NSBRI Neurovestibular Adaptation Team Strategic Plan

9.0 NEUROVESTIBULAR ADAPTATION

Team Leader: Charles M. Oman, Ph.D.
Director, Man-Vehicle Laboratory
Department of Aeronautics and Astronautics
Center for Space Research
Massachusetts Institute of Technology
77 Massachusetts Avenue, Rm. 37-219
Cambridge, MA 02139-4301
617-253-7508
617-258-8111 FAX
cmo@space.mit.edu

9.1 INTRODUCTION

The most overt change affecting an astronaut in space flight is the immediate response of the neurovestibular system to changes in gravity. NSBRI's neurovestibular adaptation research program supports research aimed at developing scientifically-based countermeasures against the vestibular problems associated with space flight: spatial disorientation, space motion sickness, oculomotor deficits, postflight postural instability and gait ataxia. Problems typically arise first when astronauts transition from 1-G to 0-G, unfortunately at a time when their physical and cognitive performance is often critical for mission success and safety. Postflight problems have been more severe after 3-5 month Mir and ISS flights than on 1-2 week Shuttle missions, showing that some components of vestibular adaptation to 0-G take place over time scales of months, rather than days. Vestibular problems are also anticipated on planetary missions when astronauts make the transition from 0-G to partial G, or from 0-G to an artificial gravity environment. Over the past two decades, many of NASA's ground and flight neurovestibular experiments have focused on quantifying the effects of weightlessness on vestibular reflex responses in humans and animals. The objective of NSBRI's neurovestibular adaptation research program is to develop countermeasures against the broad set of vestibular risks associated with long duration space flight. In priority order, these are:

9.2 RISKS [i]

1. Re-entry and landing vertigo, resulting from adaptation to the 0-G environment, and exacerbated by head movements and vehicle accelerations during reentry, approach, landing and rollout, causing spatial disorientation, instability of vision, loss of visual acuity and ability to read cockpit displays, and potentially causing manual control and system monitoring errors during this critical phase of flight.

2. Acute space motion sickness, including nausea and vomiting, which impacts crewmember productivity and could cause failures in EVA suit life support systems.

3. Postlanding imbalance, vertigo, visual instability and orthostatic hypotension, decreased tone in postural muscles, impaired locomotor coordination, causing some crewmembers to have great difficulty to stand up and egressing in emergencies.

4. Inflight spatial disorientation and reference frame problems, causing spatial memory and navigation problems during emergency egress, EVA height vertigo, and operational difficulties during docking and remote manipulation.

5. Chronic space motion symptoms, including fatigue, "space stupids", decreased vigilance, drowsiness, loss of motivation, anorexia, dehydration, and other effects, resulting in increased incidence of operational errors and decreased crew work capacity

6. Vestibular and biomechanical Coriolis effects of artificial gravity (AG), including disorientation, nausea, vomiting, and loss of coordination which offset the potential positive physiological benefits of AG.

7. Irreversible vestibular function changes after long duration exposure to weightlessness, radiation, environmental toxins, stress, isolation, or immobilization, causing functionally important deficits in central or peripheral vestibular function, development, plasticity, or acceleration of the normal aging process.

9.3 GOALS

The ultimate goal of NSBRI's neurovestibular research program is to develop countermeasures that ultimately will to allow crewmembers to: avoid disorientation, meet the physical requirements of emergencies, treat motion sickness without side effects, and safely control vehicles and systems.

Risk –Based Goals

1. Reduce the risks of reentry and landing vertigo.
2. Reduce the risks of acute space motion sickness
3. Reduce the risks of postlanding imbalance, vertigo, visual instability and orthostatic hypotension.
4. Reduce the risks of inflight spatial disorientation and reference frame problems.
5. Reduce the risks of chronic space motion sickness.
6. Reduce the risks of Coriolis effects of artificial gravity.
7. Reduce the risks of irreversible vestibular function changes.

Non-Risk Based Goals

1. Develop improved methods for diagnosis, monitoring and treatment of human vestibular disease and the balance and disorientation problems associated with aging and inactivity.
2. Integrate research and analysis.

National Space Biomedical Research Institute
NEUROVESTIBULAR ADAPTATION RESEARCH PROGRAM

Table 9.1. Project Research Activities

PI/Project	Risk(s) Addressed	Countermeasure Target	Experimental System	Phase 1 Activities: Focused Mechanistic Research	Phase 2 Activities: Preliminary Countermeasure Development Research	Phase 3 Activities: Mature Countermeasure Development Research
BLOOMBERG/ Understanding Full-body Gaze Control During Locomotion	Postlanding imbalance, vertigo, visual instability.	• Monitoring and Diagnosis (Prediction) • Training	Human, treadmill walking	Understand how body segments absorb heel strike, and adapt to VOR gain changes.	Determine how visual acuity changes during locomotion	Assess postflight locomotion and gaze performance and fitness for return to activities of daily living.
DORNHOFFER/ Pharmacological Countermeasures for Space Motion Sickness	• Acute space motion sickness • Chronic space motion sickness	• Pharmacological agents • Diagnosis (prediction)	Human, off axis rotating chair	Assess drug effectiveness and side effects on P50 AEP, memory, learning	Assess otolith responses measuring torsional eye movements in off axis rotating chair.	Recommend appropriate drugs and side effect assessment techniques.
OMAN/ Visual Orientation and Spatial Memory and Countermeasures	• Inflight spatial disorientation & reference frame problems • Acute space motion sickness • Chronic space motion sickness	• Monitoring and diagnosis (assessment & prediction) • Training • Environmental manipulation	• Human, physical and virtual environments • Animal (Long Evans rat) in 1-G and parabolic flight	• Assess role of frame & polarity cues in human visual orientation • Determine 3D head direction cell coding in 1-G and 0-G.	Develop 0-G 3D spatial memory and navigation training techniques.	Implement preflight and inflight orientation training techniques, path marking techniques, interior layouts.

RESCHKE/ Modification of Eccentric Gaze Holding	• Re-entry & landing vertigo • Postlanding vertigo & visual instability • Peripheral & central vestibular changes	• Monitoring and diagnosis (assessment & prediction) • Training	Human, normals and cerebellar patients, tilted and on centrifuge.	Determine how body tilt and proprioception, and centrifugation influence centripetal drift of gaze.	Develop methods to determine whether gaze-holding is impaired following spaceflight, why it fails in patients, and how it can be remedied.	Develop training countermeasures to reduce gaze-holding deficits.
SHELHAMER/ Context-Specificity and Other Approaches to Neurovestibular Adaptation	• Re-entry & landing vertigo • Postlanding vertigo & visual instability	• Monitoring and diagnosis (assessment & prediction) • Training	• Human, 1-G sled and parabolic flight. • Animal (primate), sled	• Determine context cues for VOR and saccade adaptation, and effects of torsional misalignment in 1-G and parabolic flight. • Determine whether context specific adaptation transfers between eye and limb movements	Determine whether saccadic or cyclovergence adaptation may be useful countermeasures.	Develop appropriate assessment methods and context specific adaptation training countermeasure.
WALL/ Advanced Techniques to Assess and Counter Gait Ataxia	• Postlanding imbalance, vertigo & visual instability	• Monitoring and Diagnosis (Prediction) • Training • Prosthesis	• Human, walking on disturbance platforms and circular treadmill. • Tactile prosthesis.	Quantify body, head & gaze response to perturbed and circular walking.	• Develop portable locmotion disturbance platform for use at JSC. • Develop tactile prosthesis and dynamic balance exercises	• Define standards for postflight locomotion and gaze response to disturbance. • Evaluate effectiveness of tactile prosthesis and dynamic balance exercises

YOUNG/ Neuro-Vestibular Aspects of Artificial Gravity Created by Short-Radius Centrifugation	• Vestibular & biomechanical effects of artificial gravity • Acute space motion sickness • Chronic space motion sickness	• Monitoring and diagnosis (assessment & prediction) • Training • Environmental manipulation • Pharmacological agents	Human, short radius centrifuges and rotating chair.	Determine how context cues influence VOR, perception, and motion sickness adaptation, and which kind of conflict cues drive adaptation.	Determine optimal conditions for developing VOR and limb movement adaptation to Coriolis effects. Determine whether drugs affect Coriolis adaptation	In concert with other teams, develop short-radius, intermittent centifugation countermeasure for muscle, bone, cardiovascular, and vestibular reconditioning.

9.4 DESCRIPTION AND EVALUATION OF THE CURRENT PROGRAM:

NSBRI's neurovestibular research program is led by Dr. Charles Oman (MIT) assisted by Drs. Bernard Cohen (Mt. Sinai School of Medicine) and Conrad Wall (Harvard Medical School/Mass Eye and Ear Infirmary). The program consists of seven projects, three of which were initiated in 1997, and the remainder in 2000. Tables 9.1 summarize the risks, experimental paradigms, and countermeasure type targeted by each project. Project specific aims are tabulated in Appendix 1, and more details are available at www.nsbri.org. Note that most projects address several risks. Most of the projects resemble small NIH Program Project Grant, in that they involve multiple experiments conducted concurrently by multidisciplinary teams, and several involve collaborations between investigators at different institutions. The emphasis has been on physiological and behavioral research in humans, but three projects also utilize animal models. Our current project portfolio addresses – in part - all seven of the critical path risks. Most of the projects have countermeasures concepts defined and in development, (though two currently have not yet reached that stage). However, there remain significant strategic gaps in the current program, partly due to funding limitations and also to the particular thematic distribution of successful proposals obtained from the most recent NSBRI research announcement (NSBRI 00-001).

These strategic gap areas include:

- Vertigo on rentry and landing.
- Vestibular/autonomic/emetic physiology
- Postflight neurovestibular rehabilitation
- Mechanisms and detection of pathological vestibular function change.

Vertigo on Rentry and Landing clearly represents a "Class I" risk to astronauts, as an episode – particularly in the process of landing – could potentially lead to the loss of the vehicle and her crew. Although the landing vertigo problem has been manageable on 1-2 week missions, it is likely to become a significant problem if shuttles remain in orbit (e.g. docked with ISS) for longer periods, and if night landings become more common. This risk currently has the highest NSBRI vestibular program priority, but was not formally identified until after the current round of projects was selected. McClusky, Clark, and Stepaniak (2001) found shuttle landing flight technical error (height over threshold, and distance, vertical velocity, and airspeed speed errors at touchdown on 9 missions) correlated with intensity of postlfight neurologic symptoms (9 missions, 8 subjects). Vestibular and related somatosensory factors may have contributed to pilot induced oscillations on several Shuttle landings. JSC flight surgeons confirm that vestibular disturbances are commonly more severe after ISS increments than after short duration shuttle flights. Shuttle pilots practice landing procedures on orbit using laptop flight simulators, but cannot experience the vehicle accelerations or make head movements in a gravitational environment until the actual re-entry is flown. Though Shuttle pilots are aware of the danger, and voluntarily limit head movements, vehicle accelerations cannot be avoided. Vertigo and nystagmus cause well known difficulties reading flight instruments and displays. The Shuttle has some autoland capability, but it is not available at all landing sites. Autoland

capability does not completely resolve the problem, since pilots must still have sufficient visual acuity to monitor displays used in landing. Reentry vertigo has been recognized since the earliest days of the Shuttle program, but its operational significance has probably been masked by the traditional "can do" attitude of military-trained pilots who believe they can concentrate on their instruments and "fly through" episodes of vertigo. The Shelhamer and Reschke projects indirectly address some aspects. However none of our current projects focus specifically on rentry disorientation, acuity loss due to vehicle and/or head movement, or and resulting inappropriate control flight path error. Research is needed to document the head movements and vehicle accelerations pilots experience, and to better understand the types of otolith-tilt-translation-reinterpretation, G-excess-like and other somato-gravic illusions they produce. Controlled tests on recently returned crewmembers in motion simulators and the Shuttle Training Aircraft will probably be needed so that its then possible to develop an appropriate 1-G experimental simulation, and design improved procedures, controls and displays. Countermeasures to pre-adapt crewmembers or display/flight control changes and training procedures which reduce disorientation and flight technical error will be required.

Acute space motion sickness also represents a Class I risk during EVA, since the Shuttle space suit ("EMU") has no containment bag. In 1980s, Hamilton Standard (P. Heimlich) noted vomitus in the LiOH canister creates exothermic reaction, and shuts down EMU primary vent loop. Frozen vomitus in secondary vent nozzle could shut down the secondary vent loop, leaving only a few minutes of residual in suit O2 remaining. Vomitus is biologically active, so if there is an episode, the suit cannot be reused unless completely refurbished on the ground. Vomitus volume could be somewhat reduced by eating/drinking less frequently, but this is often inappropriate. Modifying the suit to include a vomitus containment receptacle has been considered, but is expensive and may be impractical. Risk is serious if emergency EVA is required. Risk exposure currently is currently reduced by prohibition of non-emergency EVAs before flight day 3. One in-suit vomiting episode has occurred, but before actual EVA began. Acute vomiting episodes – even during IVA – are momentarily disabling. Drug or behavioral countermeasures are needed which reliably and quickly reduce probability of vomiting. Feasibility of EMU modifications to reduce susceptibility or provide containment should be reinvestigated. Opening the early-mission window for EVA by 1-2 days will add useful flexibility in mission planning, and improve overall STS-ISS productivity. In addition to new agents, improved methods of rapid drug treatment which are less painful than the present method of intramuscular injection, and which could be used for treatment during EVA are highly desirable. Currently the Dornhoffer and Young neurovestibular projects, and the Putcha project on the Smart Medicine team are looking at some aspects of drug effectiveness, delivery systems, and side effects, but a broader effort – perhaps involving new drugs and techniques – and research to define the physiology of the vestibular-emetic linkage is needed. The vestibular/autonomic/emetic area is challenging because of its interdisciplinary aspects. The physiological basis of the sensory conflict theory and the linkage to emetic centers remains unknown. Existing anti-motion sickness drugs have been empirically discovered. A breakthrough in vestibular/autonomic/emetic physiology could have important implications for development of targeted pharmacologic countermeasures. NASA and NIH have not provided major funding for vestibular-emetic research since the early eighties. However new research avenues have been potentially opened in the intervening years the development of modern molecular neuroscience and functional imaging techniques. Given the almost universal human

susceptibility to motion sickness, basic research in this area could yield dramatically important results.

Postlanding imbalance, vertigo, visual instablility, and orthostatic hypotension remain concerns for all Shuttle and ISS crewmembers, particularly in the event an emergency requires rapid egress from the vehicle. Although recent cardiovascular and neuromuscular countermeasures have been successful on ISS, neurovestibular balance problems remain a problem for some individuals. Many returning crew tested cannot run 1000 ft on a treadmill. It is clear that the problem is not entirely due to changes in muscle strength or fatigability. Some crewmembers find that they need days to weeks to recover normal locomotion, and some have troubled by "0-G flashbacks", which are a concern when driving a car, riding a bicycle, or flying an aircraft. Countermeasures are therefore needed to assess their fitness for return to activities of daily living, and also the special avocational activities of an astronaut. Currently the Wall and Bloomberg projects are developing postflight locomotion and visual acuity assessment techniques, and investigating possible methods to pre-adapt returning crewmembers, to mitigate the risk of injury resulting from an accidental fall. The Shelhamer and Reschke projects address related oculomotor aspects. The Wall project is investigating the possibility of providing a balance prosthesis for returning crewmembers, but a broader effort is needed in the area of neurovestibular rehabilitation of crewmembers. The latter is, in turn, part of the larger challenge of postflight multi-system astronaut rehabilitation. NSBRI's nutrition, physical fitness, and rehabilitation program has not yet had resources to work in this area. An integrated, multidisciplinary, practical approach is essential. However, most of the clinical techniques used today are empirical, guided by qualitative theories about the relative advantages of adaptation vs. sensory substitution. Hypothesis-driven research techniques and quantitative assessment techniques are only slowly entering the field. Astronauts differ physiologically from vestibular patients in important ways. There is no widely accepted 1-G research analog for the space environment that can be used for neurovestibular rehabilitation studies in a manner analogous to the way bed rest or leg suspension in neuromuscular rehabilitation studies. It is not clear how to optimize the readaptation and functional recovery of returning flight crews, or how neurovestibular, neuromuscular, bone, and cardiovascular rehabilitation techniques may interact. NSBRI's Cardiovascular and Chronobiology teams have been interested in the question of vestibular contribution to cardiovascular orthostatic regulation, and projects led by Ray and Morin are currently investigating this. Further neurovestibular research is needed to determine the functional importance of the vestibular contribution to postflight hypotension in humans, and to evaluate potential countermeasures (e.g. inflight centrifugation).

Inflight spatial disorientation, navigation and reference frame problems have a higher incidence among crewmembers inside space stations (Mir, ISS) than on Shuttle, due to their more complex 3D interior architectures (Richards, et al, 2001). Shuttle crewmembers visiting Mir frequently became lost. Cognitive reference frame problems complicated the Mir crew's response to the collision with the Progress spacecraft in 1997. On ISS, crew debriefs have documented operational errors and robotic teleoperation problems caused by multiple frames of reference and visual reorientation illusions. Oman's project has been defining the visual cues which contribute to static orientation perception, and developing potential countermeasures for spatial memory problems, include preflight visual orientation and navigation training – perhaps

using appropriate virtual reality techniques or ground simulators – and revised, evidence based human factors standards for spacecraft architecture and egress path signage. Additional research is also needed on EVA and teleoperation related issues: Shuttle and RMS operators say it is difficult to interrelate three dimensional information concurrently displayed in several different reference frames. Mir and ISS crewmembers occasionally report height vertigo when the Earth is in their lower visual field, and for some the experience has been momentarily disabling. The lack of visual references cues during the dark half of each orbit has caused disorientation and concern among some ISS EVA crew.

Chronic space motion sickness symptoms affect 75% of crewmembers to some degree during the first 3-5 days in space, and impair the average physical and mental efficiency of crewmembers, and cause profound somnolence, nausea related inability to follow procedures, and loss of initiative. The impact on operational capability of the crewmember equals or exceeds the somnolence produced by other aberrant circadian cues associated with spaceflight. Though acute space sickness problems are generally confined to the first week, several cases lasting weeks have been noted in the Russian program, and there is reason to believe chronic low grade symptoms ("sopite syndrome") may persist in some crewmembers for weeks. Existing drugs were developed to prevent and treat acute space motion sickness, and have significant side effects. They may not be the best agents for treating chronic space motion sickness symptoms. The Dornhoffer and Young projects are currently investigating the effects of several anti-motion sickness drugs on eye movements and rates of adaptation, sensory gating, time perception, and learning. Other potential countermeasures include techniques or drugs which accelerate adaptation to weightlessness, or which to block or treat symptoms without unacceptable cognitive or circadian side effects.

Artificial gravity (AG) remains a potentially important multi-system countermeasure for neuromuscular, bone, cardiovascular and neurovestibular dysfunction in 0-G. As a neurovestibular countermeasure, AG is a double-edged sword: it likely could be used to pre-adapt crewmembers for return to planetary gravity. However, the Coriolis effects on inner ear endolyph flow and on moving limbs creates disorientation, nausea, vomiting and loss of coordination whenever the movement is not along or about the axis of AG system rotation. Unless the head and body are mechanically restrained, motion sickness can be a serious problem. Coriolis problems can be reduced by employing a large radius, but large radius AG spacecraft systems are likely several decades away. However, short radius (2-3 m) systems could be developed now which fit inside Shuttle or an ISS module. In a rotating artificial gravity environment, with the body's principal oriented perpendicular to the axis of rotation, the direction and magnitude of the vestibular Coriolis effects depend on which way the crewmember happens to be facing. The extent to which a person can adapt in a context specific way to vestibular and biomechanical Coriolis stimuli was unclear, and has been the major focus of the Young project. Establishing the values of AG system radius and RPM, and the duration/repetition rate of AG sessions which are effective for neuromuscular, bone, cardiovascular and neurovestibular therapies remain a NSBRI wide priority.

Pathological peripheral and central vestibular function changes potentially could occur after long duration exposure to 0-G, radiation, or environmental toxins, stress, isolation, or body immobilization, however relatively little is yet known about these phenomena. There is no

conclusive evidence that prolonged (months to years) exposure to 0-G produces irreversible vestibular changes, but only half a dozen individuals have yet flown beyond 6-8 months, and to a large extent we lack the diagnostic techniques, analogous to clinical audiometric testing, sensitive enough to detect such changes at an early stage. We cannot confidently predict the potential long term effects of weightlessness (including systemic changes in body calcium for example) on the vestibular end organs, on the otolith-ocular and otolith-spinal reflexes, and know if they are reversible. The Wall, Bloomberg, Shelhamer, Dornhoffer and Reschke projects are working on improved methods for quantitative assessment of vestibulo-ocular and postural reflexes. However, there is no program yet in place for long term follow up of long duration crewmembers. Anatomical changes have been seen in vestibular sensory epithelia in animals on flights of several weeks and longer, but the functional significance of these changes is unclear. The effects of radiation exposure on the vestibular end organs and central vestibular system (e.g. brain stem, cerebellum, thalamus, hippocampus) have not been established. The effects of gravity on the formation and distribution of otolith crystals within the labyrinth is not well understood. Loose otoconia will presumably float benignly in 0-G, but returning crewmembers may be susceptible to disorienting effects (e.g. canalithiasis) during landing and postflight.

The neurovestibular team expects to maintain a strong record of scientific productivity. As of the spring of 2002, 23 manuscripts were published or submitted. Between 1997 and 2000, the initial 3 projects published 14 journal articles, along with 3 reports, 6 graduate theses, 23 abstracts, with 15 manuscripts accepted or in review. Eight articles have been accepted for a special issue of the Journal of Vestibular Research in 2003. Eleven graduate students and 10 postdoctoral trainees participated in the research. Two students interned at NASA JSC, and one is now employed there. In addition, progress is reported annually in written and oral presentations to the NSBRI External Advisory Council. There are significant inter-project and inter-team collaborations and coordinations, as shown in Table 9.2. For example, Drs. Wall, Oddson and Bloomberg are coordinating their locomotion research, and developing a portable locomotion testing platform. Dr. Minor (Shelhamer project) has assisted Dr. Taube in developing a semicircular canal blocked animal preparation. There is a strong interaction with NASA JSC. Drs. Shelhamer, Solomon, and B. Cohen are working with JSC clinical colleagues on development of a postflight neurological assessment battery. Drs Wall and Oddson are constructing a portable locomotion test platform for the Neurophysiology lab at JSC. Dr. Shelhamer serves on the JSC Medical Branch Neurophysiology Integrated Project Team. Dr. B. Cohen serves on the Critical Path Project Review Board. Dr. Oman, Mr. J. Richards, Dr. J. Clark (JSC) and Dr. Marshburn (JSC & Smart Med. Team) prepared a retrospective summary of Mir neurovestibular episodes. The team maintains a web site to provide project science details. Drs. Wall and Oman worked with members of the NSBRI Education and Outreach Team at Harvard Medical School to develop a vestibular case study for use in high schools ("Cecilia's Story"), and Dr. B. Cohen participated in the summer high school outreach teaching program at Mt. Sinai. The team has held panels at the Aerospace Medical Association and Neural Control of Movement meetings. The team also co-sponsored the 6th Symposium on the Role of the Vestibular Organs in Space Exploration in Portland, Oregon Oct. 1-3, 2002. This symposium was a satellite to the concurrent Barany Society meeting, and continued the series initiated at Pensacola in the 1960s and 70s. The symposium provided an opportunity for team members to

present their results, and interact with more than a hundred other investigators from the NASA NRA program, and the international neurovestibular scientific community. Further symposia are planned at three year intervals.

Table 9.2. Integration Activities

	BLOOMBERG **Full Body Gaze Control**	**DORNHOFFER** **Pharmacological Countermeasures**	**OMAN** **Visual Orientation & Spatial Memory**	**RESCHKE** **Eccentric Gaze Holding**	**SHELHAMER Context Specific Adaptation**	**WALL** **Gait Ataxia**	**YOUNG** **Artificial Gravity**
Internal Communication	H. Cohen	• Garcia-Rill • Paule • Wyuts • Van DeHeyning	• Howard • Shebilske • Taube • Harris • Jenkin • Liu • Stuerzlinger	• Paloski • Wood • Leigh • Kornilova	• Minor • Zee • Angelaki • Zhou • Wu	• Raphan • Bloomberg • Oddson • Raphan • Solomon	• Young • Hecht • Mast • DiZio • Lackner • Paloski • B.Cohen
Integrated Experiment Development	Integrate with JSC postflight protocols	• Integrated Test Battery (P50 AEP, time perception, short term memory, learning) • OT assymetry	0-g parabolic flight HD Cell (Oman/Taube) Spatial memory experiments (Oman/Shebilske)	Leigh and Wood	Semicircular canal plugging technique (Taube/Minor).	Raphan & Wall Compare separate and combined countermeasures.	Young and DiZio/Lackner
Sample Sharing	Collaborative experiments using Balder Platform with Wall/Oddson	Dornhoffer and Wyuts		Coordinate US (Reschke) and Russian (Kornilova) data collection and analysis			
Synergistic Studies of Opportunity	Coordinate neuro-rehabilitation with Lupton (Nutrition & Fitness) nd with JSC Neurophysiology Integrated Project Team	• Coordinate with Putcha drug research project (Smart Med Team).	Coordinate performance assessment method development with Neurobehavioral team. Visual display techniques developed by Howard used by Oddson; also Wood&Meck (Cardiovascular team)		Coordinate development with JSC Neurophysiology Integrated Project Team	• Coordinate rehabilitation with Lupton (Nutrition & Fitness). • Coordinate with NIH and DOD vestibular prosthesis development	• Planning of human-powered centrifuge (Bone, Nutrition & Fitness, Cardiovascular, Neurovestibular)

9.5 OBJECTIVES AND STRATEGIC ACTIVITIES

The objective of NSBRI's neurovestibular adaptation research program is to develop countermeasures against the vestibular risks of space flight. NSBRI research teams normally particpate in steps 1-7 of the countermeasures development process. After the neurovestibular problems are initially discovered and phenomenologically described (phase one), our NSBRI research team hypothesizes the physiological mechanisms and/or cognitive processes responsible for neurovestibular risks; performs the necessary focused mechanistic research to validate these hypotheses (phase two); formulates potential countermeasures, and then does the ground and/or parabolic flight experiments to establish their efficacy (phase three). Basic research (CRLs 1-3) was the focus during the initial years of the NSBRI program, and still may be an appropriate project component, but in the coming years the major project focus should be on definition, development and feasibility testing of specific practical countermeasure concepts (CRLs 3-7). Multidisciplinary approaches and mathematical modeling techniques are encouraged. Most research will initially be done in ground laboratories or in parabolic flight. We then work with JSC to evaluate whether the countermeasures are practical in an operational environment, sometimes via simulation(phase four), and an independent, non-advocate group reviews the case for using the countermeasure. The countermeasure is evaluated on the ground using surrogate subjects, and then ultimately in flight.

The specific long term goals of NSBRI's neurovestibular research program correspond to each of the seven space flight risk areas. An eighth programmatic goal – to develop improved methods for diagnosis and treatment of vestibular disorders on Earth is also identified. Tables 9.1-9.8 below outline the progression of research required to develop countermeasures for each risk area and goal - in an ideal program. Though the seven existing projects fit well within this framework, the the overall scope of a broad based neurovestibular program significantly exceeds the resources currently available.

Table 9.1 Achieving Goal 1: Reducing the risk of vertigo on rentry and landing

Countermeasure Development Phases

Phase 0: Observational & Phenomenological Research

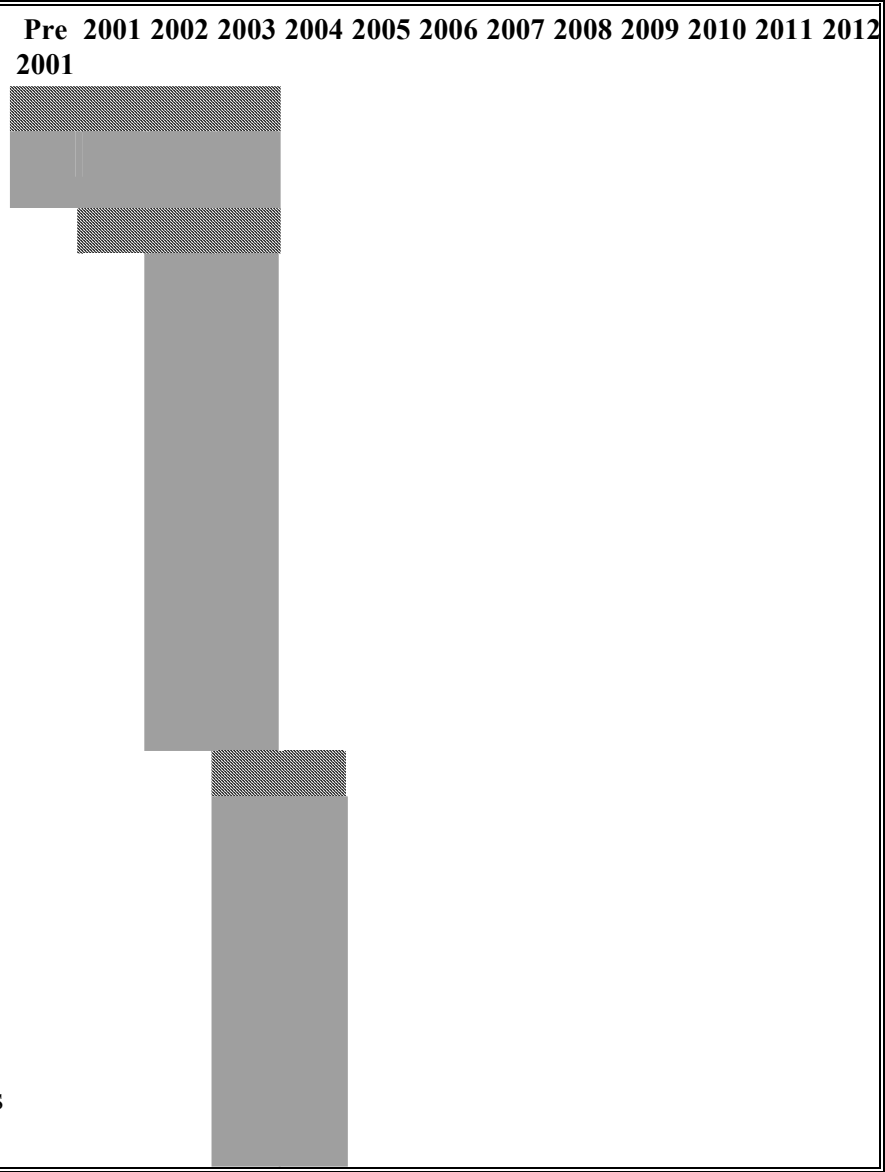
- Review existing data on effect of vertigo on shuttle flight technical error, postflight visual acuity, and gaze stability.

Phase 1: Focused Mechanistic Research

- Monitor and quantify shuttle pilot head movements, vehicle accelerations, and characterize the visual environment of the shuttle flight deck.
- Quantify incidence and magnitude of nystagmus, disorientation loss of visual acuity, gaze stability, and VOR components in returning crews.
- Quantify effect on simulated landing performance parameters.
- Define pilot tasks and head movements in manual, autoland, and emergency landings.
- Develop mathematical models for nystagmus, perception, manual control errors; vehicle loss scenarios.
- Quantify manual control and visual acuity loss under analogous disorientation conditions induced in simulators.

Phase 2: Preliminary Countermeasure Development Research

- Conduct simulations to define how changes in pilot role (supervisory vs. manual), procedures or head up/head down display format could reduce impact.
- Develop preflight training techniques to preadapt subjects to otolith-tilt-translation-reinterpretation and G-excess illusions.
- Use models and data to define potential procedural changes to reduce disorientation.
- Define and valuate potential in flight preadaptation techniques or in flight landing rehearsal countermeasures.



Phase 3: Mature Countermeasure Development Research

- Develop integrated landing vertigo countermeasure, and verify feasibility.

Phase 4: Countermeasure Evaluation & Validation

- Testing of integrated countermeasure procedure

Phase 5: Operational Implementation of Countermeasure Strategy

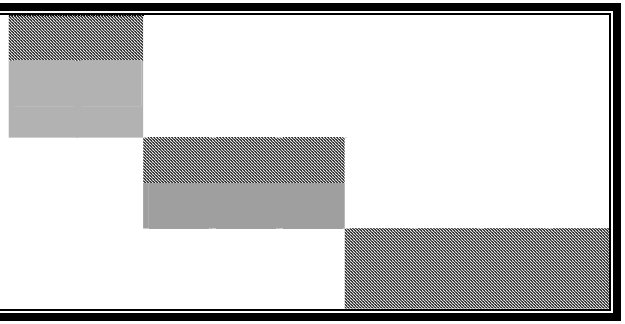


Table 9.2 Achieving Goal 2: Reducing the risk of acute space motion sickness

Countermeasure Development Phases	Pre 2001	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Phase 0: Observational & Phenomenological Research													
Phase 1: Focused Mechanistic Research													
• Determine side effects of existing anti-motion sickness drugs (e.g. effects on sensory-motor adaptation, eye movements, alertness).													
• Determine effects of 0-G on drug bioavailability and effectiveness.													
• Determine role of head movements, visual and haptic cues in triggering space motion sickness.													
• Evaluate potential non-pharmacologic countermeasures (e.g. parabolic flight preadaptation, movement restriction, haptic cues, biofeedback, etc.)													
• Define options for minimizing impact of vomiting episode in space suit.													
• Define physiological basis of sensory conflict and emetic linkage in animal models													
• Identify new pharmacologic agents which could specifically block the emetic linkage or increase rate of sensory-motor adaptation.													
• Determine what physiological factors determine individual susceptibility.													
• Determine role of brainstem and cerebellar mechanisms in adaptation.													
Phase 2: Preliminary Countermeasure Development Research													
• Develop anti-motion sickness drugs targeted at sensory conflict, emetic linkage or adaptive mechanisms using animal models.													
• Evaluate non-pharmacologic motion sickness countermeasures.													
• Develop improved drug delivery and side effect monitoring techniques.													
• Evaluate techniques for mitigating impact of EVA emesis.													

Phase 3: Mature Countermeasure Development Research

- Develop behavioral and pharmacological countermeasures and test in humans

Phase 4: Countermeasure Evaluation & Validation

- Testing of behavioral and pharmacological countermeasure.

Phase 5: Operational Implementation of Countermeasure Strategy

Table 9.3 Achieving Goal 3: Reducing the risk of postlanding imbalance, vertigo and orthostatic hypotension

Countermeasure Development Phases	Pre 2001	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Phase 0: Observational & Phenomenological Research • Postflight neurologic exams, posture platform and treadmill assessments. • Determine incidence of sensory-motor flashbacks.													
Phase 1: Focused Mechanistic Research • Develop reliable techniques for quantifying postural, locomotor and gaze control deficits in returning astronauts. • Determine how head and body motor strategies influence visual acuity and ability to stand, walk and run. • Determine whether training (e.g. "learn how to learn") helps normal subjects rapidly adapt to analog stimuli. • Determine whether there is a significant vestibular contribution to orthostatic hypotension and dizziness. • Determine physiologic basis for intra-individual differences in magnitude and duration of postflight symptoms and signs. • Determine effect of acute motion sickness on circadian and cardio regulatory systems.													
Phase 2: Preliminary Countermeasure Development Research • Develop normative database for postflight postural, locomotor and gaze assessment techniques, and relate test parameters to functional performance loss. • Define preflight and inflight preadaptation techniques. • Define and develop appropriate sensory aids to assist temporarily disoriented crewmembers. • Identify and evaluate potential neurovestibular and neuromotor rehabilitation techniques. • Identify potential operational changes which would reduce crew susceptibility to postflight injuries. • Determine whether vestibular-autonomic factors can be manipulated to decrease susceptibility to postflight orthostatic hypotension and dizziness.													

Phase 3: Mature Countermeasure Development Research

- Develop integrated countermeasures and test in human volunteers

Phase 4: Countermeasure Evaluation & Validation

- Testing of integrated countermeasure

Phase 5: Operational Implementation of Countermeasure Strategy

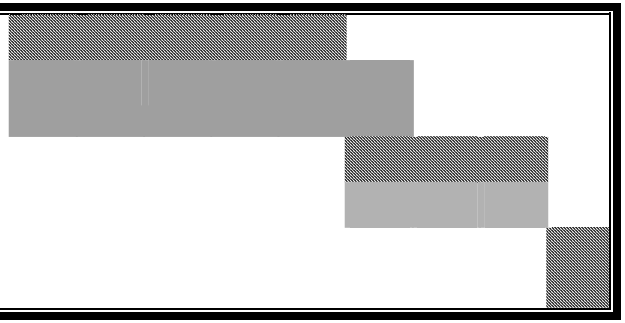


Table 9.4 Achieving Goal 4: Reducing risk of inflight spatial disorientation and reference frame problems.

Countermeasure Development Phases

Phase 0: Observational & Phenomenological Research

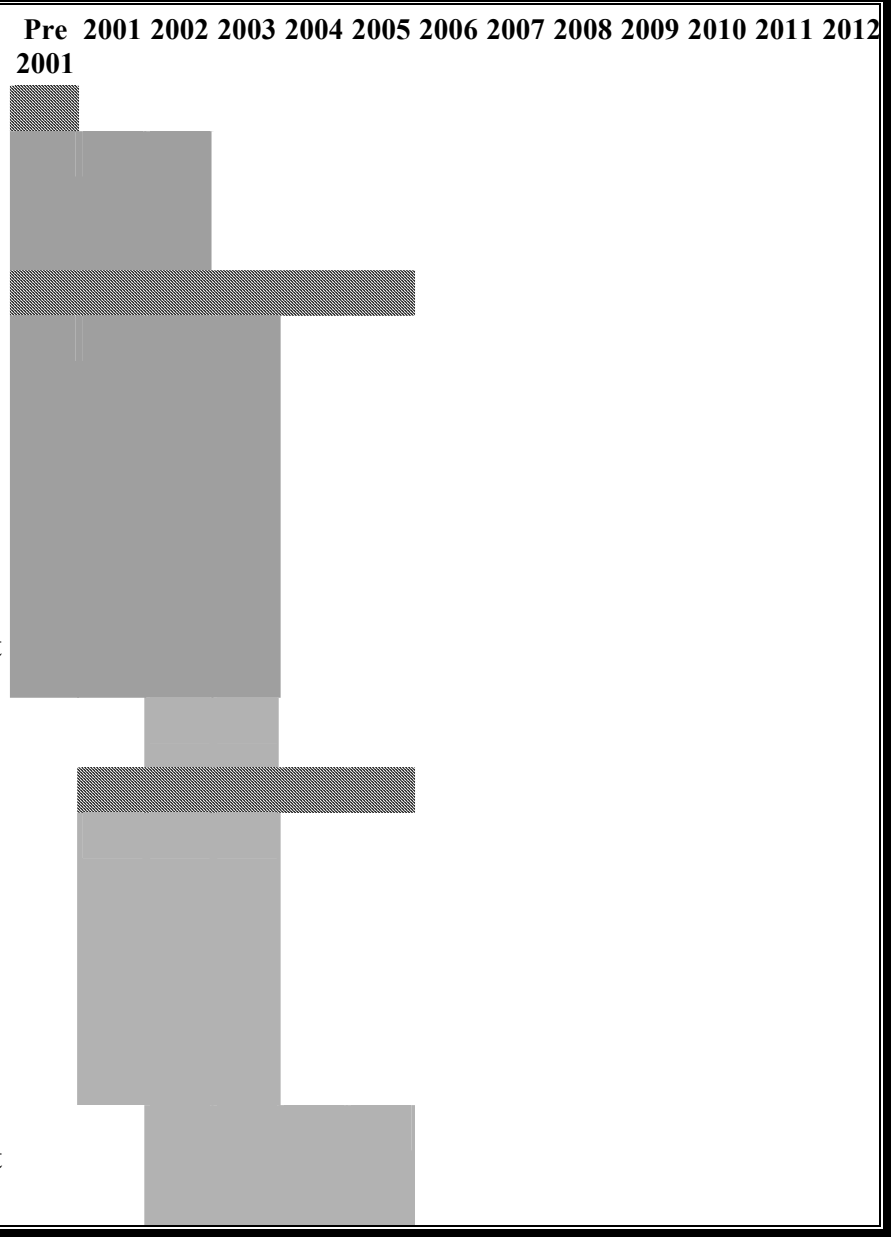
- Postflight crew debriefs, task analyses and workstation evaluations.
- Assess ISS remote manipulation controls and displays to define frame-of-reference issues.

Phase 1: Focused Mechanistic Research

- Determine how vestibular and environmental visual cues contribute to spatial disorientation, navigation, height vertigo and frame-of-reference problems.
- Determine how gravitational orientation of human subjects influences the relative weighting of sensory cues.
- Determine whether/how "place" and "direction" is neurally coded in 3 dimensions, and limits of human abilities to interrelate multiple reference frames..
- Develop techniques for assessment of individual mental rotation and spatial memory skills, and susceptibility to height vertigo.
- Evaluate use of virtual reality techniques for studies of EVA height vertigo.

Phase 2: Preliminary Countermeasure Development Research

- Develop generic (e.g. "learn how to learn") and/or environment specific training techniques (e.g. using virtual reality or neutral buoyancy) which could help normal subjects retain spatial memory while performing 0-G analogous tasks.
- Develop improved techniques for 3D egress path marking, "you-are-here" maps.
- Revise NASA Standard 3000 for spacecraft interior architecture and workstation layout.
- Identify operational changes which would reduce crew susceptibility to inflight spatial disorientation and EVA height vertigo.



Phase 3: Mature Countermeasure Development Research

- Develop countermeasures and test in human volunteers

Phase 4: Countermeasure Evaluation & Validation

- Testing of countermeasures

Phase 5: Operational Implementation of Countermeasure Strategy

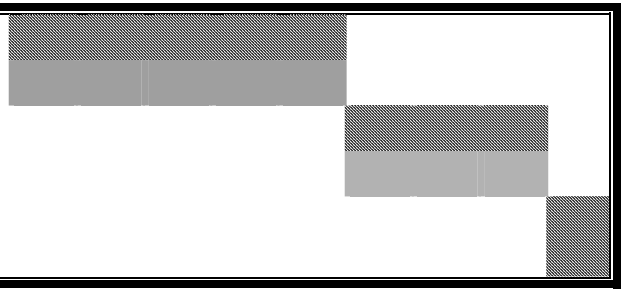


Table 9.5 Achieving Goal 5: Reducing the risk of chronic space motion sickness symptoms.

Countermeasure Development Phases

Phase 0: Observational & Phenomenological Research

- Correlate postflight crew debriefs, neurologic exams, retrospective task analyses, crew performance, diet, sleep, and drug use data.

Phase 1: Focused Mechanistic Research

- Identify anti motion sickness drugs and delivery methods suitable for longer duration administration, and which will combat sopite syndrome symptoms.
- Develop techniques to quantify attention deficits, somnolence, vigilance and short term memory loss in chronic motion sickness.
- Develop methods to quantify attention deficits, short term memory loss, ability to multi-task, somnolence, and vigilance.

Phase 2: Preliminary Countermeasure Development Research

- Test anti-sopite drugs on normal subjects experiencing chronic motion sickness symptoms (e.g. produced in rotating rooms or by prism wear). Evaluate for both effectiveness and cognitive and circadian side effects.
- Identify operational changes which would reduce crew susceptibility to and impact of chronic space motion sickness.

Phase 3: Mature Countermeasure Development Research

- Develop countermeasures and test in human volunteers

Phase 4: Countermeasure Evaluation & Validation

- Testing of countermeasures

Phase 5: Operational Implementation of Countermeasure Strategy

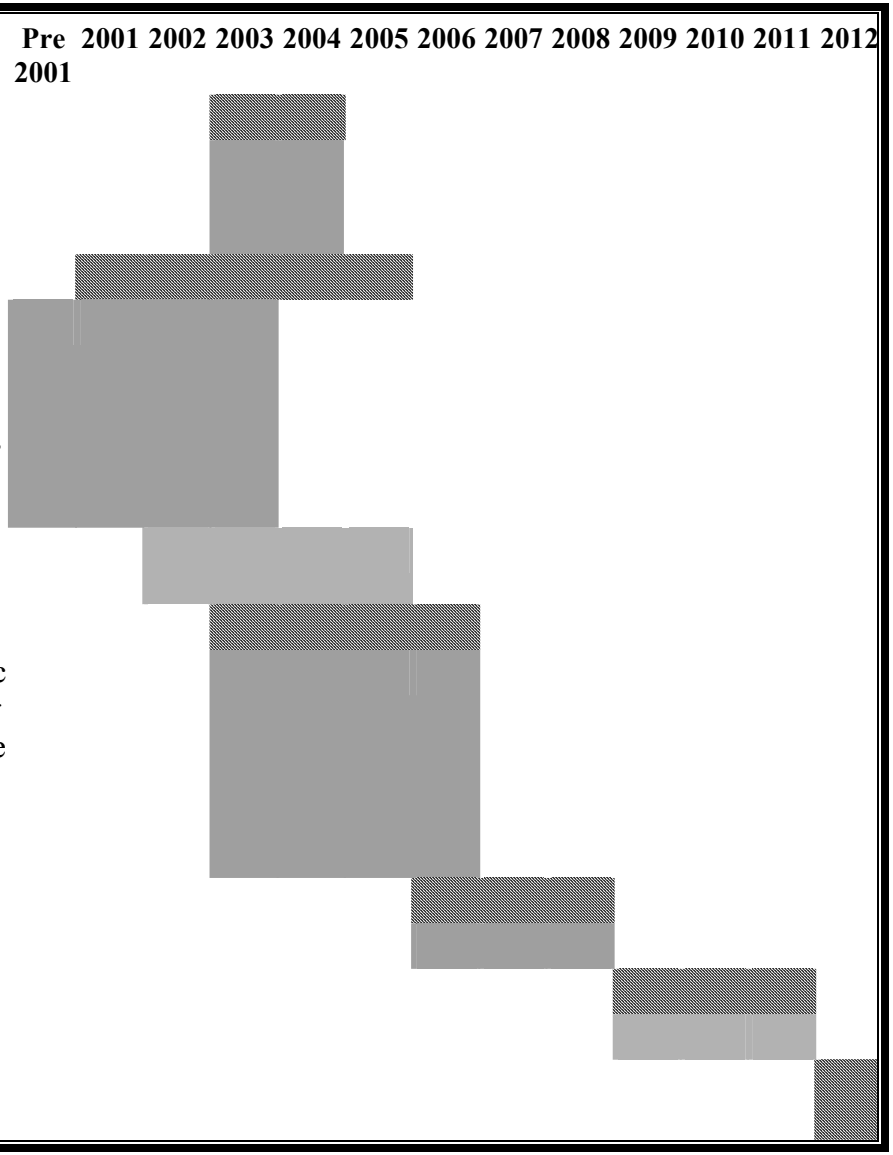


Table 9.6 Achieving Goal 6: Reducing the risk of artificial gravity related disorientation, nausea, vomiting and loss of coordination.

Countermeasure Development Phases	Pre 2001	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Phase 0: Observational & Phenomenological Research													
Phase 1: Focused Mechanistic Research • Determine whether human subjects show context specific oculomotor and sensory-motor adaptation to vestibular Coriolis stimulation. • Determine how radius, RPM, G level, duration, and repetition rate limits for subjects oriented perpendicular to the angular velocity vector. • Determine whether adaptation generalizes to different rotation environments. • Evaluate intermittent artificial gravity as a potential countermeasure for adverse cardiovascular, musculo-skeletal and neurovestibular effects of long duration spaceflight, using analog models.													
Phase 2: Preliminary Countermeasure Development Research • Evaluate short radius centrifuge designs for use as a multi-system countermeasure on ISS class missions. • Determine optimal adaptation schedule for chosen radius, RPM. • Define medium large radius centrifuge concepts for eventual use on planetary missions.													
Phase 3: Mature Countermeasure Development Research • Develop countermeasure protocols and test in human volunteers													
Phase 4: Countermeasure Evaluation & Validation • Evaluate prototype short radius centrifuge countermeasure in flight.													
Phase 5: Operational Implementation of Countermeasure Strategy													

Table 9.7 Achieving Goal 7: Reducing the risk of permanent vestibular function change .

Countermeasure Development Phases

Phase 0: Observational & Phenomenological Research

- Evaluate postflight crew debriefs and neurologic exams of long duration crew for evidence of irreversible vestibular changes, and exposure of crew to significant radiation or environmental toxins.
- Retrospective testing of vestibular function using currently available techniques of previously flown long duration crewmembers.

Phase 1: Focused Mechanistic Research

- Investigate effects of prolonged 0-G exposure on otolith formation and resorption, vestibular sensory epithelia in animal models, and identify potential mechanisms.
- Determine effects of potential environmental toxins (e.g. carbon monoxide, ethylene glycol) on central and peripheral vestibular function.
- Determine effects of radiation exposure on central and peripheral vestibular function.
- Determine the effect of age, stress, isolation, and immobilization on vestibular function.

Phase 2: Preliminary Countermeasure Development Research

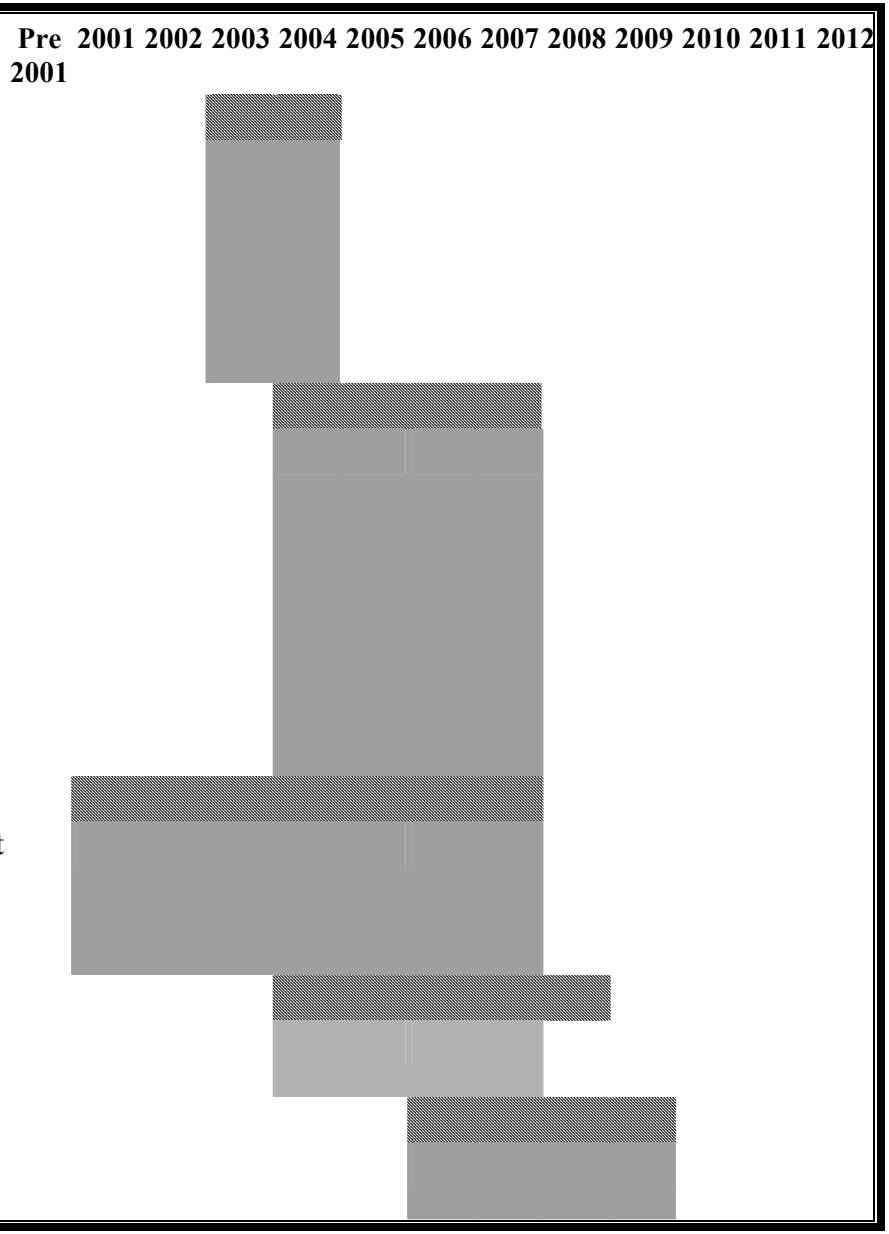
- Develop sensitive techniques for early detection of impairment of peripheral and central vestibular function.
- Develop appropriate evidence-based countermeasures, based on understanding of physiologic mechanisms.

Phase 3: Mature Countermeasure Development Research

- Testing of normals and vestibular patients using new techniques.

Phase 4: Countermeasure Evaluation & Validation

- If evidence for long duration changes warrants, continue countermeasure development.



Phase 5: Operational Implementation of Countermeasure Strategy

- Retrospective testing of previously flown long duration crewmembers using new techniques.

Table 9.8 Achieving Goal 8: Improving methods for diagnosis and treatment of vestibular disorders on Earth.

Countermeasure Development Phases	Pre 2001	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Phase 0: Observational & Phenomenological Research													
Phase 1: Focused Mechanistic Research • Define the physiological mechanisms responsible for otolith formation and resorption, and vestibulo-ocular, vestibulo-collic, and vestibulo-spinal reflex adaptation. • Define physiological basis of motion sickness, including sensory conflict and emetic linkage in animal models. Identify pharmacologic agents which could specifically block the emetic linkage or increase rate of sensory-motor adaptation. • Define the role of the vestibular system in cardiovascular regulation. • Determine effects of potential environmental toxins (e.g. carbon monoxide, ethylene glycol) on central and peripheral vestibular function. • Determine effects of radiation exposure on central and peripheral vestibular function. • Determine the effect of age, stress, isolation, and immobilization on vestibular sensory epithelia in animal models, and identify potential mechanisms.													
Phase 2: Preliminary Countermeasure Development Research • Develop anti-motion sickness drugs targeted at sensory conflict, emetic linkage or adaptive mechanisms using animal models. • Evaluate non-pharmacologic countermeasures for motion sickness. • Identify and develop sensory aids and rehabilitation techniques for use by vestibular patients. • Develop sensitive techniques for early detection of impairment of vestibular function with particular emphasis on diagnosis of otolith related pathologies. • Develop appropriate evidence-based countermeasures, based on understanding of physiologic mechanisms.													

Phase 3: Mature Countermeasure Development Research

- Testing of normals and vestibular patients using new techniques.

Phase 4: Countermeasure Evaluation & Validation

- Continue countermeasure development.

Phase 5: Operational Implementation of Countermeasure Strategy

- Deploy countermeasures in a clinical setting.

Some projects are transitioning research products beyond CRL5 this year. For example, the Wall project is finishing a locomotion evaluation platform which will be used by JSC in testing, and the Bloomberg project is using some components developed with NSBRI support in JSC astronaut testing. The Oman project is preparing a proposal for preflight astronaut spatial memory training, and a draft revision of NASA Standard 3000 for work area layout and architecture. The Young project team wrote a preliminary plan last year for potential use of an AG countermeasure on a proposed (but since cancelled) Shuttle/Spacehab mission. There have also been useful negative results. For example, Dornhoffer recently showed that lorazepam 1 mg. p.o. was ineffective against laboratory coriolis induced motion sickness.

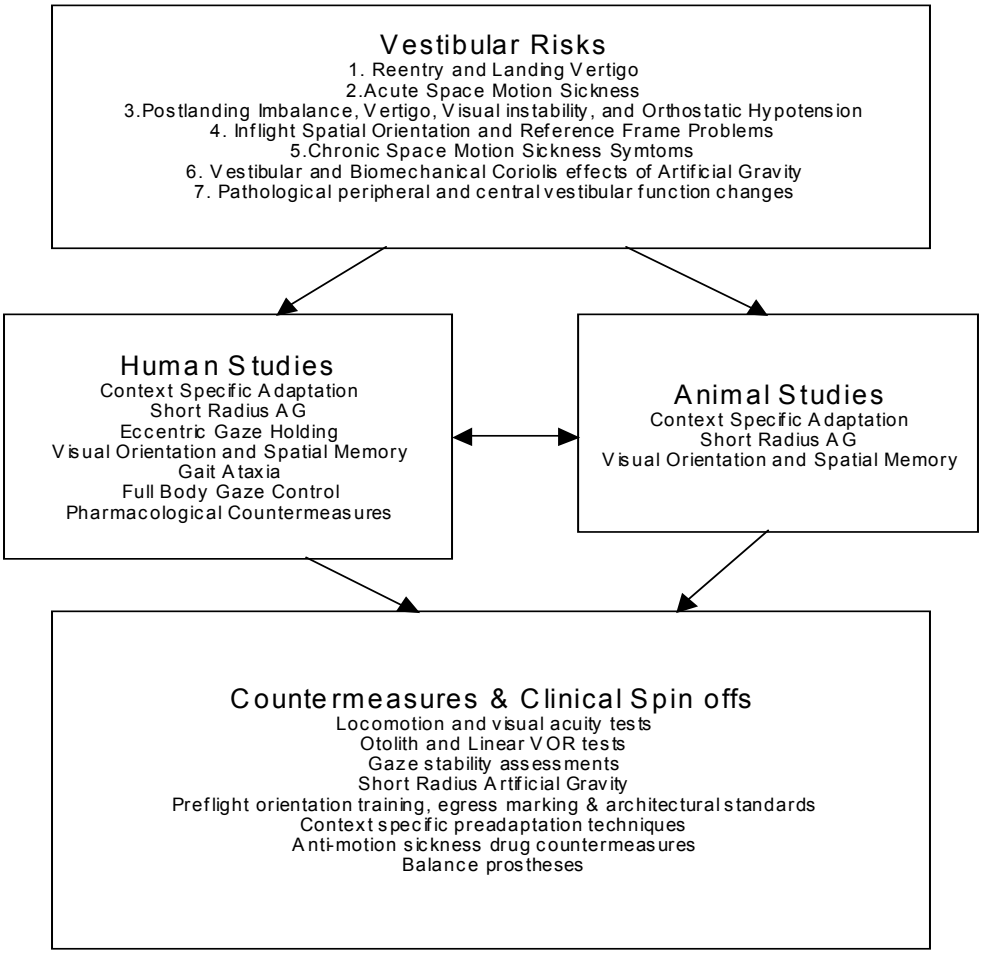
Realistically not all of the current countermeasures development efforts will be successful. Those projects which fail to generate countermeasures concepts (Step 3) will be discontinued . When countermeasures concepts prove ineffective (Step 4), the thrust of the project will be redirected. Developing an effective working relationship with our NASA scientific and clinical colleagues is a priority for our team during the next five years. Once countermeasure reliability is established assessment using preflight/postflight testing (e.g. locomotion and dynamic acuity tests) is relatively straightforward. Ground facilities needed for neurovestibular research include a neurovestibular testing laboratory for pre and postflight experiments, equipped with angular, linear, and artificial gravity stimulus devices, 3D eye movement, whole body kinematic, otolith, posture and locomotion testing and immersive VR display equipment. Access to the VMS Shuttle landing simulator and the Shuttle Training Aircraft for studies of landing vertigo and JSC immersive VR facilities for preflight visual orientation training is also forseen.

Other types of countermeasures (e.g. those involving environmental manipulations such as artificial gravity) can ultimately only be validated via spaceflight. The loss of the oribiter Columbia, NASA budget caps, ISS construction and the limits on the number of ISS crewmembers at “core complete” will significantly limit what can be accomplished in orbit during this decade. Eventually access to space flight and opportunities for sophisticated experimentation will increase. There are several basic human and animal neurovestibular experiments (associated with the hypothesis testing phase of countermeasures development level 3) that will eventually require access to ISS and Shuttle crewmembers preflight, inflight and postflight for large n longitudinal studies. Orbital research facilities include a short or medium radius human centrifuge for both neurovestibular adaptation research and countermeasure use. Also needed will be second generation eye, head, and body movement research equipment with capabilities beyond those currently aboard the ISS-Human Research Facility.

9.6 SUMMARY

During the next 3-5 year time span, through a balanced program of basic and applied research the neurovestibular team expects to define, understand and prevent or resolve many of the neurovestibular risks of spaceflight, and obtain important new insights which will have application here on Earth to the treatment of dizzy patients. It will require a multi-investigator, multi-disciplinary effort, carefully coordinated with JSC colleagues in neurophysiology and medical operations (e.g. postflight testing) and engineering (e.g. orbiter flight deck, EVA, and teleoperation

systems) and also with other NSBRI teams, particularly in the areas of artificial gravity (Cardiovascular, Bone, and Muscle teams), vestibular-autonomic function (Cardiovascular, Chronobiology), and drug development (Smart Medicine, Behavioral & Psychosocial). The emphasis will likely remain on human physiological and behavioral experiments, supported by mathematical modeling techniques and complemented where essential by studies in animals. Returning astronauts say that neurovestibular problems are the most overt ones associated with human spaceflight. In some phases of almost every mission, disorientation and vomiting present potentially life-threatening risks. In some NSBRI disciplines, there is hope that a single drug or technique could provide a "magic bullet" to eliminate a risk. Sensory-motor systems involve many complex, interacting physiological mechanisms, so resolution of the neurovestibular problems of spaceflight will require a broad effort, and may at first yield only incremental progress. However important practical breakthroughs are possible, and are well within the reach of a team that maintains a balanced view of the most important scientific, clinical and operational questions.



APPENDIX I

NSBRI Neurovestibular Adaptation Team project investigators, their institutions, the critical path risks addressed, experimental model, specific aims, countermeasure types and countermeasure development strategy of the seven current projects are:

Context-Specificity and Other Approaches to Neurovestibular Adaptation.
PI: Mark J. Shelhamer,
CoIs: Minor, Zee, Angelaki, Zhou, Wu.
Institutions: Johns Hopkins U. School of Medicine, Washington U., U. Mississippi Med Ctr.
Critical path risks addressed: 1. Vertigo on rentry and landing., 3. Postlanding imbalance and vertigo.
Experimental models: Human and animal (primate)
Countermeasure Types: assessment, prediction, training.
Current readiness level: 2
Specific Aims:

- Is torsional eye position a context cue for saccade adaptation ?
- Does a rest interval between stimuli promote adaptive consolidation ?
- Can cyclovergence adaptation provide a countermeasure to ocular torsion changes in parabolic flight ?
- How do pursuit and LVOR deficits correlate in cerebellar lesioned monkeys ?
- How do pursuit and LVOR adaptation transfer across frequencies in humans and monkeys
- Can LVOR adaptation be trained with pursuit stimuli, and how do cerebellar lesions influence adaptation.
- Does head tilt adaptation of saccades and VOR transfer to arm movements in monkeys ?
- What is the best way to induce context specific LVOR adaptation in humans ?
- Does the naso-occipial LVOR also show context specific adaptation ?

Neuro-Vestibular Aspects of Artificial Gravity Created by Short-Radius Centrifugation
PI: Laurence R. Young.
CoIs: Hecht, Oman, Mast, DiZio, Lackner, Paloski, B. Cohen,
Dai, M. Cohen, Welch, Stone.
Institutions: MIT, Brandeis, NASA-JSC, Mt. Sinai Hospital, NASA-Ames.
Critical Path Risks: 6. Artificial Gravity, 2. Acute space motion sickness, 5. Chronic space motion sickness
Experimental model: Human
Countermeasure Types: assessment, training, environmental manipulation, drugs.
Current readiness Level: 4
Specific Aims: Using short and medium radius centrifuges and rotating chairs, to determine:

- How context cues influence VOR, perception and motion sickness adaptation.
- What is the role of sensory-motor (non-vestibular) adaptation to AG ?
- What types of sensory conflict drive adaptation ?
- What are the optimal duty cycles and inter-session intervals ?
- Does body orientation re gravity provide a context cue ?
- In what way does adaptation generalize to different rotating environments?
- How does intermittent training influence the accuracy of head movements ?
- How does promethazine affect adaptation and eye movements in humans and monkeys ?

Modification of Eccentric Gaze-Holding,
PI: Millard F. Reschke
CoIs: Paloski, Kornilova, Wood, Leigh
Institutions: NASA-JSC, IBMP/Moscow, BCM, University Hospitals of Cleveland
Critical Path Risk: 1 Vertigo on reentry and landing, 3, postlanding vertigo, 7. peripheral or central vestibular changes.
Experimental model: Human

Countermeasure types: assessment, prediction, training.
Countermeasure Readiness Level: 2
Specific Aims:

- Effect of tilt and proprioception on centripetal drift time constant
- How rebound nystagmus provides adaptive compensation.
- How centrifugation influences gaze holding.
- Why adaptation fails in cerebellar patients.
- Whether gaze-holding is impaired immediately following spaceflight.

Visual Orientation and Spatial Memory.
PI: Charles M. Oman.
CoIs: Howard, Shebilske, Taube, Hecht, Harris, Jenkin, Liu, Stuerzlinger. Institutions MIT, York University, Dartmouth Medical School, Wright State University.
Critical path risk: 4. Inflight spatial disorientation and frame of reference problems, 2. Acute space motion sickness etiology.
Experimental models: Human and animal (rat)
Countermeasure types: assessment, prediction, training, environmental manipulation. .
Countermeasure Readiness Level: **5**
Specific aims:

- Human visual orientation. Effects of visual frame, polarity, brightness, motion, and gravireceptor cues on the subjective vertical, eye movements, and limb movements.
- Three dimensional spatial memory and spatial frameworks. Generic and environment specific preflight and onboard virtual reality training methods, interior architectural standards, and escape path countermeasure design and evaluation.
- Neural coding of spatial orientation. How do visual, vestibular, gravireceptive, proprioceptive, and motor pathways drive limbic head direction cells in the rat, as a model for visual reorientation illusions in astronauts.

Advanced Techniques to Assess and Counter Gait Ataxia
PI: Conrad Wall III
Co-Is:Bloomberg, Oddson, Raphan, Solomon.
Institutions: Mass Eye and Ear Infirmary, NASA-JSC, Boston University, Mt. Sinai Hospital, U. Penn.
Critical Path Risks: 3. Postlanding imbalance, instability, vertigo.
Experimental model: Human
Countermeasure types: assessment, prediction, training, prosthesis.
Countermeasure Readiness Level: 5
Specific Aims:

- Quantify body, head, & eye coordination during perturbed straight walking. And also:
- during straight and circular walking on a circular treadmill.
- while ascending/descending stairs.
- while wearing a tactile prosthetic countermeasure.
- assess effect of dynamic balance exercises.

Understanding Full-Body Gaze Control During Locomotion
PI: Jacob J. Bloomberg, Jacob
Co-I:H. Cohen.
Institutions: NASA-JSC, Baylor College of Medicine
Critical Path Risks: 3. Postlanding imbalance, instability, vertigo, and hyptension.
Experimental model: Human
Countermeasure types: assessment, prediction, training.
Countermeasure Readiness Level: 5
Specific Aims: How are eye, head, trunk, and lower limb movements coordinated. Specifically:

- How do eye, head, trunk, and legs absorb heel strike while treadmill walking? How do subjects adapt to magnifying and minifying lenses ?

- To reduced degrees of freedom, for example wearing a neck brace ?
- To wearing knee braces ?

Pharmacological Countermeasures for Space Motion Sickness.
PI: John L. Dornhoffer
CoIs: Garcia-Rill, Paule, Van De Heyning.
Institutions: U. Arkansas for Medical Sciences, National Center for Toxicological Res., U. Hospital, Antwerp.
Critical Path Risks: 2. Acute space motion sickness, 5 Chronic space motion sickness.
Experimental model: Human
Countermeasure types: assessment, prediction, pharmacological.
Countermeasure Readiness Level: 5
Specific Aims: (2 year project)

- What are the effects of lorazepam, meclizine, promethazine, and scopolamine on coriolis induced motion sickness symptoms ?
- How do these drugs affect reticular sensory gating (P50 double click auditory evoked potential), time perception, short term memory, and learning ?

---

[i] Note: The critical path project (criticalpath.jsc.nasa.gov) originally (1998) defined a set of five risks:

1. Disorientation and inability to perform landing, egress, or other physical tasks, especially during/after G-level changes (Acute spontaneous and provoked vertigo, nystagmus, oscillopsia, poor dynamic visual acuity)
2. Impaired neuromuscular coordination and/or strength (Gait ataxia, postural instability)
3. Impaired cognitive and/or physical performance due to motion sickness symptoms or treatments, especially during/after G-level changes (Including short term memory loss, reaction time increase, drowsiness, fatigue, torpor, irritability, ketosis)
4. Vestibular contribution to cardioregulatory dysfunction (Postlanding orthostatic intolerance, sleep and mood changes)
5. Possible chronic impairment of orientation or balance function due to microgravity or radiation (Imbalance, gait ataxia, vertigo, chronic vestibular insuffciency, poor dynamic visual acuity)

However, it was subsequently recognized that this set of five risks did not adequately describe the operational impacts of vestibular problems on long duration shuttle and ISS flights, or reflect the difference in mission criticality of landing vs. inflight vs. postflight disorientation, or the acute vs. chronic effects of space sickness. It was difficult to define a focused research program based on this set. Therefore, in early 2002 the Neurovestibular team redefined the risks and critical questions in this research area into the set described in this strategic plan.