Human Research Program
Human Health Countermeasures Element
Sensorimotor Risk
Standing Review Panel (SRP)
Final Report

November 2009

I. Executive Summary & Overall Evaluation

The Sensorimotor Risk Standing Review Panel (SRP) met at the NASA Johnson Space Center on October 4-6, 2009 to discuss the areas of future research targeted by the Human Health Countermeasures (HHC) Element of the Human Research Program (HRP). Using evidence-based knowledge as a background for risks, NASA had identified gaps in knowledge to address those risks. Ongoing and proposed tasks were presented to address the gaps. The charge to the Sensorimotor Risk SRP was to review the gaps, evaluate whether the tasks addressed these gaps and to make recommendations to NASA's HRP Science Management Office regarding the SRP's review. The SRP was requested to evaluate the practicality of the proposed efforts in light of the realistic demands placed on the HRP. In short, all tasks presented in the Integrated Research Plan (IRP) should address specific risks related to the challenges faced by the astronauts as a result of prolonged exposure to microgravity. All tasks proposed to fill the gaps in knowledge should provide applied, translational data necessary to address the specific risks.

Several presentations were made to the SRP during the site visit and the SRP spent sufficient time to address the panel charge, either as a group or in separate sessions. The SRP made a final debriefing to the HRP Program Scientist, Dr. John B. Charles, on October 6, 2009.

Taking the evidence and the risk as givens, the SRP reached the following conclusions: 1) the panel is very supportive of and endorses the present activities of the Sensorimotor Risk; and the panel is likewise supportive of the gaps and associated tasks in the IRP; 2) overall, the tasks addressed the gaps in the IRP; 3) there were some gaps and tasks that merit further enhancement and some new gaps/tasks that the SRP recommends.

The SRP was pleased with the current gaps and tasks, but has the following recommendations for areas which merit further focus and enhancement or consideration as new gaps/tasks:

1. The SRP believes that study designs incorporating longitudinal evaluations of a particular crewmember's sensorimotor performance over the course of a mission, or ideally over that crewmember's lifetime, will yield the optimal understanding of sensorimotor risks and their mitigation. Performance in the sensorimotor domain varies widely across individuals. Within-subject studies are therefore vital to optimize the knowledge gained in this area, especially with the small subject pools typical of space science studies.

   Many of the existing tasks within the HHC and Space Human Factors and Habitability Elements already incorporate within-subject comparisons. The SRP urges further

enhancement of within-subject designs wherever possible. The SRP envisions several task designs that expand the current portfolio in this critical area. These are described in the first section of the detailed report.

2. The SRP recommends a study of the extent to which prehabilitation training that fosters the ability to adapt to novel sensorimotor environments results in enhanced performance of mission-related tasks. A secondary goal of such training would be to familiarize crewmembers with the sensations and illusions that can occur as the system encounters and adapts to such novel environments. This could enhance a crew's ability to recognize and cope with such effects when they arise during a mission.

3. The SRP also recommends that studies be undertaken to measure the alterations in sensorimotor performance and adaptation that accompany the use of drugs such as promethazine to counter space motion sickness.

4. In addition, the SRP believes that the clarity of the sensorimotor portion of the HRP would be improved by including problems with space vehicle egress (especially under emergency conditions) as an explicit risk to be addressed. Although many present and planned tasks already address the mitigation of this risk, the SRP believes that clearly expressing their purpose would improve the current HRP IRP.

5. Finally, the SRP raised concerns regarding changes that might occur in the human nervous system as a result of exposure to conditions of prolonged space missions.

II. Critique of Gaps and Tasks

The SRP was charged with evaluating the gaps and tasks to address the following risk:

RISK OF IMPAIRED ABILITY TO MAINTAIN CONTROL OF VEHICLES AND OTHER COMPLEX SYSTEMS

A. List of Current Gaps and Tasks in IRP

Gap SM1: What is the relationship between the mode of in-flight exercise and post-flight sensorimotor performance?

- Data mining activities for Sensory-Motor Discipline. (Sensory DM). (Performance)

Gap SM2: What is the time course of recovery of sensorimotor function after long duration space flight?

- Data mining activities for Sensory-Motor Discipline. (Sensory DM) (Recovery)

Gap SM4: Can previous performance data be correlated with clinical observations?

- Data mining activities for Sensory-Motor Discipline. (Sensory DM) (Performance)

Gap SM5: What are the effects of disorientation and inter-individual differences on supervisory control, docking, RMS, etc.?

- Data mining activities for Sensory-Motor Discipline. (Sensory DM)

Gap SM6: Can a seated manual/visual performance assessment after long-duration spaceflight be completed?

- Assessment of Operator Proficiency Following Long-Duration Spaceflight (OpProf)
- Ambiguous Tilt and Translation Motion Cues After Space Flight/Otolith Assessment during Post-Flight Re-Adaptation. (ZAG/Otolith)
- Development of Countermeasures to Enhance Sensorimotor Adaptation. (SM Adaption)

The SRP determined that the above listed gaps and tasks in the current research portfolio are relevant and are the proper gaps and tasks to address the risk. The SRP endorses the gaps and tasks listed above, with recommendations for gaps/tasks to enhance and add outlined in Section I (Executive Summary) and detailed in part B of Section II of this report that immediately follows.

B. SRP Recommendations of Gaps and Tasks to Enhance and Add

1. Considering its conclusion regarding the desirability of longitudinal evaluations of a particular crewmember's sensorimotor performance and adaptive capabilities (item 1 in the Executive Summary), the Sensorimotor Risk SRP makes the following recommendations:

SENSORIMOTOR KNOWLEDGE GAP FOR BASELINE VESTIBULAR FUNCTION RELATING TO VESTIBULAR-DEPENDENT SENSORIMOTOR PERFORMANCE AND ADAPTATION

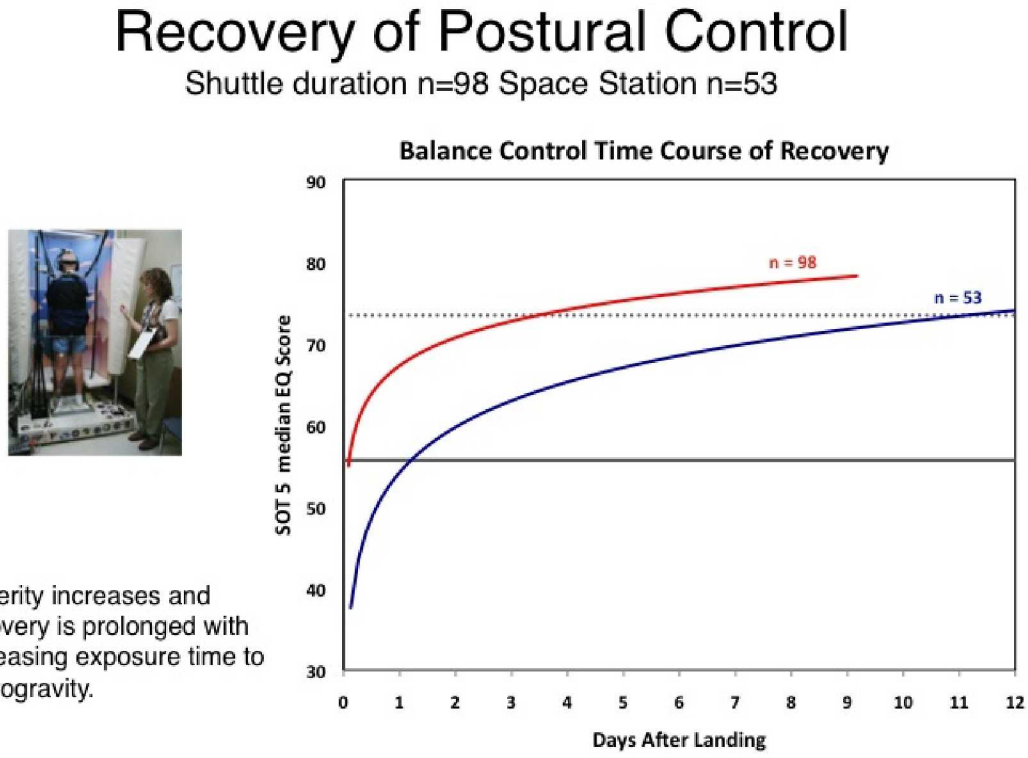
The Sensorimotor Risk SRP agrees that establishment of 'space normal' is a critical 'first step' toward understanding the extensive physiological alterations induced by exposure to changing gravitational environments, including microgravity. Evidence to date strongly supports the hypothesis that removal or reduction of linear acceleration stimuli to the vestibular otolith receptors initiates extensive sensorimotor re-organization of physiological systems, including control of key body segments (e.g., eye movements, postural and limb control). Successful task completion in microgravity therefore depends upon optimal central nervous system adaptation to altered inputs to the otolith sensors (Paloski, et al., 2009; Paloski, et al., 1999).

Knowledge Gap: No baseline data exist for the quantitative, longitudinal assessment of vestibular-dependent adaptation to changing linear acceleration environs, including microgravity. The proposed baseline vestibular function tests are currently in wide clinical use for assessment, monitoring and management outcome analysis (evidence based medicine) of vestibular function in patients with vestibular disorders. In order to establish 'space normal' and other standards of vestibular sensory contributions to sensorimotor adaptations to microgravity, the SRP recommends that an obligatory set of baseline vestibular function tests be established for inclusion with other tests of physiological status. Testing should begin with astronaut candidates and continue with periodic monitoring of vestibular function, perhaps during annual physical examinations. These data will provide comparison and correlation with specific human performance tasks and, if implemented, proposed R+0 field tests (Paloski, et al., 1999).

EVIDENCE

The proposed tests of vestibular function are fully analogous with other tests of physiological function such as visual acuity. Without such data, it is impossible to establish quantitative, evidence-based recommendations for crew health and safety relative to sensorimotor disruption, adaptation and recovery upon exposure to changing gravity environs. For example, it is known that postural stability is disrupted following both short- (Space Shuttle) and long-duration (ISS) flights. Disruption of postural control is much more severe and persists longer following return from ISS long-duration flights. (See the figure and graph below taken from Dr. Bloomberg's presentation to the SRP on October 5, 2009.)

The vestibular-induced changes following return from ISS long-duration flights are severe enough that return to baseline on computerized dynamic posturography (CDP - assessment of vestibular-dependent postural control) is a medical requirement for safe return to duty following ISS flights. It is therefore essential to develop countermeasures for mitigation of the disruption of postural control induced by extended duration flights to moon and Mars. The SRP proposes that both vestibulo-ocular and vestibulospinal operational data from individual crew members during, and upon exposure to changes in gravitational environs be performed in order to identify and advise crew with regard to risks and how to mitigate performance risks.



Red line: Shuttle post-flight recovery dynamics.

Blue line: Space Station post-flight recovery dynamics.

GAPS

The sensorimotor disruption of postural control is otolith-mediated and the recovery dynamics of the vestibulospinal system have been documented (Paloski, et al., 1993). However, a comparatively limited documentation of the vestibulo-ocular (VOR) effects of ISS long-duration flights is available. With the anticipated use of the Orion vehicle for NASA space missions, the landing environment becomes quite different from that of the Space Shuttle. The Orion Crew Exploration Vehicle (CEV) is designed for a parachuted landing on water. The integrity and stability of the CEV may be compromised upon landing, e.g., in rough seas. Astronauts may be required to egress Orion quickly upon landing, and before they have had opportunity to re-adapt to terrestrial gravity. Exiting Orion can be extremely demanding, as the astronauts would have to cope with the rolling and pitching of the vehicle in the open seas, would have to climb upward on a ladder to exit from the top, would have to descend a ladder, and would have to deal with these imposed roll and pitch accelerations against the background of Earth's gravity. Without extensive training and good human engineering design, along with pre-habilitation strategies, crewmember's safety will likely be compromised. Furthermore, landing the Orion CEV on uneven terrain may cause the vehicle to tumble and come to rest in an off-nominal orientation. Successful egress by the microgravity-adapted crew will likely be compromised without effective countermeasures.

PROPOSED TESTS OF VESTIBULAR FUNCTION (For review see Eggers & Zee (Eds.) 2009)

The SRP proposes the following vestibular function tests in order to establish risk factors and develop countermeasures, including rapid rehabilitation strategies for exposure to changing microgravity environs and return to Earth. Emphasis will be placed upon obtaining otolith function tests.

1) Ocular Vestibular Evoked Vestibular Myogenic Potentials (oVEMPs)
2) Cervical VEMPs (cVEMPs)
3) Computerized Dynamic Posturography (CDP)
4) Dynamic Visual Acuity (DVA)
5) Active and Passive Visual-vestibular Interaction Tests (Specific tests TBD)
6) Hand-Eye-Head Interaction Tests

(Specific test protocols TBD after consultation with flight surgeons)

The SRP also proposes that the above test results be correlated with results of field tests of sensorimotor function.

DELIVERABLES

Receiver-operator curves (sensitivity, specificity and clinical efficiency) will be developed for use by flight surgeons advising individual crewmembers regarding sensorimotor risks based upon results of longitudinal data from the above tests.

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2. Considering item 2 of the Executive Summary concerning prehabilitation training that fosters the ability to adapt to novel sensorimotor environments, the Sensorimotor SRP makes the following recommendations:

LEARNING TO LEARN: A PRE-ADAPTATION APPROACH TO MITIGATE SPACEFLIGHT RELATED SENSORIMOTOR DEFICITS

BACKGROUND

Traditionally, it has been thought that motor learning follows a specificity of learning principle, which suggests that learning is specific to the learning context and the task performed. In contrast, recent evidence demonstrates that facilitation of learning, or "learning to learn", is possible (Bock, et al., 2001; Roller, et al., 2001; Seidler, 2004). That is, participants learn a new skill, independent from those recently experienced, more quickly if they first participate in multiple bouts of learning (reviewed in Seidler, 2010). NASA's portfolio of sensorimotor research already includes NSBRI-funded work developing countermeasures to enhance sensorimotor adaptation using the "learning to learn" approach. The Sensorimotor Risk SRP was quite enthusiastic about this approach and discussed it at length. The SRP came up with several components that it thought would enhance this very important research plan, which are outlined in this section.

EVIDENCE

NASA's HRP Sensorimotor Evidence Book provides a detailed review of extensive research documenting that spaceflight alters sensorimotor control. Specific effects include changes in locomotion, gaze control, dynamic visual acuity, and perception. The approach being taken in Dr. Jacob Bloomberg's laboratory is development of a "prehabilitation" paradigm to increase adaptability of the sensorimotor system prior to spaceflight, thereby increasing the rate of adaptation to gravitational force transitions.

The potential utility of pre-adaptation training for astronauts is high – it is a countermeasure that could be performed prior to spaceflight, with booster training conducted during a mission. The increased adaptability arising from the learning to learn approach has been shown to endure for up to a month following initial training (Bock, et al., 2001; Roller, et al., 2001). The benefits of

learning to learn have been shown to extend across a range of participants and settings. For example, older adults exhibit a comparable magnitude of learning acceleration following multiple adaptation experiences to that of young adults (Seidler, 2007a, 2007b). This approach was used as early as 1989 to pre-habilitate balance while walking in monkeys prior to labyrinthectomy (Igarashi, et al., 1989) and resulted in better performance stability over the three month post-labyrinthectomy period. More recently, prehabilitation exercises, along with gentamicin, have been used in patients with cerebellar-pontine angle tumors prior to surgery as a means of reducing post-operative dizziness and vertigo (Magnusson, et al., 2007).

As stated above, the Sensorimotor Risk SRP is quite enthusiastic about the work that is already being done to develop "learning to learn" into a pre-flight countermeasure. The SRP has some suggestions that it believes would further enhance this approach; the first is to determine the generalizability limits of this effect. For example, it is of interest to know whether participants that engage in the current training protocol (variations in visual flow displays and support surface translations) exhibit faster adaptability in the pre-adaptation trainer (PAT). Do they adapt better to the microgravity and hypergravity conditions of parabolic flight? Do they adapt more readily to the g-force transitions experienced in spaceflight? The SRP believes that addressing these questions is a natural extension for the work that is currently being conducted by Dr. Bloomberg and would allow for further validation of prehabilitation as a countermeasure.

Our second suggestion is to develop and administer a pre-flight adaptability assessment. This would support our overall recommendation for more consistent longitudinal assessments of individual astronauts. It could also serve to indentify those individuals who experience particular difficulty with microgravity and partial gravity adaptation, and they could then receive targeted interventions. "Booster" training protocols could also be developed for in-flight use when the crew is nearing the time for gravitational transitions such as a lunar or Mars landing or return to Earth. The SRP believes that one potential indirect benefit of this individualized approach is that it may increase astronauts' self-awareness of their deficits and their ability to self-assess their performance at different time points during a mission. This may aid decision making for choices such as when to rely on automatic pilot systems and when booster adaptive training should be conducted.

In summary, the Sensorimotor Risk SRP strongly supports the work that is already being done to develop pre-adaptive countermeasures. The SRP believes that addition of the components described above will further enhance the beneficial impact of this program. In particular, the SRP feels that if "at-risk" individuals are not identified and targeted for pre-adaptation, the program runs the risk of greater washout of astronauts from the program.

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3. Considering its concerns regarding the alterations in sensorimotor performance and adaptation that accompany the use of drugs such as promethazine to counter space motion sickness (item 3 in Executive Summary), the Sensorimotor Risk SRP makes the following recommendations:

THE USE OF PROMETHAZINE (PHENERGAN) TO TREAT SPACE MOTION SICKNESS

OVERVIEW

The SRP concluded that the use of promethazine to treat space motion sickness should be re-evaluated. Space motion sickness usually resolves within 3-4 days when astronauts enter weightlessness but would be expected to recur when astronauts enter fractional gravitational states in space (e.g., when nearing Mars) and could impair the ability of astronauts to operate complex equipment appropriately during a Mars landing.

DOSE-DEPENDENT SIDE-EFFECTS

Promethazine has been the standard treatment of space motion sickness for several decades (Graybiel and Lackner, 1987). While it effectively reduces the symptoms of motion sickness, it has a number of adverse effects, both dose-dependent and idiosyncratic. Promethazine has a complex pharmacologic effect, as it is a histamine (H1) antagonist but is also a dopamine antagonist and has anti-cholinergic properties. It has been well documented to produce a number of dose-dependent side effects, many of which could hinder effective vehicular navigation.

These include sedation, dizziness (rarely true vertigo), and confusion. Studies on Earth have demonstrated substantially impaired performance during tests of alertness and coordination after receiving promethazine (Cowings, et al., 2000).

EXTRAPYRAMIDAL SIDE-EFFECTS

Because promethazine blocks dopamine receptors, it shares the "extrapyramidal" side effect profile of other dopamine antagonists. While promethazine infrequently causes these side effects, they would prove to be extremely disabling and potentially fatal if they did occur. These complications include acute dystonia (intense contraction of a group of synergist muscles, often affecting the neck), tremor, and oculogyric crises (involuntary eye closure) (Schwinghammer, et al., 1984). The most severe, albeit rare, potential side effect of promethazine is the neuroleptic malignant syndrome, characterized by intense muscle rigidity, fever, and marked confusion. This syndrome could be fatal if it occurred during space travel (Mendhekar and Andrade, 2005).

ALTERNATIVES TO PROMETHAZINE

Several highly effective anti-emetic medications with much more benign side-effect profiles have been developed over the past two decades, and these could serve as replacements for promethazine. The majority of these drugs are serotonin antagonists, block 5-HT_3 receptors, and are used to treat nausea and vomiting associated with chemotherapy (see Navari, 2009 for a review). Drugs in this category, dolasetron, granisetron, and ondansetron, function as symptomatic therapy, similar to promethazine. An alternate approach would be to use a drug that modulates the mechanism in the brain that is responsible for space motion sickness. Cohen and colleagues have provided convincing evidence that motion sickness in one-g relates to the velocity storage integrator in the brainstem (see Cohen, et al., 2008 for a review). Suppressing velocity storage with GABA agonists, such as baclofen, could potentially suppress space motion sickness more directly than the symptomatic therapies described above. Any of these alternate drugs, if considered as potential treatments for space motion sickness, would need to be extensively evaluated. This evaluation could include Earth-based provocative testing and testing during parabolic flight. Any potential cognitive or motor side effects would also need to be carefully characterized.

CONCLUSIONS

While promethazine has effectively reduced space motion sickness, the SRP is concerned that it may cause significant cognitive and motoric side effects that could impair the ability of astronauts to navigate vehicles during a Mars landing. Alternative drugs are likely to be equally effective but to produce milder side effects.

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4. Considering its recommendation that problems with space vehicle egress should be identified as an explicit risk to be addressed by the HRC (item 4 in Executive Summary), the Sensorimotor Risk SRP submits the following recommendations:

SENSORIMOTOR RISK FOR VEHICULAR EGRESS (PARTICULARLY FOR WATER EGRESS UNDER HIGH SEA STATE CONDITIONS AND FOR EMERGENCY EGRESS UNDER ALL CONDITIONS)

BACKGROUND

In the course of discussions of risks that result from sensorimotor effects of exposure to microgravity, the Sensorimotor Risk SRP noted the probable need to incorporate an additional risk in the HRP IRP. This additional Sensorimotor Risk comes on the back of the previously unrecognized problems resulting from the degradation of visual acuity and oculomotor control associated with thrust oscillations of the Ares launch vehicle. This risk is primarily associated with anticipated structural and operating environmental considerations regarding the Orion capsule, as well as generally underestimated problems associated with safe egress by microgravity-adapted crews from space vehicles in general.

EVIDENCE

"Sensorimotor integration plays a critical role in the control of posture and movements, and so is essential for locomotion and using tools. On exposure to an altered gravitational environment, there are changes in the sensory signals originating from the vestibular system, particularly those coming from the otolith organs. These changes have major effects on visual and spatial orientation, and on mobility during spaceflight and on return to Earth. Disturbances occur more frequently on longer-duration missions, and complete recovery can take weeks and, in some cases, months. Disorientation, impaired visual acuity, and postural instability can have profound effects on the performance of sensorimotor tasks, including piloting the spacecraft or making an

emergency egress. Further, assistance is often required even for normal vehicle egress following long duration missions (Review of NASA's Biomedical Research Program, 2000).

It is well known that multiple sensory systems contribute to accurate spatial orientation and the control of movement. On Earth, gravity plays a fundamental role in both spatial orientation and locomotion, and the vestibular, proprioceptive, and haptic receptors are all particularly sensitive to gravitational stimulation. In the absence of gravity, astronauts initially rely on vision alone, and they often misperceive their orientation with respect to the environment, misinterpret visual information, and experience visual reorientation illusions. Eventually, the astronauts adapt to the microgravity environment, and develop new ways of relating to the external world. In space, terrestrial patterns of locomotion, which are highly gravity-dependent, are eventually replaced by other modes of body translation and movement that do not depend on gravity. As they adapt to their new and virtually gravity-free space environment, the astronauts become exquisitely capable of moving around with great accuracy and precision (e.g., Skylab films of J.Kerwin entering the LBNP). Although they become highly adept at self-motion in space, their former patterns of locomotion and their terrestrial motor capabilities become degraded, as documented in multiple publications that show diminished balance control, greater gaze instability during locomotion, and restricted movement of the head, as well as increased variability in the step cycle (Bloomberg, et al., 1997; Layne, et al., 1997; Paloski, et al., 1992; Reschke, et al., 1994; Reschke, et al., 1987). Although recovery of balance control occurs rapidly over the first twelve hours post-flight, it may not return to pre-flight baseline values for weeks, (Paloski, et al., 1992) and the locomotory capabilities of astronauts within the first minutes of being reintroduced to a gravitational field have not been studied to date.

GAPS

With the anticipated use of the Orion vehicle for NASA space missions, the landing environment becomes quite different from that of the Space Shuttle. Orion will not be glided to a runway landing at a well-specified location, as with the Shuttle; rather, it is designed for a parachuted landing on water. The integrity of the vehicle may be compromised upon landing, or the sea state at the time of landing may make the vehicle unstable, extremely uncomfortable, or even uninhabitable for any appreciable period of time. Not only can the astronauts be required to exit Orion quickly upon landing, and before they have had any opportunity to re-adapt to terrestrial gravity, but the task of exiting Orion can be extremely demanding. The astronauts would have to cope with the rolling and pitching of the vehicle in the open seas, would have to climb upward on a ladder to exit from the top, would have to descend from the vehicle, and would have to deal with the imposed roll and pitch accelerations against the background of Earth's gravity. It is unlikely, without extensive training and good human engineering design, that the astronauts could promptly, safely, and successfully exit the vehicle under these conditions. Further, landing the Orion vehicle on land on uneven terrain can cause the vehicle to tumble and come to rest in an inverted orientation. Possible damage to vehicle integrity under these conditions is a distinct possibility, again requiring immediate and rapid egress by the microgravity-adapted crew. Emergency egress may be the first task that astronauts are required to perform when they first return to a gravitational field; studies to determine their capabilities immediately upon return should be given a high priority.

TASKS

1. Determine both normal pre-exposure values and immediate after-effects of microgravity exposure on locomotion, ladder climbing (and descending), and the ability to grasp and support body weight in dynamic environments.
2. Examine the ability of astronauts to orient and locomote both before and immediately after spaceflight.
3. Develop training programs, human-centered designs, and/or automated assist mechanisms to allow rapid emergency egress from Orion-type vehicles both on land and at sea.

The Sensorimotor Risk SRP notes that tasks 1 and 2 are already being pursued within existing NASA research programs.

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5. The Sensorimotor Risk SRP also raised concerns about changes in the human nervous system that might result from conditions prevailing during long duration space missions. This is addressed in the final section of the SRP's recommendations:

BRAIN REORGANIZATION AS A RESULT OF MICROGRAVITY CONDITIONS

BACKGROUND

In the course of discussions of risks and gaps that result from sensorimotor effects of exposure to microgravity, the Sensorimotor Risk SRP noted the need to incorporate an additional risk/gap under the HRP IRP. The need for this additional Sensorimotor risk/gap is supported by studies that have identified brain structural changes as a result of microgravity exposure, particularly in the somatosensory cortex and the cerebellum. Changes in brain structure and function may play a direct role in spaceflight-associated sensorimotor deficits, and further may impact the long-term health of astronauts, particularly in advanced age when brain volume loss occurs. The Institute of Medicine also suggested that brain reorganization occurring as a result of microgravity exposure should be considered an additional risk in their review of the Sensorimotor Evidence Book.

EVIDENCE

There is sufficient evidence in the literature to suggest that the brain may undergo structural remodeling similar to that seen in bone and muscle as a result of microgravity exposure, radiation and vascular changes associated with spaceflight. Both positive and negative plasticity may occur, including cortical reorganization associated with behavioral experience and volumetric losses. It has been known for quite some time that the brain's topographical organization is not fixed, but rather can undergo extensive remodeling, even in the adult brain. These changes occur in response to skill learning (cf. Karni et al., 1998; Xerri, et al., 1999), sensory deprivation (Merzenich, et al., 1983), and recovery from brain insult such as stroke (Cramer, et al., 1997; Cao, et al., 1998). The SRP suggests that experience-dependent cortical plasticity is likely to be evident in the brains of astronauts following microgravity exposure, specifically in the motor and the vestibular cortical regions. Astronauts must undergo adaptive modification of their movements in space in order to adjust to changes in sensorimotor signals occurring in microgravity. Furthermore, they must re-adapt to the 1G environment upon their return to Earth.

The evidence supports the idea that microgravity results in cortical reorganization of somatosensory and vestibular sensory systems. Research with rats demonstrated that brain structural changes occur as a result of microgravity exposure, particularly in the somatosensory cortex (Krasnov, 1994; D'Amelio, et al., 1998; Newberg, 1994) and the cerebellum (Holstein, et al., 1999). These changes include a decreased number of synapses and degeneration of axonal terminals. Krasnov (1994) reviewed data showing structural changes in the somatosensory cortex, and suggested that they imply reduced afferent input to the primary somatosensory cortex (S1). D'Amelio, et al., (1998) studied immunoreactivity of the gamma-aminobutyric acid (GABA) receptors in the hindlimb representation area of rat S1 after simulated microgravity (hindlimb unloading) for 14 days. The number of GABA immunoreactive cells were reduced in comparison to control animals. Presumably, spaceflight and prolonged unloading results in reorganization of reflex activity in hindlimb muscle groups, producing altered afferent signals to the somatosensory cortex. This altered feedback information likely produces the cortical changes.

Radiation exposure also seems to differentially affect sensorimotor brain regions, resulting in

neuronal loss (Newberg, 1994). Ross (1993, 1994) demonstrated that hair cells in the rat utricular macula undergo extensive plasticity as a result of spaceflight, with a large (40-55%) increase in synapse number. This plasticity remained evident following the flights, even after posture control in the rats had returned to normal. These findings strongly suggest that brain volumetric and functional measures should be evaluated pre- and post-flight.

Changes in cerebral blood flow as a result of microgravity exposure may also contribute to brain reorganization. Following spaceflight, astronauts have reduced arterial pressure and cerebral blood flow velocity as measured with transcranial Doppler (Bondar, et al., 1993). Similarly, Gazenko, et al., (1981) found that astronauts show reduced cerebral blood flow pulsatility, as measured with impedance rheography, when in a head-down tilt posture following spaceflight. Other studies have demonstrated a microgravity dose-dependent effect, with cerebral vasoconstriction following long-term flight not resolved after a period of five weeks (Charles, et al., 1996; Gazenko, et al., 1981; Watenpaugh & Hargens, 1996). It is thought that this increased vasoconstriction is an adaptive response to the increased cranial pressures experienced while in the microgravity environment. Blood vessel remodeling can occur relatively quickly, with as little as two weeks of head down tilt on Earth resulting in increased vessel wall thickness and vessel diameter in the brain vasculature and concomitant decreases in the lower extremity vasculature (Folkow, 1987; Mao et al., 1999). What is not known is how the increased cerebral vasoconstriction affects brain tissue reactivity during the performance of cognitive and motor tasks. Vasoconstriction, combined with other maladaptive neural changes due to heightened stress and radiation levels in space (reviewed by Newberg, 1994), may result in a change in baseline measures of brain blood flow. Thus, this should be considered a cross cutting topic with relevance to sensorimotor, radiation, behavioral, and vascular groups.

Brain volumetric losses occur during normal human aging, with both gray and white matter structures in the anterior portion of the brain showing particular vulnerability to loss (cf. Raz et al., 2004; Sullivan, et al., 2008). If astronaut brains undergo substantial volumetric degeneration during spaceflight, they may be at risk of accelerated aging effects. On a more positive note, targeted interventions have been successful at slowing and in some cases even reversing brain volumetric declines during aging. For example, a twelve week aerobic exercise intervention with previously sedentary older adults resulted in increased brain volume in the structures that undergo differential loss with age (anterior gray and white matter structures, Colcombe, et al., 2006) and increased recruitment of task-relevant brain structures during cognitive task performance (Colcombe, et al., 2004). Visuomotor task practice has also been associated with increases in brain volume in both young (Draganski, et al., 2004) and older adults (Boyke, et al., 2008) in task-relevant brain structures. The SRP believes that an appropriate first step to evaluate the significance of this risk would be to conduct pre- and post-flight brain structural and functional assessments, such as MRI and functional MRI (fMRI).

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C. Conclusions

The Sensorimotor Risk SRP concludes that current NASA programs addressing sensorimotor risks within the Human Health Countermeasures (HHC) and Space Human Factors and Habitability (SHFH) Elements are doing a very good job in addressing the important issues within the SRP's domain. In line with this, recommendations within Section II-B, Parts 1 and 2 of the detailed report consist of endorsements of current programs and suggestions of possible enhancements. Section III-B, Part 4 of the report recommends reclassifying capsule egress as an explicit risk but also notes that appropriate work is already underway in mitigating this risk.

Section II-B, Part 3 of the report recommends an ongoing re-evaluation of the appropriateness of current treatment of space motion sickness in the light of continuing advances in drugs that have more targeted actions than the current drug of choice, promethazine. NASA has the capability of carrying out such a re-evaluation if it is decided that it has a high potential for enhancing the safety and efficiency of upcoming missions as this SRP believes.

Section II-B, Part 5 of the report identifies an area of risk that is not yet explicitly included in the HHC and SHFH Elements. This area also relates as a gap, as it pertains to the possibility of sensorimotor impairment impacting the risk of the ability to maintain control of vehicles in long duration space missions. The SRP's discussion with Dr. Jacob Bloomberg revealed that he is aware of the risk of changes in the human nervous system produced by prolonged space missions beyond low Earth orbit. He and many other SRP panel chairs concurred that it is appropriate to undertake research in this area as part of the planning for such missions. Non-invasive structural and fMRI scans would be a good starting point for such investigations.

III. Discussion on the Strengths and Weaknesses of the Integrated Research Plan (IRP)

Strengths of the IRP

- Logical approach to define task demands, i.e. working tasks during the various stages of the mission
- Focus on best-evidence available to apply to the safety and performance of the crew
- Interest in more fundamental top-down questions
- Experienced investigators and staff
- The SRP endorses the current portfolio of research gaps/tasks

Weaknesses of the IRP

- A limitation is the small number of subjects who are engaged in different activities, which could pose a challenge for having longitudinal studies
- There needs to be some resolution between crew medical privacy and the need for data. Need better access to de-identified data
- No baseline data exist for quantitative longitudinal assessment of vestibular-dependent adaptation to microgravity-induced sensorimotor transitions
- Refer to Section II for specific recommendations of gaps/tasks to enhance in the portfolio of the IRP

IV. Discussion of Element Specific Questions in Addendum and/or Any Other Issues or Concerns the Panel Chooses to Address.

1. Are there obvious, unrealistic aspects in the IRP schedule?

- There are no unrealistic aspects in the IRP schedule that were noted by the SRP.

2. Is the portfolio of tasks sufficiently complete to acquire an adequate description of the risks?

- The SRP endorsed the current portfolio of tasks and the SRP has recommendations for enhancement of current gaps/tasks and addition of new gaps/tasks, as described in Section II of this report. Refer to Section II for specific recommendations.

3. Is the portfolio of tasks developing the appropriate technologies?

- The current portfolio of tasks is developing the appropriate technologies. In light of the SRP recommendations in Section II of this report, new technologies may need to be developed.

4. Does the portfolio contain a sufficient number of countermeasure development tasks?

- Yes.

5. Is the portfolio properly balanced among risk description, countermeasure development, and technology development activities?

- The SRP panel determined the current portfolio is properly balanced.

6. Are the appropriate analogs being used?

- The SRP had no discussions on this matter.

7. Is it reasonable to begin complete countermeasure work prior to complete description of risks?

- The SRP had no discussions on this matter.

V. Sensorimotor Risk SRP Charge

The SRP is chartered by the Human Research Program (HRP) Program Scientist at the NASA Johnson Space Center (JSC). The purpose of the SRP is to review and provide analysis on the status and progress of HRP Elements and Projects. Your report will be provided to the HRP Program Scientist and will also be given as a courtesy to the HHC Element and Projects at JSC.

The SRP should (to the fullest extent practicable):

1. Evaluate the ability of the Integrated Research Plan (IRP) to satisfactorily address the risk by answering the following questions:
   A. Have the proper Gaps have been identified to address the Risk?
      i) Are all the Gaps relevant?
      ii) Are any Gaps missing?
   B. Have the proper Tasks have been identified to fill the Gaps?
      i) Are the Tasks relevant?
      ii) Are any Tasks missing?

2. Identify the strengths and weaknesses of the IRP, *and* identify remedies for the weaknesses, including answering these questions:
   A. Is the risk addressed in a comprehensive manner?
   B. Are there obvious areas of potential integration across disciplines that are not addressed?

3. Address (as fully as possible) the questions provided in the charge addendum and to comment on any additional information provided to the Panel that is not addressed in #1 or #2 above.

4. Expect to receive review materials at least five weeks prior to the site visit.

5. Participate in a SRP teleconference to discuss any issues, concerns, and expectations of the review process approximately three weeks prior to the face-to-face meeting
   A. Discuss the SRP charge and address questions about the SRP process
   B. Identify any issues the SRP would like to have answered prior to the site visit

6. Attend the SRP meeting and tour at NASA/JSC
   A. Attend Element and risk panel presentations, question and answer session, and briefing
   B. Prepare a draft report including recommendations from the SRP that will be briefed to the Program Scientist by the SRP chairperson or panel. The report should address #1 and #2 above, the questions in the charge addendum, and any other information considered relevant by the SRP.

7. Prepare a final report (within one month of the site visit) that contains a detailed evaluation of the risk and provides specific recommendations that will optimize the scientific return to the HRP. The final report should provide a comprehensive review of Item #1 and #2 above, address the questions in the addendum to the charge, and any additional information the SRP

would like to provide.

8. Consider the possibility of serving on a non-advocate review panel of a directed research proposal or on a solicited research peer review panel; or otherwise advise the Program Scientist.

Addendum to charge: (Element Specific Concerns):

1. Are there obvious, unrealistic aspects in the IRP schedule?
2. Is the portfolio of tasks sufficiently complete to acquire an adequate description of the risks?
    a. For example, will "space normal" be adequately defined?
3. Is the portfolio of tasks developing the appropriate technologies?
4. Does the portfolio contain a sufficient number of countermeasure development tasks?
5. Is the portfolio properly balanced among risk description, countermeasure development and technology development activities?
6. Are the appropriate analogs being used?
7. Is it reasonable to begin countermeasure work prior to complete description of risks?

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