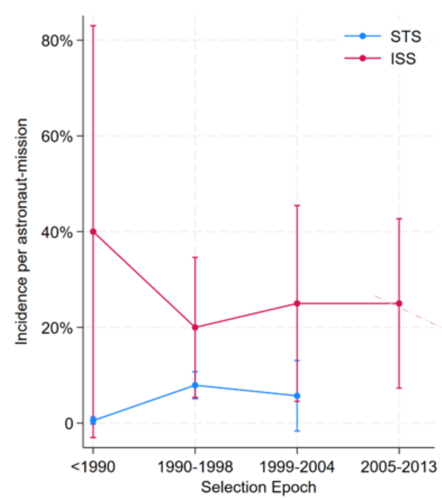
Inflight occurrences of subclinical signs and symptoms of depression and anxiety

- Total STS incidence: 0.039 (CI: .026 -.053) per astronaut-mission
- Total ISS (Exp. 1-68) incidence: 0.22 (CI: .13-.315) per astronaut-mission

STS and ISS incidence by Selection Epoch

Selection Epoch	STS	ISS
< 1990 classes	.005 (0- .012)	0.40 (CI: 0-.83)
1990-1998 classes	.079 (.051 - .11)	0.20 (CI: .053 - .35)
1999-2004 classes	.057 (0-.13)	0.25 (CI: .045 - .45)
2005-2013 classes	N/A	.25 (CI: .073-.423)
>2013 classes		None Observed

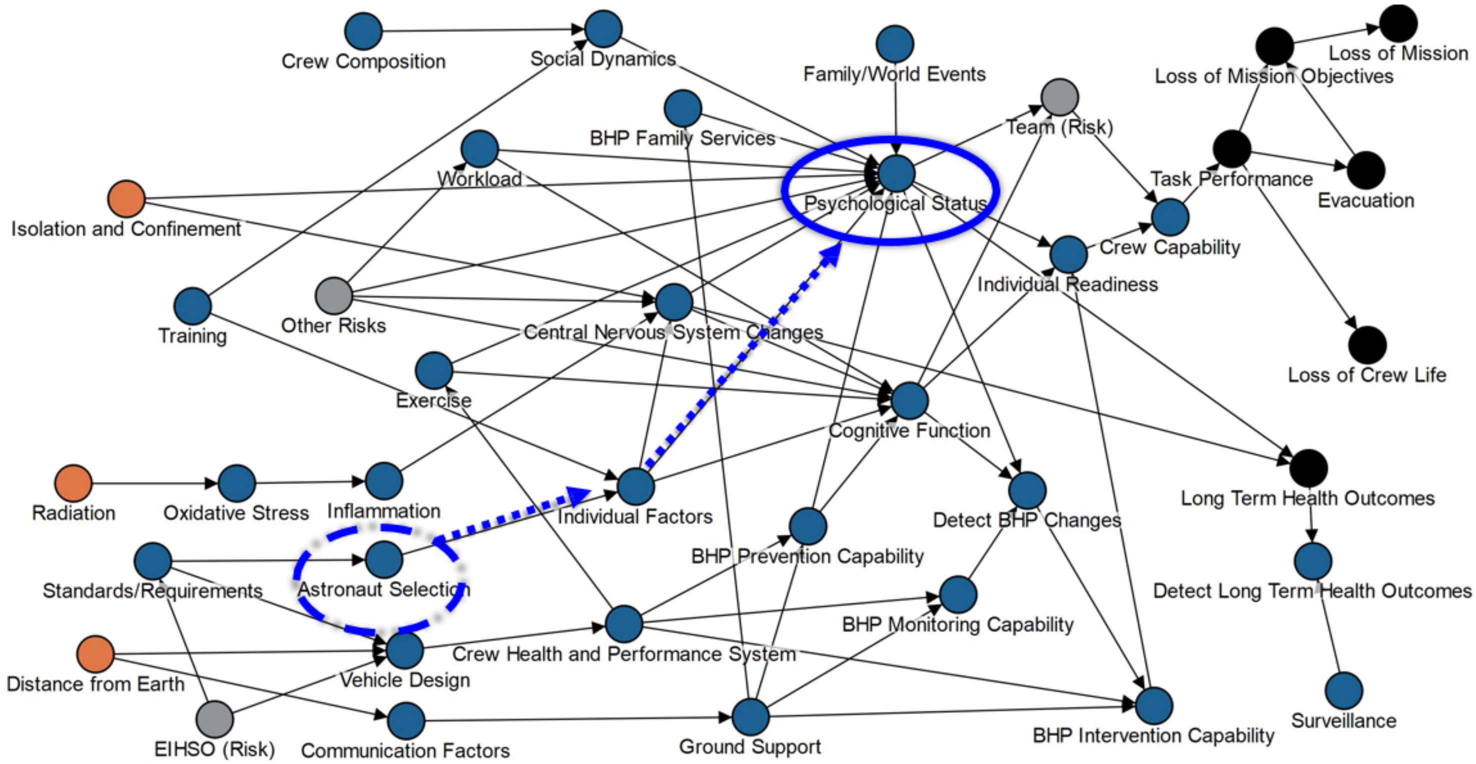
**preliminary trends; conclusions should be tempered by confounds such as increases in CM support over time across all risks (e.g., family support, exercise, etc.)



LSAH Data Request #27041; HLS Program

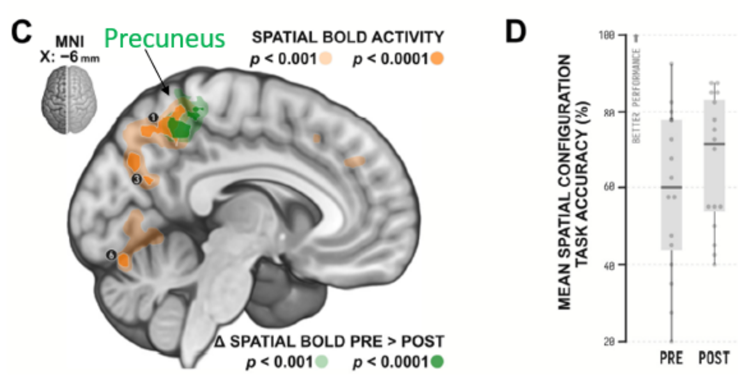
STS: Space Transportation System

DAG – Selection to psychological status



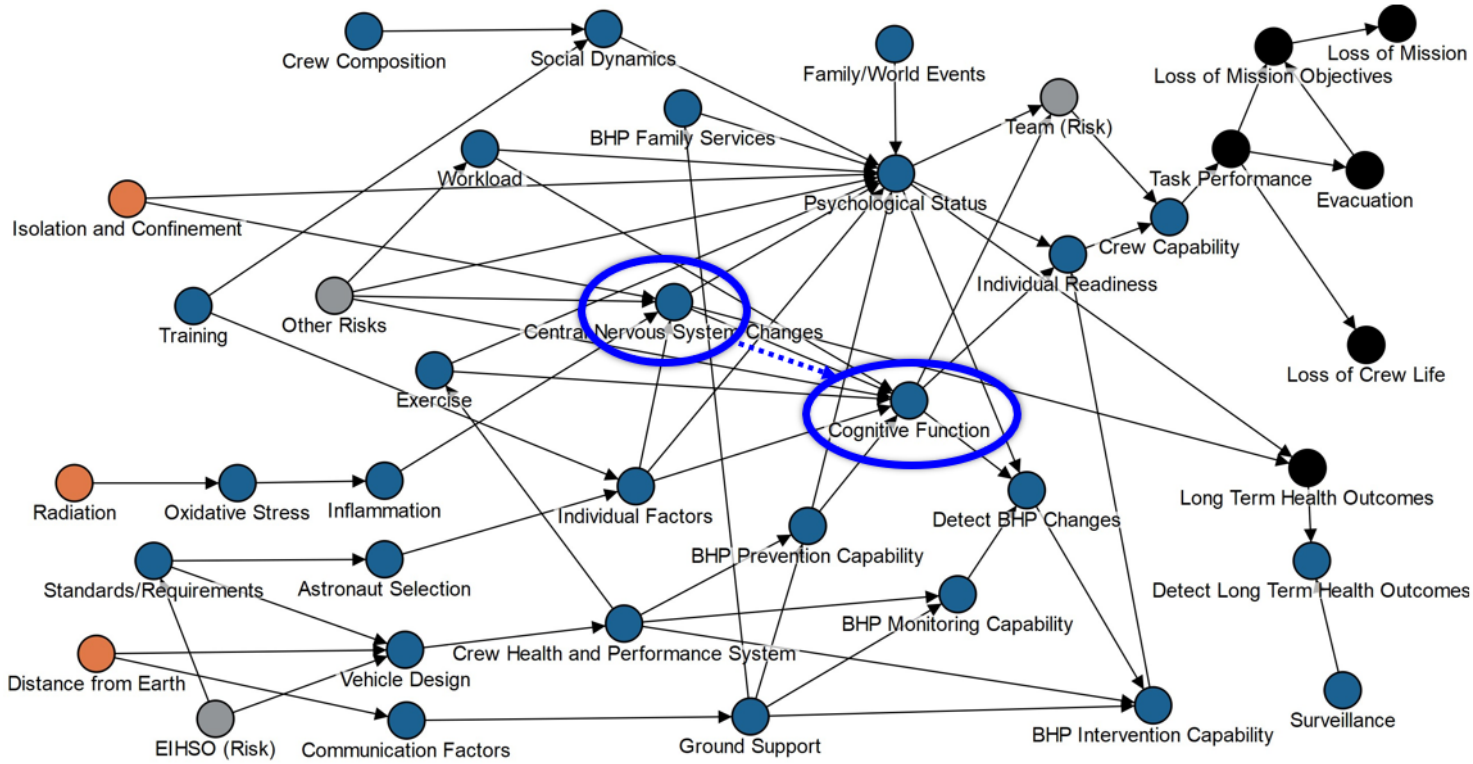
Cognitive impacts of observed changes in brain structure and function remains unknown

- Evidence of brain structural and functional changes pre to post spaceflight
  - White matter microstructure (Doroshin et al., 2022)
  - Functional connectivity (Jillings et al., 2023; Salazar et al., 2022)
  - Perivascular space (Barasino et al., 2022; Hupfeld et al, 2022)
  - Ventricular volume (Hupfeld et al., 2022; McGregor et al., 2022)
- May be in[illegible] flight duration and previous flight experience (Hupfeld et al., 2020; Hupfeld et al., 2022)
- Relationship with cognitive performance is uncertain
  - In part due to lack of data
  - Observed changes may be adaptive or compensatory (Burles et al., 2023; Salazar et al., 2022)

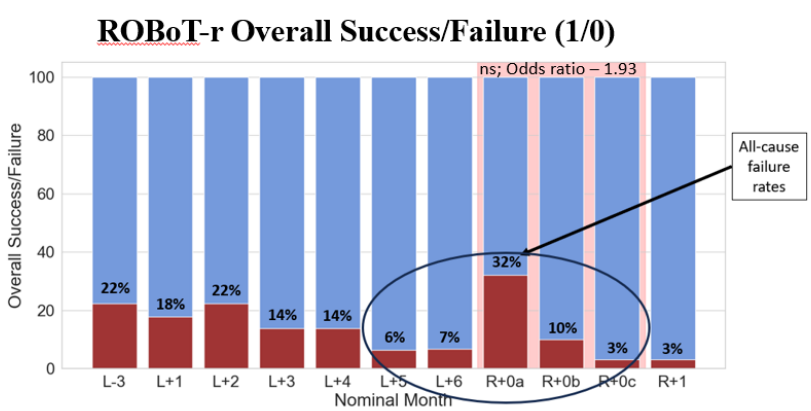


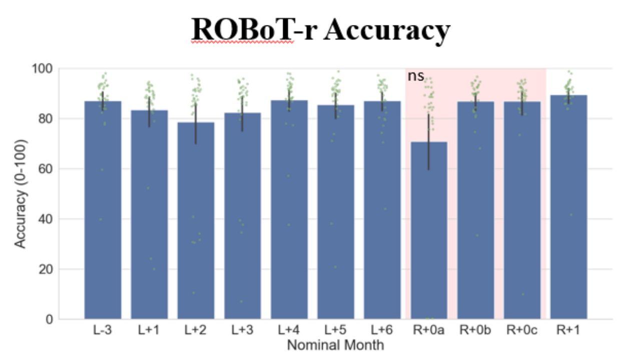
Burles et al, 2023

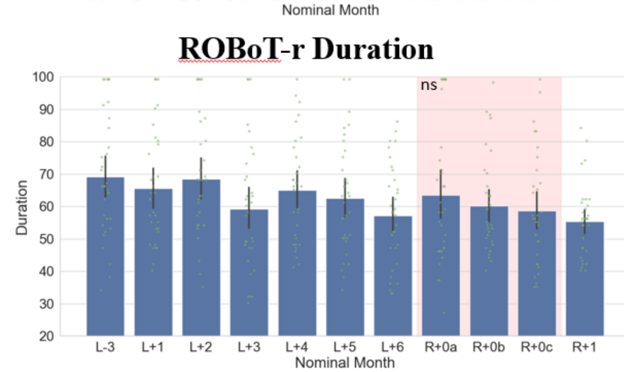
DAG – Central nervous system changes may impact cognitive functions



Operational performance at-risk immediately post landing



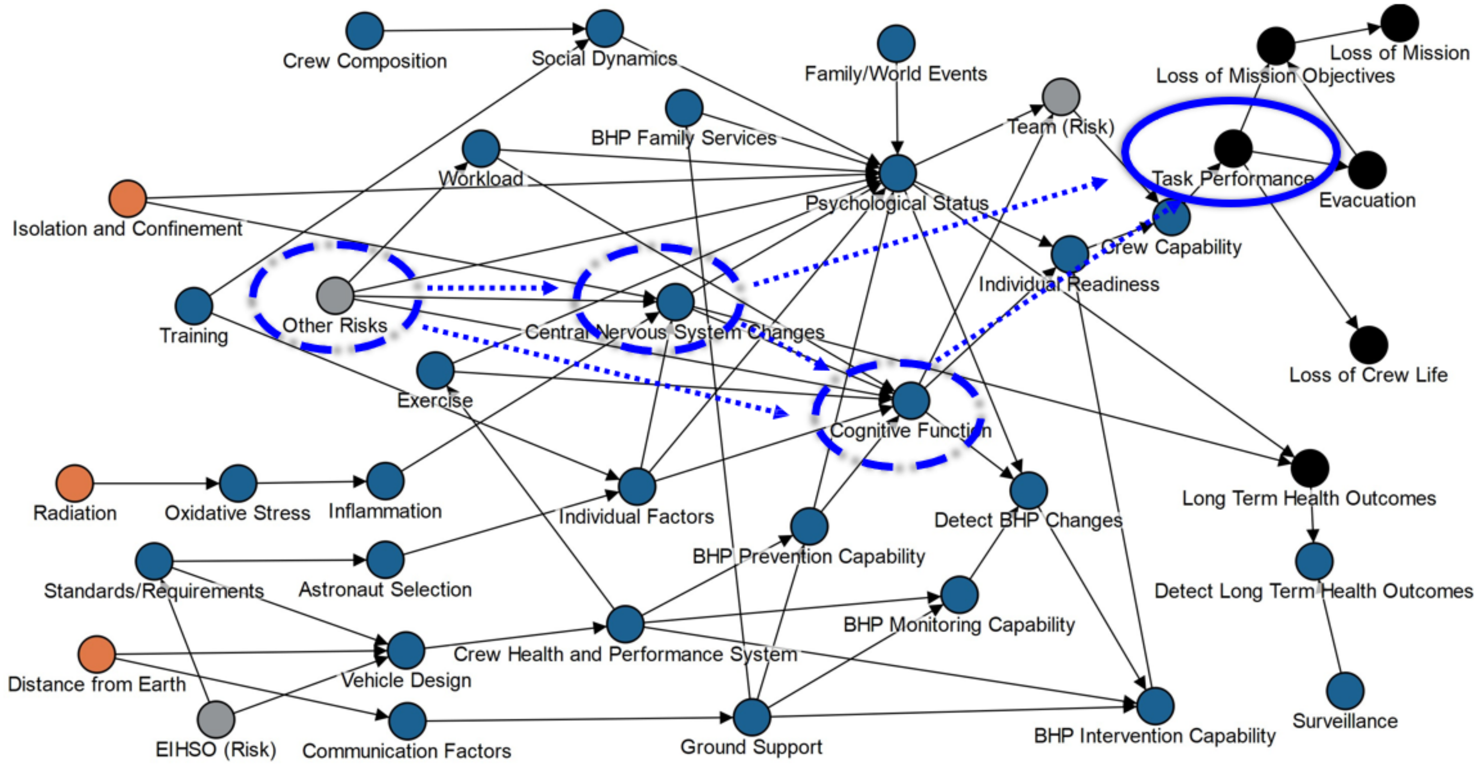




Strangman & Ivkovic 2023, HRP Investigator's Workshop

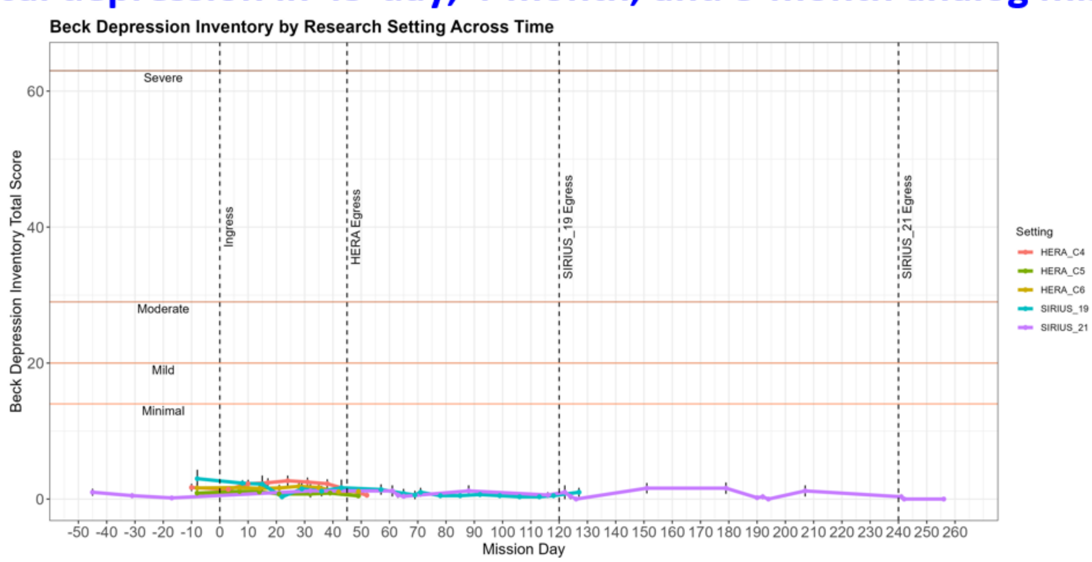
ROBoT-R Robotic On-Board Trainer for Research is used for astronaut training on the Canadarm2 track-and-capture activities.

DAG – Complex pathways can lead to performance impacts



11.1.2 Behavioral Changes: Evidence from Studies in Analogs of Spaceflight

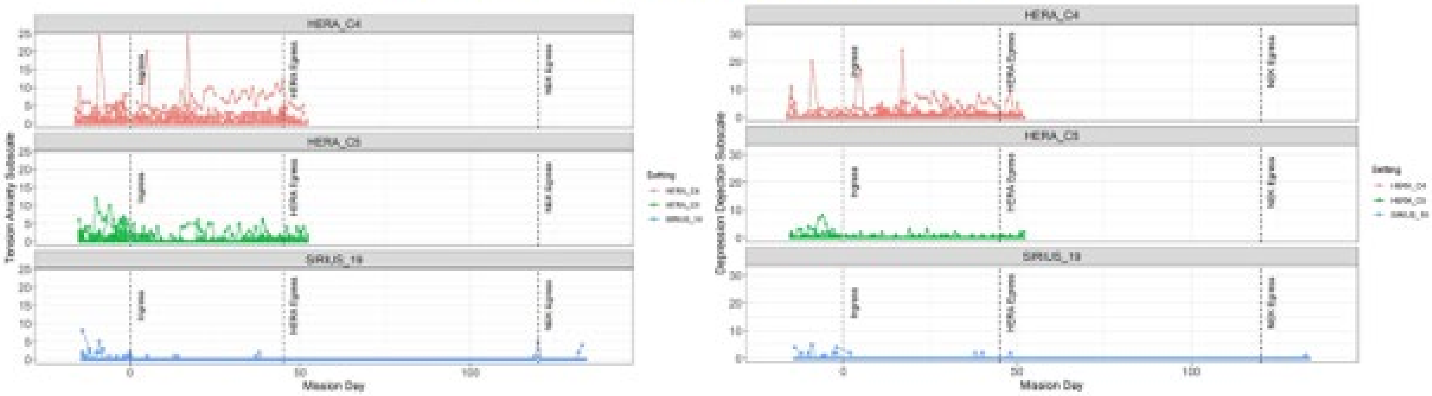
No clinical depression in 45-day, 4-month, and 8-month analog missions



BHP Lab Harmonization HERA C4/C5, SIRIUS19, ISS; BHP Lab HFBP-EM in HERA C6 & SIRIUS 21 (PI: Bell)

BHP	Behavioral Health and Performance
HERA	Human Exploration Research Analog
HFBP - EM	Human Factors and Behavioral Performance – Exploration Measures
SIRIUS	Scientific International Research In a Unique terrestrial Station. This refers to a series of spaceflight simulation missions conducted in Russia

Changes in affect observed in the contend of mission stressors In some but not all crewmembers

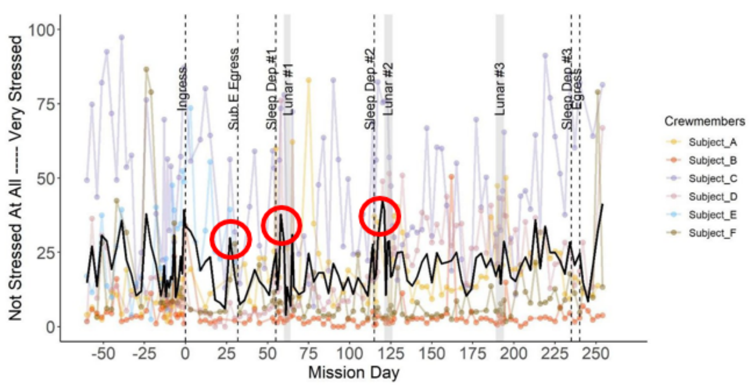


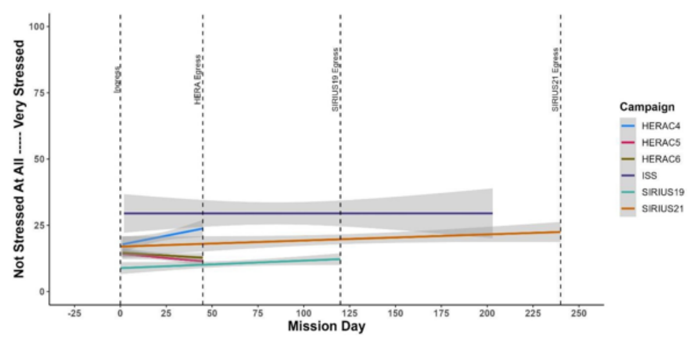
Profile of Mood States

BHP Lab Harmonization HERA C4/C5, SIRIUS19

Changes in stress observed in the context of mission stressors

NEK SIRIUS-21



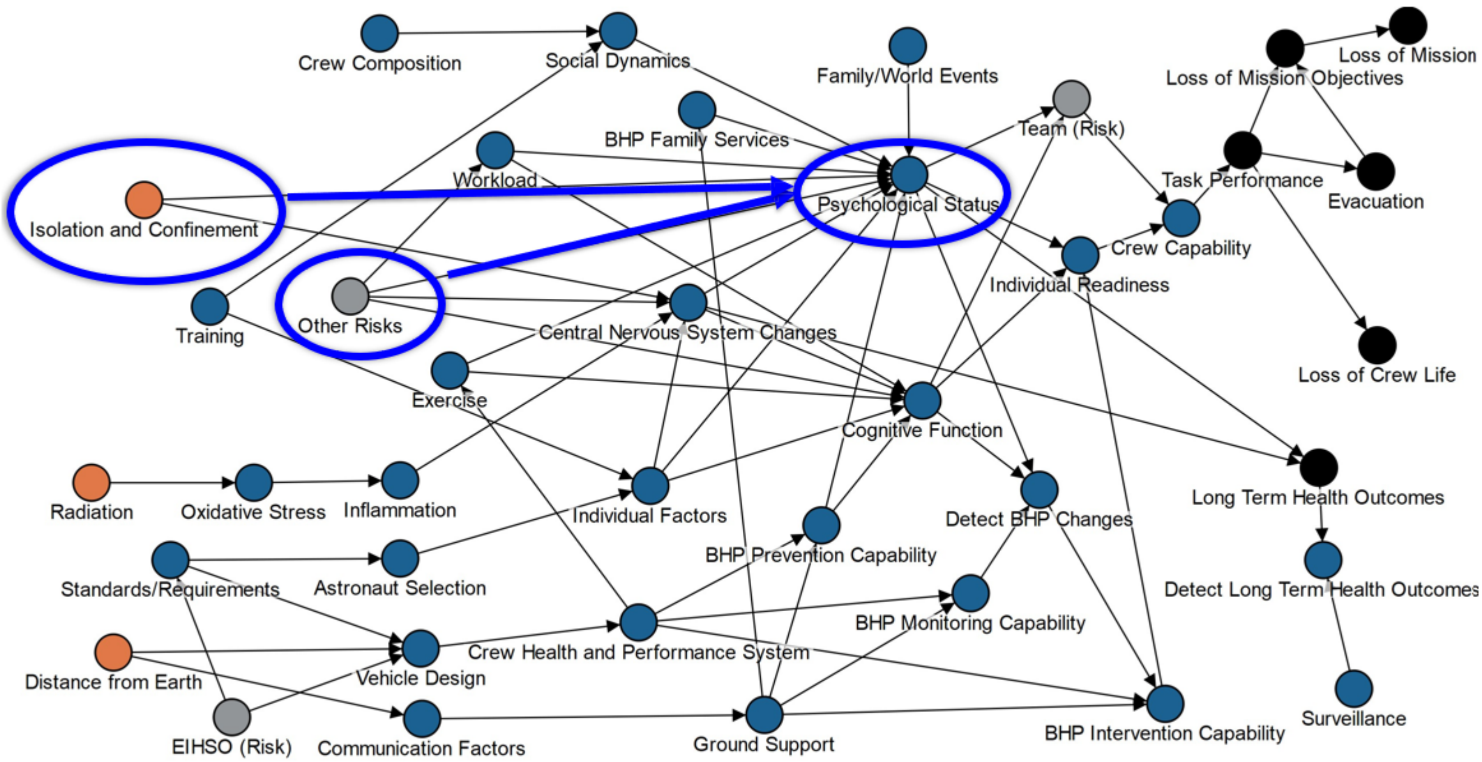


HERA C4 slope equivalent to <u>long duration</u> missions and not short duration (*p's* .007 to .03)

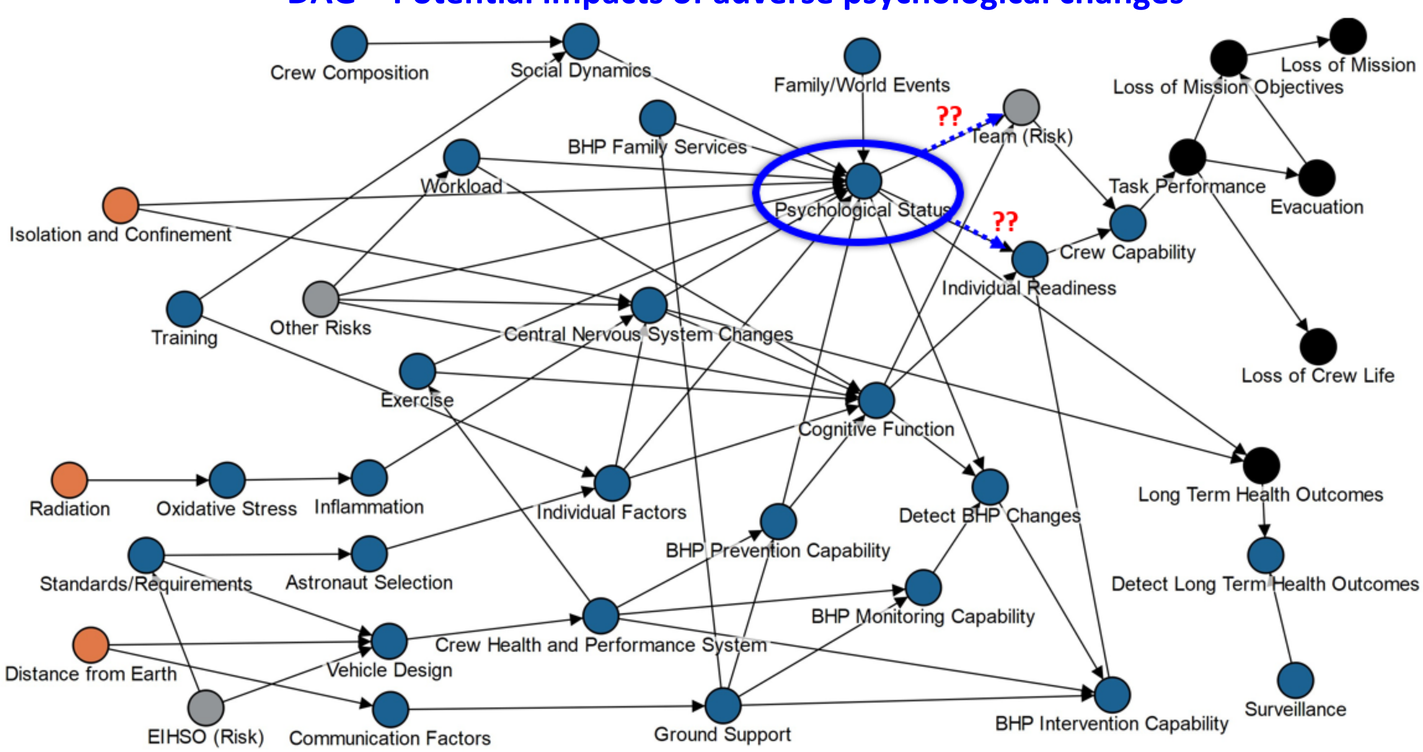
BHP Lab HFBP-EM in SIRIUS21 (PI: Bell)

Dev et al., 2024; HRP Investigator's Workshop

DAG – Exposure to spaceflight hazards and other human systems risks could lead to changes in psychological status



DAG – Potential impacts of adverse psychological changes



Positive psychology, internal physiological manifestations of negative affect, and selection standards

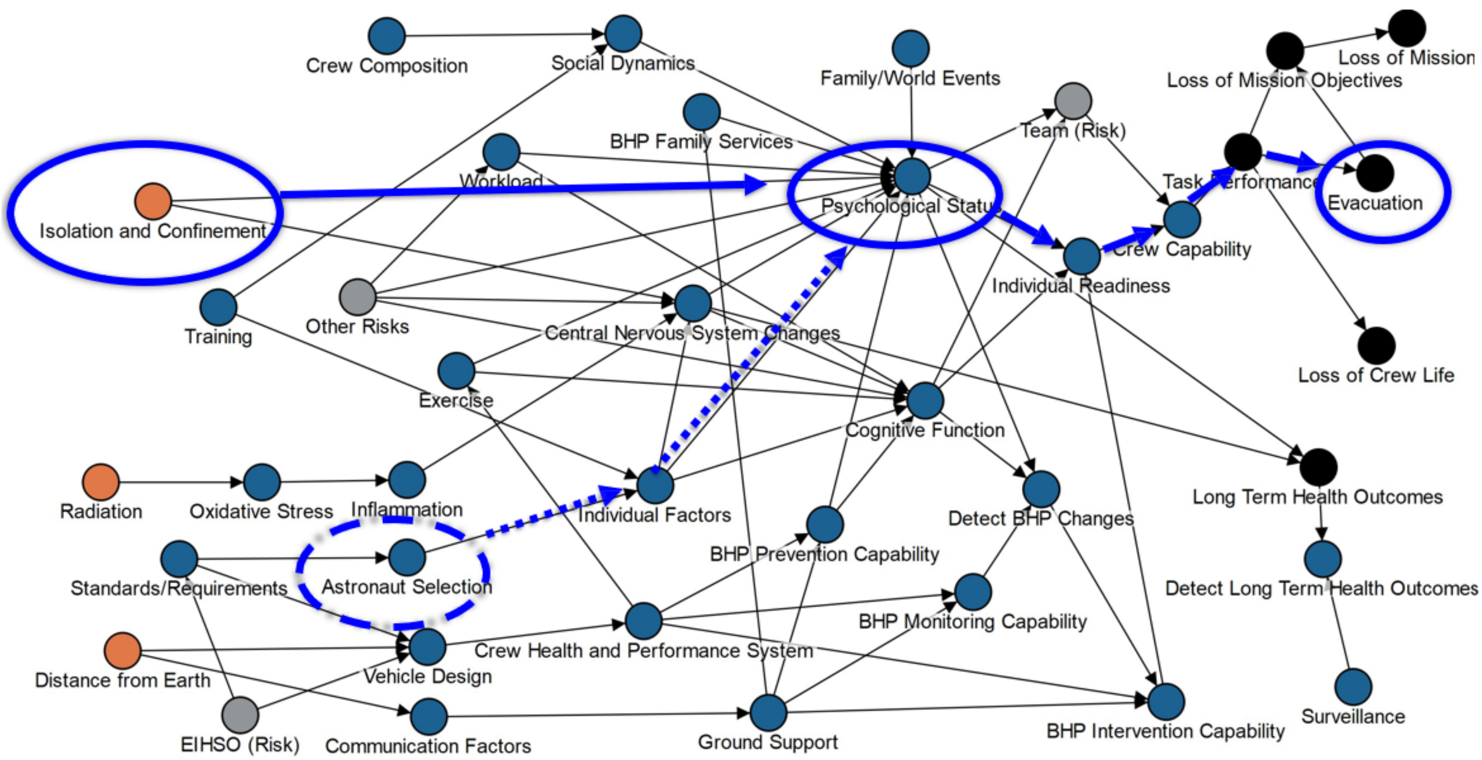
McMurdo (n = 88) and South Pole (n = 22) Winter-Over Expeditions

- Full sample: Decline in positive affect and increase somatic anxiety in both McMurdo and South Pole Antarctic stations (Alfano et al., 2021)
- No psychological screening during selection of McMurdo Station crew
  - Higher psychological distress at baseline that persists
  - 2 evacuations due to psychiatric emergencies in McMurdo station
    - Earlier changes in positive affect and cognitive anxiety (i.e., thought patterns) (Kim et al., 2021)

See Figures 1-3 in Alfano et al., 2021 and Figure 4 in Kim et al., 2023

Winter-Over Expeditions to the Antarctic provide an analog of the isolation and confinement in a hostile environment and enable studies of the potential effect of these feature of long duration spaceflight missions.

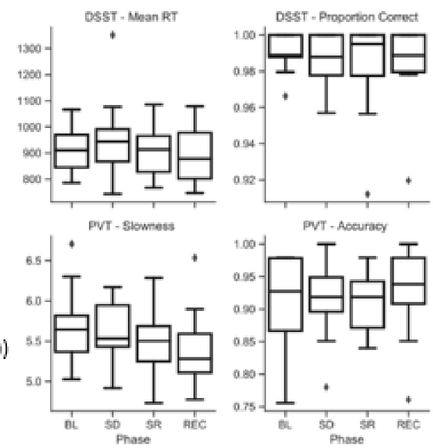
DAG – Selection may influence effects of isolation and confinement on psychological status



11.1

3. Cognitive Changes, Analog Evidence

- **Sleep restriction** (Glaros et al., 2021; Nasrini et al., 2020)
  - Decrements in sustained attention and processing speed
- **60-day head down bed rest** (Basner et al., 2021a, 2021b)
  - Initial slowing across all cognitive tasks
  - Emotion recognition continued to decline (negative valence)
  - No change in +C02 condition
- **Parabolic flight** (Stahn et al., 2020; Friedl-Werner et al., 2021))
  - Decrements in spatial cognition (0g, 1.8g) and attention (0g)
- **Enhanced spaceflight diet** (Douglas et al., 2023)
  - Associated with improved PVT performance relative to standard ISS diet condition in HERA



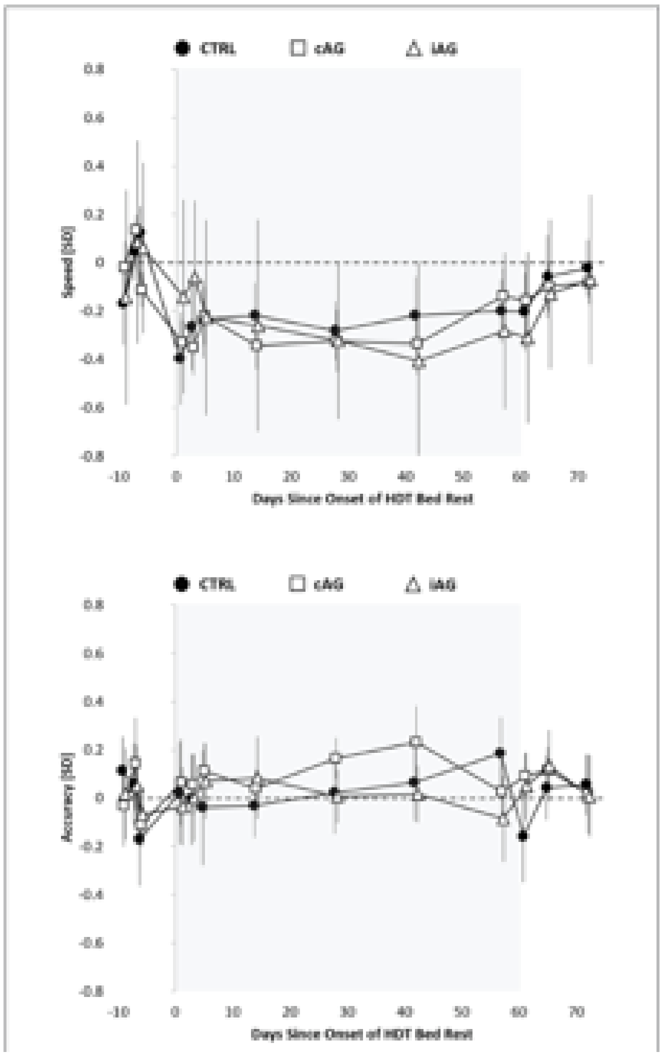
Cognitive Performance During Confinement and Sleep Restriction in NASA's Human Exploration Research Analog (HERA)

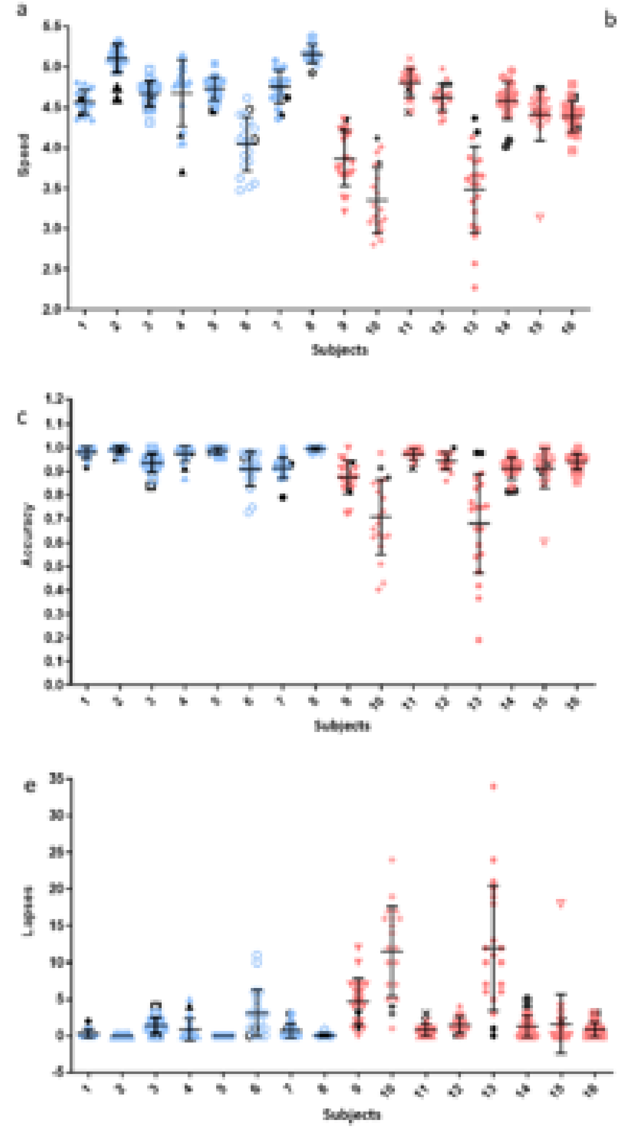
Jad Nasrini[1], Emanuel Hermosillo[1], David F. Dinges[1], Tyler M. Moore[2], Ruben C. Gur[2] and Mathias Basner[1]*

Observed changes in cognitive performance in the context of spaceflight stressors

Continuous and Intermittent Artificial Gravity as a Countermeasure to the Cognitive Effects of 60 Days of Head-Down Tilt Bed Rest

Mathias Basner[1*], David F. Dinges[1], Kia Howard[1], Tyler M. Moore[1], Ruben C. Gur[1], Christian Mühl[2] and Alexander C. Stahl[1]

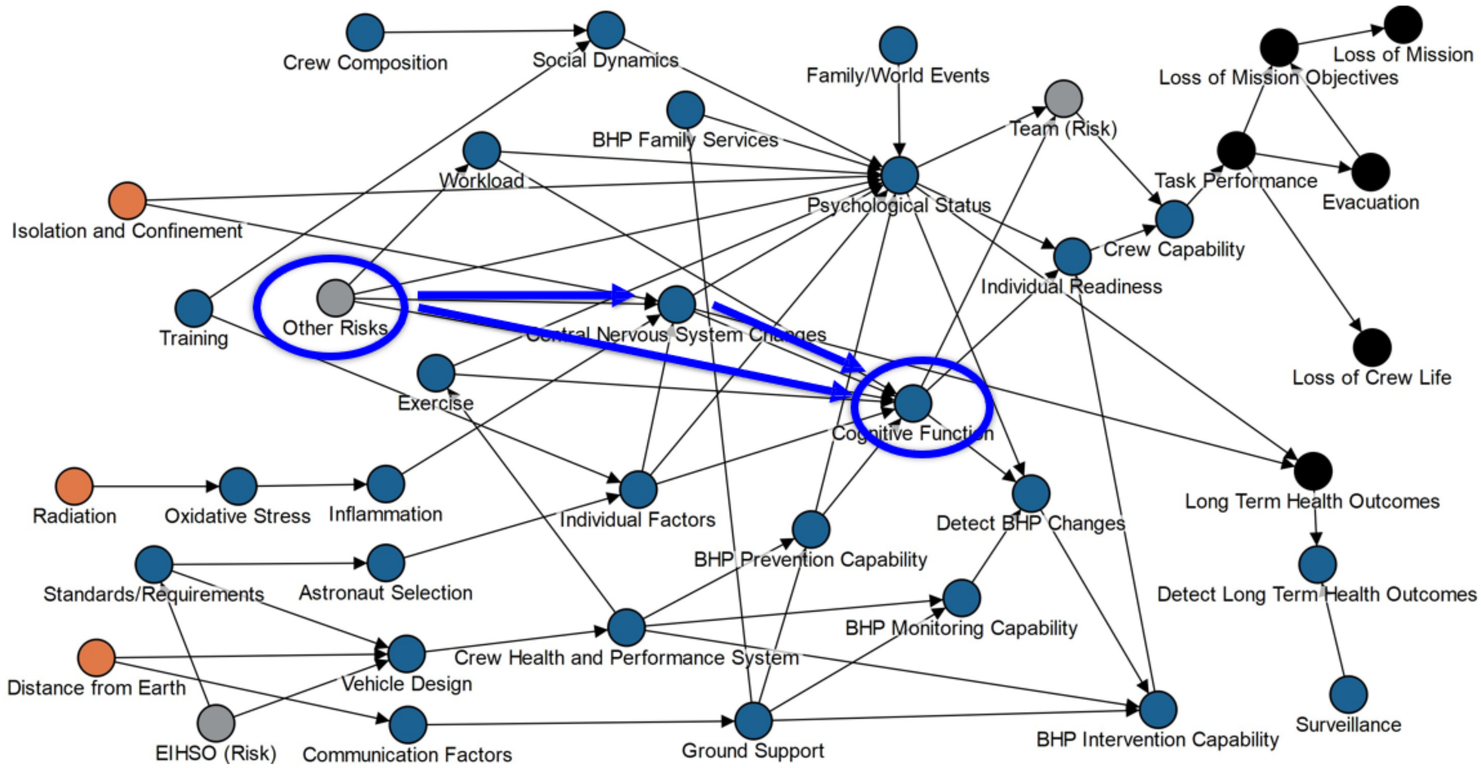




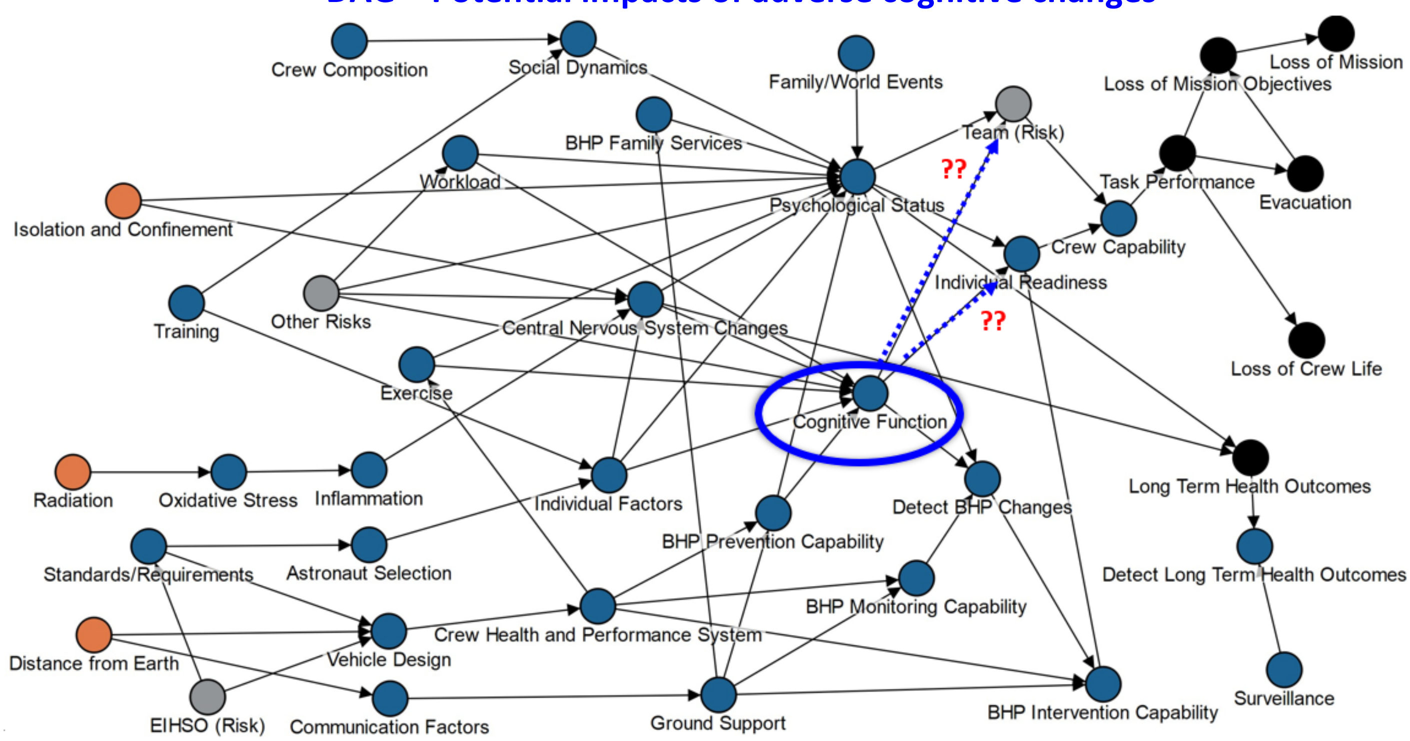
Impact of diet on human nutrition, immune response, gut microbiome and cognition in an isolated and confined mission environment

Grace L. Douglas[1,✉], Diane DeKerlegand[2], Holly Dlouhy[3], Nathan Dumont-Leblond[4], Eden Fields[3], Martina Heer[5], Stephanie Krieger[3], Satish Mehta[2], Bridgette V. Rooney[6], Manolito G. Torralba[7], Sara E. Whiting[3], Brian Crucian[1,8], Hernan Lorenzi[7,8], Scott M. Smith[1,8], Millennia Young[1,8] & Sara R. Zwart[8,9]

DAG – Other human systems risks may impact the central nervous system and cognitive functions



DAG – Potential impacts of adverse cognitive changes



Design Reference Missions (DRMs)

DRM Categories	Mission Type and Duration	Gravity Environment	Radiation Environment	Vehicle/Habitat Design	Distance from Earth		EVA
					Evacuation	Communication	Frequency
Low Earth Orbit	Short (<30 days)	Microgravity	LEO-Van Allen (<5-15 mGy)	Mid-sized volume, resupply	1 day or less	Real time	1-4 EVAs
	Long (30 days-1 year)	Microgravity	LEO-Van Allen (5-150 mGy)	Mid-large optimized volume, resupply	1 day or less	Real time	1-10 EVAs
Lunar Orbital	Short (<30 days)	Microgravity	Deep Space-Van Allen (15-20 mGy)	Small volume, self contained, resupply	3 – 11 days	Real time	Contingency EVA only or very few EVA
	Long (30 days-1 year)	Microgravity	Deep Space (175-220 mGy)	Mid-sized volume, self contained, limited resupply	3 – 11 days	Real time	Contingency EVA only or very few EVA
Lunar Orbital + Surface	Short (<30 days)	Microgravity & 1/6g	Deep Space-Van Allen (15-20 mGy)	Small volume, resupply	3 – 11 days	Real time	5 EVAs, some back to back
	Long (30 days-1 year)	Microgravity & 1/6g	Deep Space (100-120 mGy)	Mid-large sized optimized volume, limited resupply	3 – 11 days	Real time	3-4 EVA per week, 20-24 EVA hrs. per week
Mars	Preparatory (<1year)	Microgravity	Deep Space (175-220 mGy)	Midsized optimal volume, limited resupply, closed loop environment	Days – weeks	Controlled - Delayed	Contingency EVA only or very few EVA
	Mars Planetary* (730-1224 days)	Microgravity & 3/8g	Deep Space – Planetary (300-450 mGy)	Midsized optimal volume, no resupply, closed loop environment	Mission duration	No real time	2 crew x 8-hour EVA x 20 EVA days

11.1.4 Behavioral and Cognitive Conditions: Animal Studies

Rodent models indicate concern for radiation exposure at mission relevant doses

BMed Outcome	Post Irradiation Finding	Nearest term DRM
Anxiety-like Behaviors	↑ at 30 mGy (Klein et al., 2021) ↑ 70 mGy (Sorokina et al., 2021) ↑ 50 & 100 mGy, but not 200 mGy. Equivalent to sham irradiation at 12 and 18 months (Garrett et al., 2022).	**Long duration LEO & Lunar**
Depression-like Behaviors	↑ 50 mGy but not 25 or 200 mGY (Raber et al., 2019)	**Long duration LEO & Lunar**
Spatial Learning and Working Memory	↓ at 30 mGy but not 5 mGy (Klein et al., 2021) ↓ 10, 50, and 100 mGy followed by 6–20-month period of improved performance (Miry et al., 2021) = at 75 mGy (Simmons et al., 2022) ↓ at 50 mGy in males only (Garrett et al., 2022)	**Long duration LEO & Lunar**
Set Shifting & Executive Functions	↓ as low as 1 mGy (Britten et al., 2020) ↓ at 100 mGy in high performers when cog load increased (Britten et al., 2022) ↓ at 50 mGy in high performers after sleep restriction (Britten et al., 2020)	**Short duration LEO**

Cognitive resilience to radiation undermined by additional stressors: sleep fragmentation and increased task demands

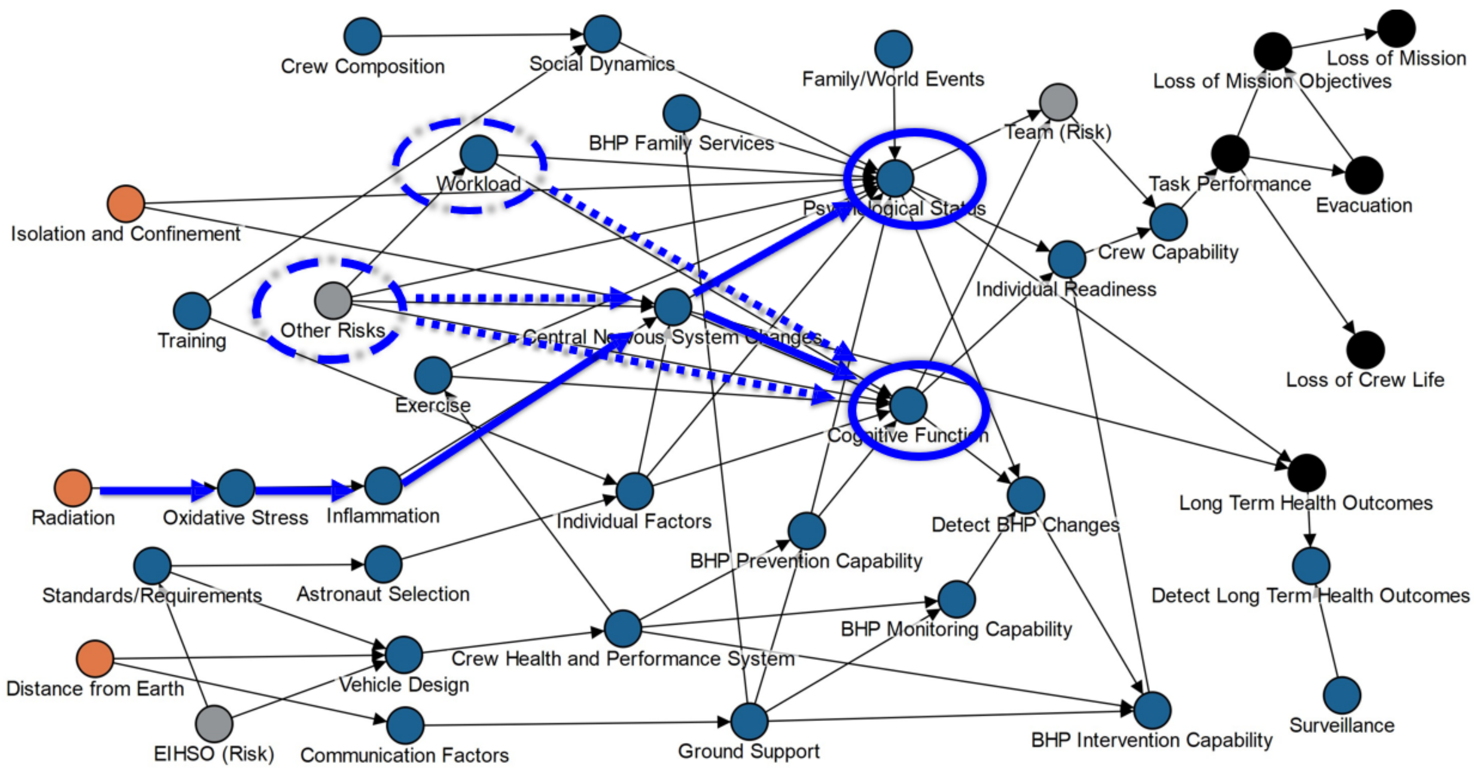
- Decrement in attentional set shifting in irradiated mice after sleep fragmentation but not in irradiated mice after normal sleep (Britten et al., 2020)

50 mGy: long duration LEO, Lunar, and Lunar Orbital; Mars
Britten et al, 2021

- Decrement in performance when causal learning and anterograde interference (rule change) demands are added to task (Britten et al., 2022) *

100 mGy: long duration LEO, Lunar, and Lunar Orbital; Mars
Britten et al., 2022

DAG – Combined impacts of radiation and other spaceflight stressors on psychological status and cognition



11.1.5 . Long-term health outcomes: epidemiology data

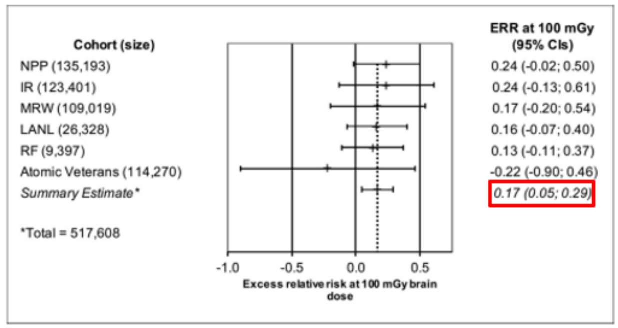
New data from Million Persons Study indicating excess relative risk of Parkinson's Disease mortality following occupational radiation exposure.

DRM Categories	Mission Type and Duration	Gravity Environment	Radiation Environment
Low Earth Orbit	Short (<30 days)	Microgravity	LEO-Van Allen (<5-15 mGy)
	Long (30 days-1 year)	Microgravity	LEO-Van Allen (5-150 mGy)
Lunar Orbital	Short (<30 days)	Microgravity	Deep Space-Van Allen (15-20 mGy)
	Long (30 days-1 year)	Microgravity	Deep Space (175-220 mGy)
Lunar Orbital + Surface	Short (<30 days)	Microgravity & 1/6g	Deep Space-Van Allen (15-20 mGy)
	Long (30 days-1 year)	Microgravity & 1/6g	Deep Space (100-120 mGy)
Mars	Preparatory (<1year)	Microgravity	Deep Space (175-220 mGy)
	Mars Planetary* (730-1224 days)	Microgravity & 3/8g	Deep Space – Planetary (300-450 mGy)

Million Person Study

Table 2
Estimated mean (mGy), median (mGy), and other brain dose statistics for 6 cohorts within the Million Person Study.

MPS cohort	Mean (mGy)	Median (mGy)	STD (mGy)	Percent ≥ 100 mGy	Maximum (mGy)
Low-LET					
Nuclear Power Plant Workers (NPP)	33.2	17.2	45.5	6.58	834
Industrial Radiography Workers (IR)	11.9	1.1	31.2	2.10	977
Medical Radiation Workers (MRW)	18.9	9.8	27.7	1.15	1080
Atomic Veterans (A-Vets)	6.9	2.6	17.7	0.05	2654
High-LET and Low-LET					
Los Alamos National Laboratory Workers (LANL)	11.6	0.8	39.4	1.78	760
Rocky Flats Workers (RF)	47.6	13.2	89.0	11.7	831



Dauer et al., 2023

ERR: excess relative risk; LET; Linear energy transfer

11.1.6 Gaps in Knowledge: Lunar Communication Delays

Impact of lunar-like comm delays on BHlth outcomes is unknown

- Impacts to PPC and private family conferences (PFC)
  - Reduced effectiveness of current countermeasures for isolation and confinement
  - Greater crew time
- Frustration or performance inefficiency related to disrupted conversations with ground

Lunar Orbital Short

4x2	Requires Characterization

HRP Research – Selected Communication Delayed Studies	0s	~10s	30s	~1m	3m	5m	20m
Individual Well-being							
Stress, frustration increased (Kintz, Palinkas et al., 2016, **ISS**; Bell et al., 2022, **harmon**.); adverse behavioral symptoms increased (adverse mood, confusion) (Basner et al., 2014, **Mars 500**; Roma, n.d., **HI-SEAS**)	x		x	x	x	x	x
Individual Performance							
Cognitive load increased (Fischer, Mosier, 2017, **lab**, **astros**); coping behaviors decreased, Van Wijk, 2018, **subs**				x		x	x
HSIA overlap; errors, time to complete task increased; hi-fi task performance decreased (Stankovic, Duda, et al., 2022, **HERA**, Draper sim)	x		x	x	x	x	
Family Connectedness							
Connectedness, satisfaction with relationships declined (Goemaere et al., 2019, **HI-SEAS**; Wu **VR**, **HI-SEAS**)							x

*0s includes ICE analogs & long-duration missions; *Bell 2022, harmonization, HERA C4/5, SIRIUS-19, ISS; *HERA: 0s,30s,1m,3m,5m; SIRIUS/NEK: 5m, HI-SEAS: 20m, NEEMO: 0s,50s,5m, 20m, ISS/Palinkas: 0s, 50s

BHlth	Behavioral health
Comm	Communication
Hi-SEAS	Hawaii Space Exploration Analog and Simulation
Mars 500	The MARS-500 was a psychosocial isolation experiment conducted between 2007 and 2011 by Russia, the European Space Agency, and China

11.1.7 Gaps in Knowledge: Exploration EVA

Impact of radiation exposure on BHlth outcomes is unknown

BENEFIT: Informative for possible mechanistic pathways → CM targets & POLs

1. **Oxidative stress**
2. **Neuroinflammation and immune response**
3. Protein expression and epigenetic regulation
4. Neuronal structure, communication, and development
5. Hippocampal neurogenesis
6. Combined stressors on behavioral health outcomes

CHALLENGE: Limited for *human* consequence characterization (translatability)

1. Evidence from animal models is highly variable:
   - Inconsistent behavioral methodologies, timelines, animal samples, dose rates
   - Dose responses are inconsistent and/or non-linear
2. Scaling methods have not been applied for translation

Identify appropriate studies → Underlying mechanisms & inflight comparisons → Scaling & translation

Inform level of evidence | **Validate BMed DAG Inform CM development** | **POLS**

POLS: Performance optimal limits

Impact of increased physical and cognitive load during future exploration EVAs on BHlth outcomes is unknown

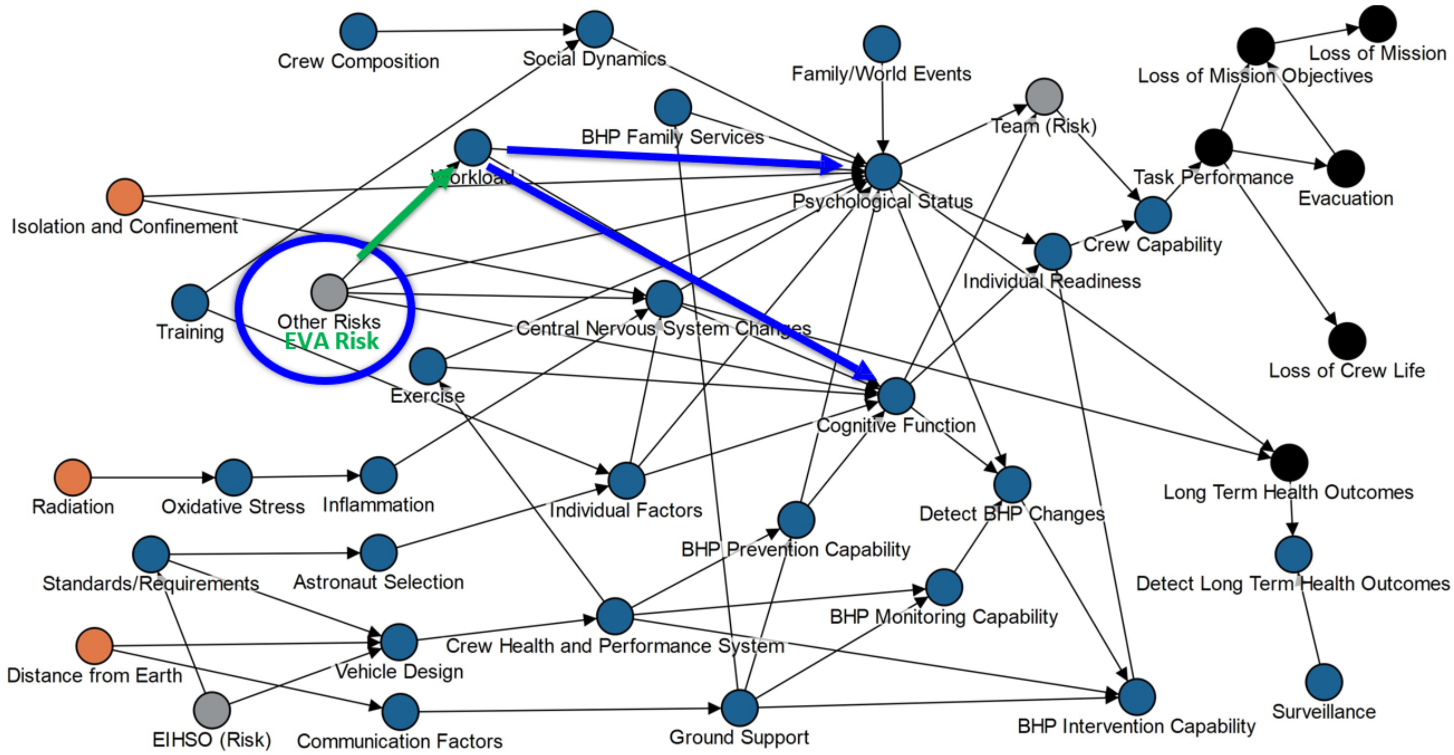
BLUF: Future Exploration EVA will be quite different from ISS and Shuttle EVA, and even previous Apollo EVAs!

Parameter	Current EVA	Exploration EVA
Tempo	8hr EVA/ ~ 2 months	8hr EVA every other day (24hr/crew/week)
Environment	Engineered Completely Characterized Microgravity Uncontaminated	Natural & Engineered **Incomplete Characterization** Partial Gravity Dust
Tasks	Construction/Maintenance	**Science** Construction/Maintenance
Skills / Training	Specific Skills/task-based NBL practice many hours	Generic Skills **Tool-based**
Mission	Specific tasks, practiced and planned	**Broadly scoped timelines** **Real-time adjustments**
Operational Support	MCC-centric Extensive personnel support	**Crew-centric** **Delayed ground support**

Norcross; EVA Risk Presentation to HSRB, Aug 2023

BLUF – Bottom line up front

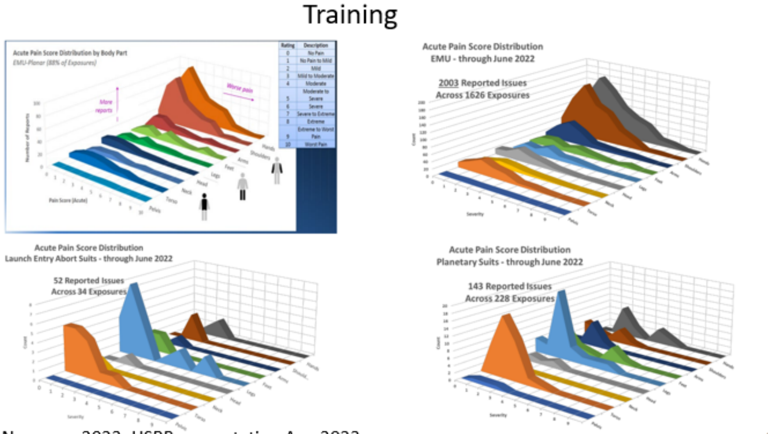
DAG – Potential Effects of EVAs on psychological status and cognitive function



11.1.8 Gaps in Knowledge: Pain

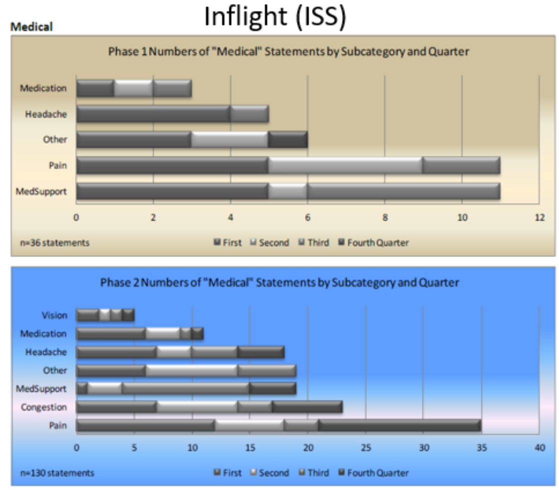
Impact of acute and chronic pain on BHlth outcomes is unknown

Training



Norcross, 2023; HSRB presentation Aug 2023

Inflight (ISS)



Stuster, 2016

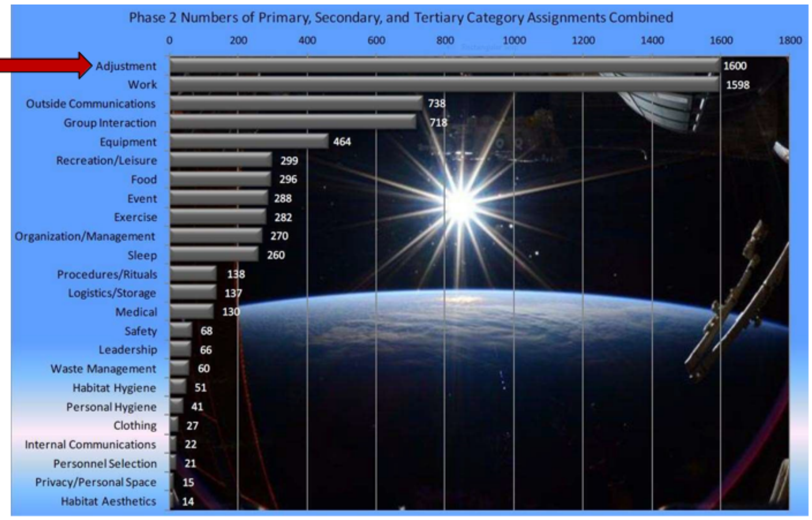
Well established (non spaceflight) literature in the bidirectional relationships between pain and cognitive/emotional outcomes

(Bushnell et al., 2013; Berryman et al., 2014; Bevers et al., 2016; Eccleston & Crombez, 1999;)

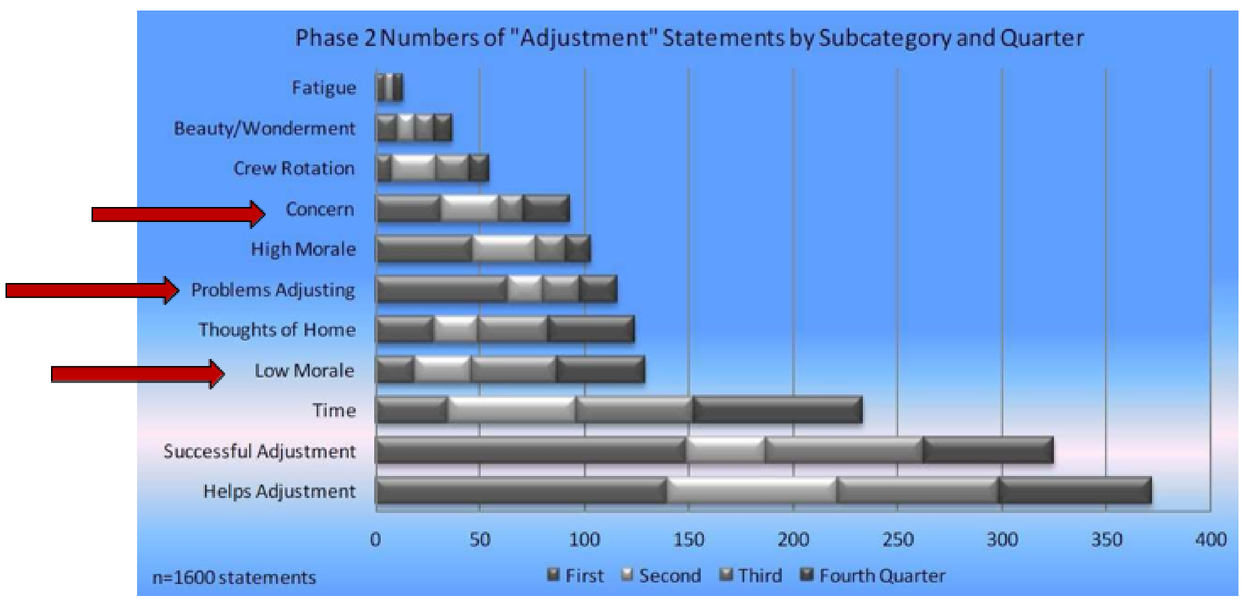
11.2 State of Knowledge – Existing Evidence Base (Rev C)
11.2.1 Behavioral Conditions, Spaceflight

Behavioral Conditions: Spaceflight (Existing Evidence Base)

- These data from the Astronaut Journals Study were collected when ISS was fully constructed with typically 6-person crews.
- Personal adjustment topics were the most frequently discussed compared to being the 3rd most common topic in the earlier construction era.
- This shift is interpreted an increasing awareness of well-being and behavioral health factors inflight, especially as mission durations increase.



Source: Stuster, 2016



Source: Stuster, 2016

- A majority of adjustment statements were positive or noted things that have been helpful to life on ISS.
- Some adverse behavioral conditions were described, despite ISS having the most comprehensive suite of behavioral health countermeasures and habitability standards and volume.

State of Knowledge – Behavioral Conditions: Spaceflight

Comments from crewmembers on ISS missions

“It's like a continuous battle against time up here... There is a lot of stress with that. It's just a continuous time battle.”

“Little details that seem so trivial bite me all the time here. I hope it will go away soon.

I need to pay better attention to the lessons that I must keep relearning.”

“I think I do need to get out of here. Living in close quarters with people over a long period of time, definitely even things that normally wouldn't bother you much at all can bother you after a while... that can drive anybody crazy.”

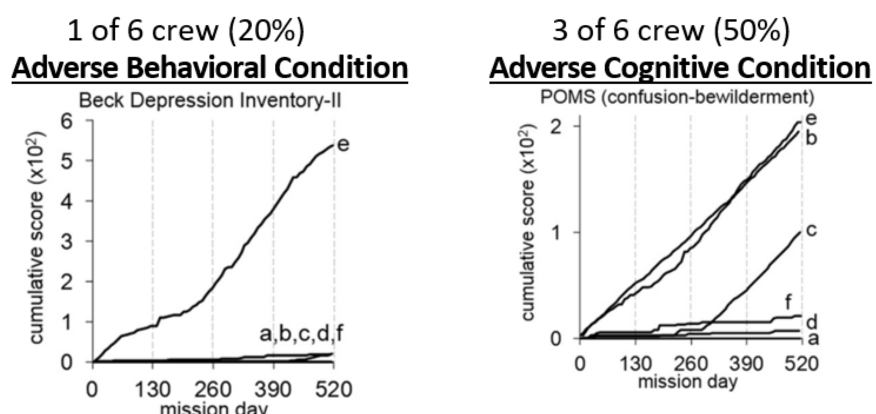
“Getting back to the family is going to be tough. I hope I can reintegrate, but I've been gone for so long it is going to be weird...”

Source: Stuster, 2016

11.2.2 Behavioral Conditions: Analogs of Spaceflight

❖ 520 days (Mars 500) (Basner et al., 2014)

- Analogs research is the only evidence extending beyond 6 months.
- While fidelity issues exist, analogs do model exploration class missions better due to no exchange of crew and minimal resupply.



Not universally experienced

- Cumulative scores throughout the mission.
    - 1 of 6 crewmembers showed a non-linear progression of depression symptoms, with an inflection point near the 6-month mark
    - Half of crew showed a linear increase in perceived cognitive symptoms throughout the mission

State of Knowledge – Behavioral Conditions, Analogs

- 8 months [(Hawaii Space Exploration Analog and Simulation (HI-SEAS III)]
  - Behavioral health influenced habitat power usage patterns (Engler et al., 2019)
  - Preliminary, non-linear decline in positive mood
    - The publication by Engler and colleagues only applied a linear trend, which indicates declining mood over time. However, a preliminary re-analysis indicates a trend for plateauing throughout most of the mission, with a steeper decline around 6 months.
    - There is some evidence of the "so called" third-quarter effect across analog studies like this. Although not all individuals or crews show this trend.

See Fig 9 in Engler et al., 2019

- Positive Affect Negative Affect Scale (PANAS)
  These data are ratios of positive activating mood (enjoyment, interest, etc.) to negative activating mood (anxiety, irritability, etc.). Higher ratios indicate brighter or more pleasant mood.

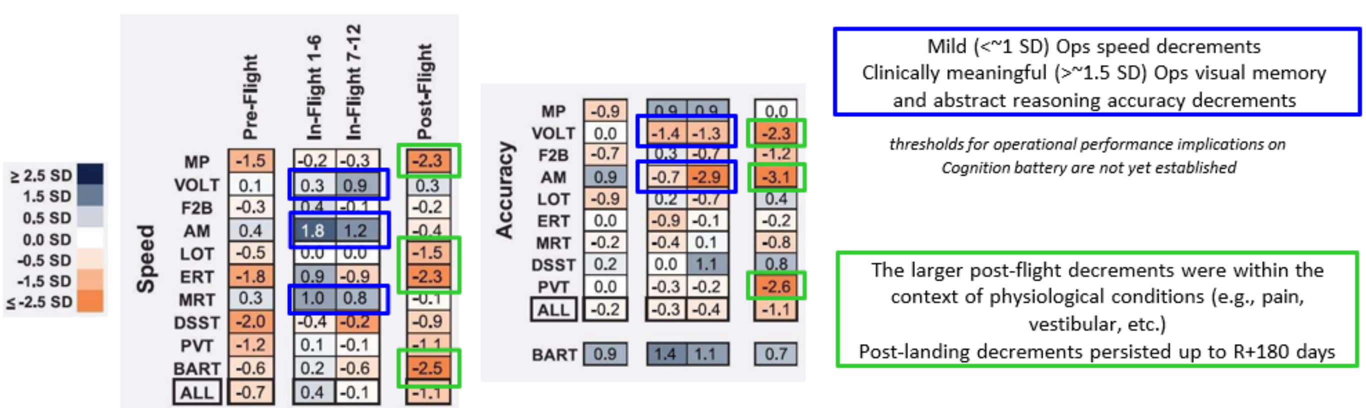
11.2.3 Behavioral Health: Analogs of Spaceflight

- 45 days [Human Exploration Research Analog (HERA)] - Daily meal replacement bars (MRB) (Sirmons et al., 2020)
  - Greater stress and unhappiness
  - Lower perceived health and energy

Food system acceptability is a contributing factor. See Fig. 5b Sirmons et al., 2020

11.2.4 Cognitive Conditions: Spaceflight

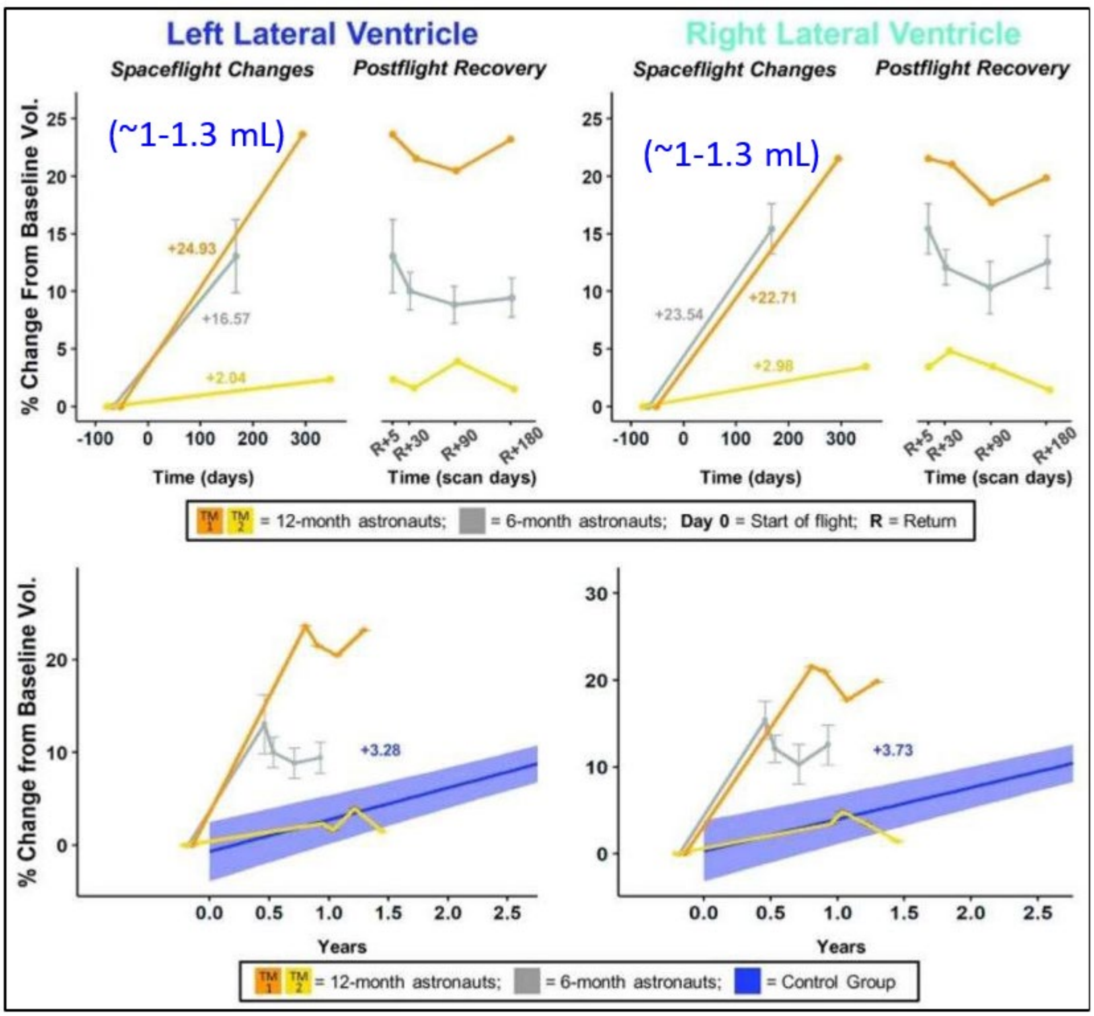
- 1 year International Space Station (ISS) Case Study (N=1) (Garrett-Bakelman et al., 2019)
  - No observed operational performance impact in the crewmember, but monitoring and Cognition battery thresholds for operational performance are advised to better characterize risk for long-duration missions.
  - Decrements post-landing are relevant for Mars surface ops. with less ground support mitigation



For readability, acronyms and abbreviation are used in the graphic above. For full term/ titles, see Acronyms and Abbreviations page

Brain Structural Changes

- Vertical brain displacement (Roberts et al., 2017; 2019) and narrowing of Cerebrospinal fluid (CSF) spaces at the vertex (Jillings et al., 2020; Roberts et al., 2017; 2019)
- Sub-clinical lateral ventricle enlargements ~10-14% (Alperin et al., 2017; Hupfeld, et al., 2020; Jillings et al., 2020; Kramer et al., 2020; Roberts et al., 2019; Van Ombergen et al., 2019)
  - Cause unknown; headward shift of blood and CSF is hypothesized (see Jillings et al., 2020; Kramer, 2020)
  - Individual variability (e.g., see figure from Hupfeld et al., 2020)
  - Unknown timecourse (onset and/or progression)
  - Normal aging changes can contribute to post-flight volume increases (Kramer et al., 2020) but may not fully account for them
    - Volume increases for most astronauts exceeded a normal aging control group by R+180 (see figure; Hupfeld et al., 2020)
  - Incomplete recovery by R+360 days (Kramer et al., 2020)
    - Larger baseline volumes correlate with more prior flight experience, less time between missions (Hupfeld et al., 2020)
- Cognitive performance and LTH implications are unknown, but concerns for forward characterization work



11.2.5 Cognitive Conditions: Analogs of Spaceflight

- 14 months (Neumayer III Station) (Stahn et al., 2019)
  - Dentate gyrus (learning and memory) and other regional grey matter volume reductions
  - Isolation and confinement can impede neurogenesis
    - Social isolation and crew dynamics (stress-immune)
    - Environmental monotony (sensory deprivation)

See Fig 1.C in Stahn et al., 2019

- Brain-derived neurotrophic factor (BDNF) mediates cognitive performance in physicians with burnout (He et al., 2017)
  - Somatic and immune response to chronic stress is a driver of cognitive decrements.
- ~9.5 months (Antarctic) (Basner et al., unpublished)
  - Mild decrements (<0.5 SD)
  - Corrected for practice and stimulus set effects
  - Variable by station
    - Implications for crew and station factors
      - Crew dynamics?
      - Habitat design?
      - Selection?

11.2.6 Cognitive Conditions: Animal Studies

- CNS radiation risk evidence from experimental animal models is highly variable
  - Limited for *human* consequence characterization (translatability questions)
    - Inconsistent behavioral methodologies, timelines, and animal samples
    - Dose responses are inconsistent and/or non-linear
    - Some acute effects seen at doses <250 milligray (mGy) and can persist
  - Informative for possible mechanistic pathways (CM targets)
    - Neuroinflammation and immune response
    - Oxidative stress
    - Protein expression and epigenetic regulation
    - Neuronal structure, communication, and development

- ❖ LTH risk of Alzheimer's disease (AD) has been observed in transgenic, disease-prone mouse models ≥ 100 mGy
  - Suggests potential risk for susceptible individuals
- ❖ Emerging cognitive risk interaction between radiation and sleep (Britten et al., 2020)
  - Attentional set-shifting performance decrement in irradiated rats with a single session of sleep fragmentation vs. normal irradiated mice with normal sleep.

11.2.7 Ops Incidence/Prevalences (Rev C)

State of Knowledge – Ops Incidence/Prevalence, Spaceflight

	Behavioral Med. Outcome	Mission Type(s)	Incidence/Prevalence	Source
	Psychiatric Disorders	Apollo through ISS	Female: 0.0036 -0.0071 person-year Male: 0.0029 - 0.0019 person-year	IMM (0 in spaceflight; model estimates based on general population aged 40-49yr)
	Depression symptoms	Mir – U.S. Astronauts	0.77 incidence-year	Marshburn, 2000
	Behavioral signs and symptoms*	Shuttle (STS-1 to STS-89)	14-day: 0.11 2.87 person-year	Billica, 2000
new	**Bereavement** (unexpected loss)	ISS (through Exp. 62)	~~2.44 per mission~~ 1.61 *per mission*	Original source: Beven, 2014 (updated to Exp. 62)
new	**Behavioral signs and symptoms***	ISS (through Exp. 40)	0.62 person-year	Antonsen et al., 2017 LSAH Data Request ID: #10912
new	**Off-Nominal WinSCAT****	ISS (through Exp. 41) ISS (Exp. 27 – 41) new version	13.2% (of 318 trials) 19% (of 120 trials)	Seaton and Kane, 2015

* Minimum estimates from retrospective medical records review (does not include BHP Ops records)

** Off-nominal does not imply an operational performance decrement; does not account for contributors to an off-nominal test session (e.g., interruption, sleep, stress, effort, etc.)

BHP Ops – Behavioral Health and Performance Operations; WinSCAT - Spaceflight Cognitive Assessment Tool for Windows

State of Knowledge – Ops Incidence/Prevalence, Analogs

	Behavioral Med. Outcome	Population	Incidence/Prevalence	Source
new	**Psychiatric Disorder** *	Military Special Forces	3.2% (N=537) Lower than general forces (selection and training effect)	Cooper et al., 2020
	Psychiatric Disorder †	Antarctic (9-10	4.5% at Australian stations 6.4% at McMurdo	Otto, 2007
	Psychiatric Disorder †	Antarctic (9-10	5.2% of crew	Palinkas et al., 2004
	Memory or Concentration Problem	Antarctic 1989 (9-10 mos.)	51.5% of crew	Palinkas, 1992

* Includes traumatic stress, mood, and anxiety disorders
† Includes adjustment, mood, personality disorder, substance use, and insomnia/fatigue problems

11.2.8 Ops Consequences

State of Knowledge – Ops Consequences - Spaceflight

Behavioral Med. Risk	Mission Type	Consequence/Impacts
Irritability (worsened by sleep loss, congestion)	Apollo 7	Adverse Team Risk dynamics Safety concern Return to flight status?
Behavioral Emergency (suspected hallucination and/or adverse crew dynamics)	Soyuz-21 Soyuz TM-2	Evacuation (LOM)
Somatic/Depression symptoms (prostate concern partly determined psychosomatic)	Soyuz T-14	Evacuation (LOM)
Irritability/Adjustment stress (high workload; austere vehicle)	Skylab 4	Work stoppage (LOMO)
Acute adjustment stress/depression (failure of experiment)	Shuttle (Payload Specialist)	Timeline/workload adjustments (LOMO) Increased stress to whole crew
Bereavement (unexpected loss of family member)	ISS (1 U.S. astronaut; 1 Cosmonaut)	Grief worsened by isolation? Secondary BHP impact to whole crew Timeline/workload adjustments (LOMO) – (social/work withdrawal ~1 week)

LOM: Loss of Mission; LOMO: Loss of Mission Objective

State of Knowledge – Ops Consequences, Analogs

	Behavioral Med. Risk	Analog Type	Consequence/Impacts	Source
new	**Depression**	Antarctic (9-10 mos) Arctic (9-10 mos)	Evacuation (at least 6x) Weight/appetite loss Crew time: monitoring individual Unplanned telemedicine sessions	Temp et al., 2020
new	**Behavioral Emergency** (suicidal ideation)	Antarctic (<30 Days)	Medical Administrative Move (transfer to another base for care)	Pattarini et al., 2016
	Behavioral Condition (signs and symptoms)	Antarctic (9-10 mos)	4.6 psychiatric patient encounters per person-week	Cushman and Parazynski (2014)
	Physical Aggression*	Antarctic (9-10 mos)	Bodily injury Arson	Vostok 1959 (axe attack) McMurdo 1981 (arson) Almirante Brown 1984 (arson) McMurdo 1996 (hammer attack) Bellinghausen 2018 (stabbing)

11.2.9 LTH – Cognitive

LTH – Cognitive, Lifetime Surveillance

- Neurodegenerative diseases (mean lifetime flight days = 34.41)
  - No evidence of increased risk or earlier onset for most neurodegenerative diseases.
  - Limitations: small sample size for prevalence estimation; outcomes in long-duration crew are unknown

LTH Outcome	N*	Records Queried**	Prevalence*	Age at Diagnosis*	General Population Prevalence	Military/Veteran Prevalence
Dementia	<5	371 (age ≥50)	**0.27-1.07%**	60-79 years	**5.05% age ≥50** **8.80% age ≥65** (Langa et al., 2017; Niu et al., 2017)	**7.5% age ≥65 U.S.** (Krishnan et al., 2005)
Essential Tremor	10	393 (age ≥40)	**2.54%**	40-80+ years	**3.40% - 4.0% age ≥40** (Dogu et al., 2003; Wennings et al., 2005)	**6.1% China** (Wang et al., 2010)
Parkinson's	<5	393 (age ≥40)	**0.25-1.02%**	40-69 years	**0.57% age ≥40 N. Am.** **1.8% age ≥65 Europe** (De Rijk et al., 2000; Marras et al., 2018)	**2% China** (Wang et al., 2010)
ALS	<5	403 (all ages)	**0.25-0.99%**	70-79 years	**0.02% ages 18-90** **0.005% N. Am.** (Bhattacharya et al., 2019; Mehta et al., 2018)	**0.01-0.05% U.S.** (Sagiraju et al., 2020)

* For confidentiality, exact cases not specified if <5; age range is categorical (not exact)
** Records search was restricted by age for each outcome to approximate population estimate methodologies
Source: IMPALA Neurological Disorders dashboard, accessed May 5, 2019. Records queried included astronauts and payload specialists.

ALS: Amyotrophic Lateral Sclerosis; IMPALA: Information Management Platform for Data Analytics and Aggregation

LTH – Cognitive, Analogs

LTH Behavioral Med. Outcome	Population(s)	Prevalence	Source
Dementia	Atomic Bomb Survivors	No increase above general population	Yamada et al., 2009
Parkinsonian-like disease w/ depression *	Biosphere 2 2-years Isolated Controlled and Confined (ICC)	1/8 crew (12.5%)	Lassinger et al., 2004

* Mission involved prolonged exposure to hypoxic atmosphere, caloric restriction, high physical workload, and psychological stress

11.2.10 LTH – Behavioral Health

State of Knowledge – LTH – Behavioral Health, Lifetime Surveillance

"There was no possible way of setting a goal that would match the goals already achieved."

(Aldrin, 1973)

LTH Behavioral Med. Outcome	Mission Type(s)	Likelihood	Source
Depression (w/ alcohol use problems)	Apollo 11	--	Aldrin, 1973
Psychiatric Disorders*	All spaceflight	Unknown	--

* Operational psychology records are confidential and unavailable for LSAH query

- Reintegration adjustment is a concern for high-profile missions and long-duration missions away from loved ones.

12. Metrics

❖ **Current: High degree of uncertainty**
- Incidence of inflight behavioral signs and symptoms of behavioral and cognitive changes *per person-year (ISS exp 40)* à current likelihood ratings (LSAH DR #10912)
- Incidence of subclinical behavioral health mood issue *per astronaut-mission (ISS exp 68) à* support current likelihood ratings (LSAH DR #27041) ***new***
- Incidence of off-nominal WinSCAT sessions – statistical deviation from baseline ***updated***
- Incidence of behavioral health condition (depression) or psychiatric emergency in analogs ***new***

❖ **Proposals for better resolution: Leverage both flight and analog settings**
- Updated operational estimates that includes comprehensive sub-clinical symptoms of both psychological and cognitive outcomes
- Frequency of intervention for BHP
- Incidence of exceeding thresholds for operational performance (requires thresholds)
- Additional cognitive risk monitoring capabilities to operations
- Characterize and monitor relevant operational outcomes or consequences

Operational Prevalence: Spaceflight

Behavioral Med. Outcome	Missions	Incidence/Prevalence	Source
Bereavement/Grief reaction (unexpected loss)	ISS (through Exp. 68/69)	1.1 % (0-6.6%) *per astronaut-mission*	Original Source: Beven, 2014 (updated through current)
Off-Nominal WinSCAT**	ISS (through Exp. 41) ISS (Exp. 27-41) version 2.0 ISS (Exp. 40-70) version 2.0	13.2% (of 318 trials) 19% (of 120 trials) 21% (of 279 trials)	Seaton and Kane, 2015 BHP Ops, December 2023
Subclinical signs and symptoms of depression and anxiety	Shuttle (STS-1 to STS-89)	0.039 (CI: .026 - .053) per astronaut-mission	LSAH Data Request ID #27041
Subclinical signs and symptoms of depression and anxiety	ISS (through Exp. 68)	0.22 (CI: .13 - .32) per astronaut-mission	LSAH Data Request ID #27041

* Minimum estimates from retrospective medical records review (does not include BHP Ops records)
5/13/2022
** Off-nominal does not imply an operational performance decrement; does not account for contributors to an off-nominal test session (e.g., interruption, sleep, stress, effort, etc.)

LTH Prevalence: Spaceflight

❖ Neurodegenerative diseases (mean [median] lifetime flight days = 58.17 [23.24])

LTH Outcome	N*	Records Queried**	Prevalence*	Age at Diagnosis*	General Population Prevalence	Military/Veteran Prevalence
Dementia	<5	377 (age ≥50)	**0.97%**	60-80+ years	**5.05% age ≥50** **8.80% age ≥65** (Langa et al., 2017; Niu et al., 2017)	**7.5% age ≥65 U.S.** (Krishnan et al., 2005)
Essential Tremor	10	397 (age ≥40)	**2.42%**	40-80+ years	**3.40% - 4.0% age ≥40** (Dogu et al., 2003; Wennings et al., 2005)	**6.1% China** (Wang et al., 2010)
Parkinson's	<5	397 (age ≥40)	**1.54%**	40-69 years	**0.57% age ≥40 N. Am.** **1.8% age ≥65 Europe** (De Rajk et al., 2000; Marras et al., 2018)	**2% China** (Wang et al., 2010)
ALS	<5	413 (all ages)	**0.24%**	70-79 years	**0.02% ages 18-90** **0.005% N. Am.** (Bhattacharya et al., 2019; Mehta et al., 2018)	**0.01-0.05% U.S.** (Sagiraju et al., 2020)

* For confidentiality, exact cases not specified if <5; age range is categorical (not exact)
** Records search was restricted by age for each outcome to approximate population estimate methodologies

Source: IMPALA Neurological Disorders dashboard, **updated August 17, 2022**. Records queried included astronauts and payload specialists.

Operational Prevalence: Analogs of Spaceflight

Behavioral Med. Outcome	Analog	Incidence/Prevalence	Source
Psychiatric Emergency (unknown type)	Antarctic McMurdo (1-7 months)	2.3% (0.1-8.4%) of crew (no psych selection criteria)	Kim et al., 2022
Depressive symptoms^	HERA Campaigns 4, 5 (45 days)	0/32 (0-12.7%) of crew	Bell et al., 2022
Depressive symptoms^	NEK-SIRIUS 19 and 21 (4 and 8 months)	0/12 (0-28.2%) of crew	Bell et al., 2022 Bell et al., 2023

Ops Consequences

Behavioral Med. Outcome	Analog	Consequence/Impacts	Source
Psychiatric Emergency (Unknown type)	Antarctic McMurdo (1-7 months)	Crew evacuation (n = 2)	Kim et al., 2022

^No clinical elevations on Beck Depression Inventory scale

13. Risk Mitigation Framework – Color Changes

❖ How do we know when we go from **red** → **yellow**?

- Key indicators and thresholds for both early and diagnostic detection
- Hybrid-autonomous capabilities for inflight monitoring, prevention, and treatment CM suite:
  - ✓ Integrated across risks and hazards; considers mission parameters
  - ✓ Provides high level actionable feedback to crew and decision-making support
  - ✓ Evidenced-based prevention and intervention CMs that can be feasibly implemented in-mission
  - ✓ Does not rely on re-supply or real time communication with ground
- LTH likelihood of neurodegenerative disease risk is characterized sufficiently low

❖ How do we know when we go from **yellow** → **green**?

- Unlikely to achieve green given resource constraints and trade-offs. However, further reduction of risk in yellow DRMs include:
  - Key indicators and thresholds for early detection, including unobtrusive tools
  - Flight validated feasible and acceptable (to crew) CMs that do not require resupply and synchronous communication/ample bandwidth

14. Risk → Standards → Requirements Flow

Risk of Cognitive of Behavioral and Psychiatric Disorders (Behavioral Health Risk)

Standard

NASA-STD-3001: NASA Space Flight Human-System Standard Vol. 1, Crew Health, Revision C – September 2023

[V1 3001] Selection and Recertification
[V1 3002] Pre-Mission Preventive Health Care
[V1 3003] In-Mission Preventive Health Care
[V1 3004] In-Mission Medical Care
[V1 3055] Surviving Crew Support
[V1 3016] Post-Mission Health Care
[V1 3018] Post-Mission Long-Term Monitoring
[V1 4011] Mission Cognitive Status
[V1 4012] End of Mission Cognitive Assessment and Treatment
[V1 4013] End of Mission Psychosocial Assessment
[V1 4014] Completion of Critical Tasks
[V1 5002] Crewmember Training
[V1 5003] Crew Medical Officer Medical Training
[V1 5008] Psychological Mission Training
[V1 6001] Circadian Shifting Operations and Fatigue Management
[V1 6004] Behavioral Health and Performance Provisions
[V1 6010] Private Psychological Communication (PPC)

NASA-STD-3001: NASA Space Flight Human System Standard Vol. 2, Human Factors, Habitability, and Environmental Health, Revision D – September 2023

[V2 3006] Human-Centered Task Analysis
[V2 10003] Operability
[V2 10001] Usability
[V2 5007] Cognitive Workload
[V2 5006] Situation Awareness
[V2 6004] Nominal Vehicle/Habitat Carbon Dioxide Levels
[V2 6013] Crew Performance Environmental Zone
[V2 6109] Water Quantity
[V2 6110] Water Temperature
[V2 6078] Continuous Nosie Limits
[V2 6079] Crew Sleep Continuous Noise Limits
[V2 6082] Annoyance Noise Limits for Crew Sleep
[V2 6084] Narrow-Band Noise Limits
[V2 6092] Vibration Exposure Limits during Sleep
[V2 7002] Food Acceptability
[V2 7011] Food and Beverage Heating
[V2 7012] Dining Accommodations
[V2 7016] Personal Hygiene Capability
[V2 7017] Body Cleansing Privacy
[V2 7021] Body Waste Management System Location
[V2 7022] Body Waste Management Privacy
[V2 7026] Body Waste Odor
[V2 7038] Physiological Countermeasures Capability
[V2 7070] Sleep Accommodation
[V2 7071] Behavioral Health and Privacy
[V2 7073] Partial-g Sleeping
[V2 7075] Clothing Exclusive
[V2 7076] Clothing Safety and Comfort
[V2 7084] Recreational Capabilities
[V2 8001] Volume Allocation
[V2 8005] Functional Arrangement
[V2 8006] Interference
[V2 8043] Window Provisioning
[V2 8045] Window Optical Properties
[V2 8049] Window Light Blocking
[V2 8051] Illumination Levels
[V2 8103] Environmental Lighting Attenuation
[V2 8055] Physiological Effects of Light (Circadian Entrainment)
[V2 8056] Lighting Controls
[V2 8057] Lighting Adjustability
[V2 9056] Use of Hearing Protection
Section 10 – Crew Interfaces
[V2 11009] Continuous Noise in Spacesuits
[V2 11011] Suited Crewmember Heat Storage
[V2 11024] Ability to Work in Suits
[V2 11025] Suited Nutrition
[V2 11029] LEA Suited Hydration
[V2 11030] EVA Suited Hydration
[V2 11033] Suited Thermal Control
[V2 11039] Nominal Spacesuit Carbon Dioxide Levels

Requirements

ISS
SSP 41000 System Specification
SSP 50005 International Space Station Flight Crew Integration Standard
SSP 50260 ISS Medical Operations Requirements Document

MPCV
MPCV 70024 Human System Integration Requirements

CCP
CCT-REQ-1130 ISS Crew Transportation Requirements Document
JSC-65993 CHSIR

HLS
HLS-HMTA-001 (Initial)
HLS-HMTA-006 (Sustained)

Gateway
GP 10000 Program
GP 10004 Subsystem for ECLSS
GP 10006 Subsystem for FSW
GP 10007 Subsystem for CHI
GP 10012 Subsystem for VSM
GP 10015 Subsystem for Crew Systems
GP 10016 Subsystem for CHP
GP 10017 Subsystem for HSR

EHP
xEVAS-SRD-001

CCP – Commercial Crew Program; EHP - Extravehicular Activity and Human Surface Mobility Program; LEA – Launch, Entry and Abort; MPCV – Multipurpose Crew Vehicle

15. High Value Risk Mitigation Targets

- ❖ Characterize risk of sub-clinical behavioral and cognitive changes during spaceflight [HSRB/LSAH]

- ❖ Characterize how Key indicators and thresholds correlate with meaningful change (HRP Human Factors and Behavioral Performance [HFBP] Element)
  - Collaborate across programs to establish onboard capabilities for in-mission monitoring

- ❖ Characterize long-term health outcomes (HRP HFBP Element; TREAT act [To Research, Evaluate, Assess, and Treat (TREAT) Astronauts Act])

- ❖ Develop and validate inflight capability to support early risk detection and CM deployment that does not rely on re-supply or real time communication with ground [HRP HFBP Element and Strategic Capability Leadership Team and the Exploration Medical Integrated Product Team]

- ❖ Establish scaling factors that translate animal outcomes to human outcomes to better characterize risk associated with radiation hazard [HRP HFBP and Radiation Elements]

16. Conclusions

- ❖ **Evidence base continues to strengthen**
  - Changes in cognitive and behavioral outcomes in response to spaceflight stressors
  - *Unknown operational outcomes*
- ❖ **Knowledge gaps**
  - Lunar communication delays→ **LxC and color change to lunar orbital short duration**
  - Exploration EVAs
  - Radiation
  - Pain
- ❖ LEO CMs appear effective but do not easily translate beyond LEO
- ❖ **Likelihood estimates have high uncertainty**
  - Weak characterization for LTH for lunar and mars DRMs
- ❖ **The behavioral medicine risk is complex and influenced by several other risks**
  - Emphasis on interacting stressors/hazards

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18. Acronyms and Abbreviations

ALS	Amyotrophic Lateral Sclerosis
AM	Abstract Matching Test
BART	Balloon Analog Risk Test
BHP	Behavioral Health and Performance
CI	Confidence Interval
CM	Countermeasure
CNS	Central Nervous System
CO_2	Carbon Dioxide
DAG	Directed Acyclic Graph
DRM	Design Reference Mission
DSST	Digit Symbol Substitution Test
ERR	Excess Relative Risk
ERT	Emotion Recognition Test
EVA	Extravehicular Activity
F2B	Fractal Two-Back Test
G	Gravity
HERA	Human Exploration Research Analog
HFBP	Human Factors and Behavioral Performance
HFBP-EM	Human Factors and Behavioral Performance-Exploration Measures
HI-SEAS	The Hawaiʻi Space Exploration Analog and Simulation
ICE	Isolated Confined & Extreme
IMPALA	Information Management Platform for Data Analytics and Aggregation
ISS	International Space Station
LDSE	Long-Duration Space Exploration
LEO	Low Earth Orbit
LET	Linear Energy Transfer

LOM	Loss of Mission
LOMO	Loss of Mission objectives
LOT	Line Orientation Test
LSAH	Long-Term Surveillance of Astronaut Health
LTH	Long-Term Health
LxC	Likelihood X Consequence
mGy	microGray
MRT	Matrix Reasoning Test
NEEMO	NASA Extreme Environment Mission Operations
NEK	Nazemnyy Eksperimental'nyy Kompleks: a Russian facility located at the Institute of Biomedical Problems of the Russian Academy of Sciences in Moscow
PFC	Private Family Conferences
POLs	Performance optimal limit
PPC	Private Psychological Conferences
PVT	Psychomotor Vigilance Test
ROBoT-R	Robotics OnBoard Trainer – Research version
SIRIUS	Scientific International Research In a Unique terrestrial Station
STS	Space Transport System
TREAT	To Research, Evaluate, Assess, and Treat
VR	Virtual Reality
VOLT	Visual Object Learning Test
WinSCAT	Windows Spaceflight Cognitive Assessment Tool