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PI Name:	Wood, Scott J. Ph.D.		
Project Title:	Non-Pharmaceutical Motion Sickness Mitigation		
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Joint Agency Name:		**TechPort:**	No
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Comments:	NOTE: PI returned to NASA JSC in January 2017. PI was at Azusa Pacific University from August 2013 – January 2017; prior to August 2013, PI was at NASA JSC.		
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Contact Monitor:	Brocato, Becky	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2022 per PI (Ed., 7/7/21)		
Key Personnel Changes/Previous PI:	Dr. Reschke retired from NASA. Dr. Jaime Bogle from Mayo Clinic was added.		
COI Name (Institution):	Pradhan, Gaurav Ph.D. (Mayo Clinic Arizona) Stepanek, Jan M.D. (Mayo Clinic Arizona) Cevette, Michael Ph.D. (Mayo Clinic Arizona) Bogle, Jaime M (Mayo Clinic)		
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Task Description:	Alterations in vestibular sensory processing following G-transitions lead to perceptual and motion sickness upon return to Earth's gravity. The use of a non-pharmaceutical mitigation for motion sickness will have several potential advantages over drug treatment options. First, the treatment would be effective immediately and for as long as needed without having to maintain therapeutic levels in the blood-stream. Second, the treatment level could be customized and continuously titrated during re-adaptation to minimize side effects while enhancing performance. The goal of our project was to validate a non-pharmaceutical tool using galvanic vestibular reduction (GVR) to better mitigate G-transitional induced motion sickness following symptom onset while customizing the treatment level to maximize crew performance. Our first specific aim was to evaluate the effect of timing on the administration of our non-pharmaceutical treatment to motion sickness. While we have previously demonstrated that our approach can mitigate motion sickness if introduced prior to the provocative stimuli, one of the goals of this study is to determine the efficacy if we administer the treatment following the onset of symptoms. Validating the efficacy following symptom onset would alleviate the need for certifying the device to be worn within the landing suit and greatly enhance flexibility to implement this treatment during recovery operations. Our first hypothesis was that efficacy of galvanic vestibular reduction to reduce motion sickness severity will depend on the timing of the administration. We tested this hypothesis by exposing subjects to provocative Coriolis cross-coupling stimuli on a rotating chair using a repeated measures counter-balanced design to compare motion sickness severity across three treatment interventions: prior to stimulus onset (Prevention), following symptom onset (Rescue), and without GVR (Control). Symptom severity was assessed using both subjective reports and objective autonomic measures (electrogastrography). We expected that the most effective administration will be GVR delivered prior to the onset of symptoms, but that it will continue to be more effective relative to placebo control even if delivered following symptom onset. Our second specific aim was to evaluate the effect of GVR amplitude on functional fitness task performance. One disadvantage of pharmaceutical approaches is that increased drug dosage is often accompanied by sedative side effects that impact functional ability. In order to leverage our non-pharmaceutical technique that allows continuous adjustments in "dosage" level throughout recovery, we must map changes in GVR level with functional performance. Our second hypothesis is that functional task performance will decline with increasing levels of galvanic vestibular reduction. We will test this hypothesis by measuring performance on a sensorimotor and cognitive test battery in steps ranging from 0mA (control) to the level of GVR thought to provide maximal motion sickness protection (2.25mA). The test battery, conducted on the same subjects as specific aim 1, will include posturography, mobility (modified Timed Up and Go) as well as other oculo-cognitive metrics. The combined deliverable from both specific aims will be to validate the efficacy of GVR when customizing the stimulus level and introducing it following symptom onset, and to understand the effects of this non-pharmaceutical approach on crew performance on functional task performance.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our project explored a non-pharmaceutical countermeasure approach using galvanic vestibular reduction (GVR) that can be customized to mitigate G-transitional induced motion sickness while optimizing sensorimotor and cognitive performance. The ability to treat motion sickness with non-pharmaceutical approaches has the benefit to not only avoid sedative side effects of the medication but also allow for flexibility to turn the treatment on and off without residual effects associated with drug metabolism. Cevette et al. (US Patent, 2014) previously measured a reduction in motion sickness symptoms and changes in electrogastrography in the GVR treatment group when external visual cues were presented through a virtual window misaligned with the vehicle direction. This technology, while still at a relatively low readiness level, has potential utility for mitigating motion sickness in terrestrial military and commercial applications (e.g., autonomous driving vehicles) with limited or misaligned external visual cueing. Understanding the operational impacts will provide a more informed evidence base for implementing this type of tool into operational settings.
	This study was conducted at the Aerospace Medicine and Vestibular Research Laboratory in Scottsdale, AZ and the test protocol was approved by the Mayo Clinic Institutional Review Board. All subjects provided a written informed consent before participating in the study. Twenty-nine healthy subjects (32.0 ±9.1 y mean ±std, 16 male/ 13 female) were recruited to participate in a repeated measures design involving four test sessions. Subjects completed a medical history questionnaire confirming they had no known history of vestibular pathology. Subjects completed a short version of a standardized motion sickness susceptibility questionnaire (MSSQ-short, Golding 2006), and recorded a simple 5 point self-rating of susceptibility from 0 = none to 4 = extreme. During the initial session all subjects were exposed to the galvanic vestibular reduction (GVR) stimulus and completed a battery of balance, mobility, and oculo-cognitive tests to evaluate the effect of GVR amplitude on functional fitness task performance. Two male subjects were unable to complete all of the testing. The remainder of the 27 subjects (32.2 ±9.4 y mean ±std, 14 male/ 13 female) completed three motion sickness sessions using a counter-balanced cross-over design to compare motion sickness severity across three treatment interventions: (1) Prevention: GVR on throughout stimulus testing, (2) Rescue: GVR on following symptom onset, and (3) Control: no GVR. The motion sickness sessions were scheduled several days apart (20 ± 40 d, mean ± std) to minimize carry-over (e.g., habituation) effects across sessions. Galvanic vestibular reduction stimulation: Galvanic vestibular reduction was delivered using a proprietary system developed at the Mayo clinic laboratory. This utilizes a multi-channel commercial galvanic stimulator (Good Vibrations Engineering Ltd, King City, ON) with custom software. The stimulator bidirectionally delivered a sinusoidal profile (2.5 Hz) with variable amplitudes from ±1.75 to ±2.25 mA to provide matching cathodal or anodal currents simultaneously to each mastoid. Motion sickness stressor: Each of the three sessions involved a series of trapezoid velocity profiles with acceleration (6 º/s2) up constant velocity of 60 º/s for 2.5 min during which 7 forward (chin to chest) and backward (return to upright) head movements were cued every 10 seconds. Although the head position was not measured, the typical range of motion for head flexion in young healthy adults is 60º. Subjects were tested in a dark room with their eyes closed and audio cueing over a chair-fixed speaker to pace the head movements and allow operator-subject communications throughout the protocol. Since the GVR stimulus was chair mounted and needed to be turned on manually, the 2 min pause between rotations was required to allow the operator to turn on the GVR during the rescue sessions. This pause also allowed time for symptom recovery and in part led to a higher-than-expected number of subjects who did not reach the symptom endpoint during the control session. Symptom reporting: During the 2 min pause between head movement sets, symptom scoring was obtained using the Pensacola Diagnostic Index (PDI) and a Subjective Discomfort Rating (SDR). The PDI provides an acute score derived

	using diagnostic criteria introduced by Graybiel et al. (1968) by obtaining the subjective intensity of eight different modalities of symptoms and signs reported on a “slight/moderate/severe” basis used to derive a weighted “malaise index”. The symptom endpoint for stopping the test was a PDI score of 8 pts, considered severe malaise. We also used the PDI to determine when to initiate the GVR during the Rescue session. During these sessions, the GVR was initiated with a moderate malaise (PDI = 3), or following 4 sets of head movements, whichever came first. The SDR used a subjective magnitude estimation scale of 0-20, with 20 indicating vomiting (Oman et al. 1986), similar to what has been used for Field Tests and Spaceflight Standard Measures. If GVR effectively suppresses vestibular sensitivity, we hypothesized subjects would experience lower symptom scores, and be able to perform more head movements before reaching the endpoint. An objective measure of sickness was also obtained using the physiological response of gastric myoelectric activity, known as the electrogastrogram (EGG). These EGG recordings were analyzed to derive the dominant power instability coefficient (DPIC) as an index for motion sickness. DPIC quantifies the stability of the power of the dominant frequency – higher DPIC values indicate higher gastric dysrhythmia, presumably in this case due to motion sickness.
Task Progress:	Motion perception reporting: A chair-mounted joystick was used to obtain objective measures of motion perception in three-dimensions during the pitch head movements. During the head movements, subjects experienced a combination of yaw rotation from the persisting horizontal canal response to the angular acceleration of the chair rotation, pitch tilt from canal, otolith and cervical cues associated with alternating the head between upright and chin-to-chest positions, and Coriolis cross-coupled roll canal cues associated with aligning the roll plane of the head relative to plane of rotation. As the horizontal canal response decays, the conflicting cues from the cross-coupled roll canal cues and otolith cues of pitch head tilt give rise to the nauseogenic effects. Subjects were trained to indicate the direction and magnitude of perceived pitch and roll tilt using the joystick so that the maximum deflection represented the magnitude of the pitch forward and backward movement. If GVR effectively suppresses vestibular sensitivity, we hypothesized subjects would experience reduced pitch and roll tilt sensation during GVR versus the control condition without GVR. Sensorimotor cognitive test battery: Our second specific aim was to evaluate the effect of GVR amplitude on functional fitness task performance. This aim was important to understand how GVR may impair performance over the range of stimulus amplitudes (0 to 2.25 mA) used to treat motion sickness. This test battery utilizes both dynamic posturography as well as a modified timed up and go (TUG) locomotion task. A third test in the battery was designed to measure cognitive performance indicators during variable workload through eye movement features. The Oculo-Cognitive Addition Test (OCAT, Pradhan et al. 2022) tracks eye movements as the subject sums three consecutive single-digit numbers displayed at various positions around an infinity-loop pattern to elicit saccades in horizontal, vertical, and diagonal directions. RESULTS: Fifteen of the 27 subjects were not susceptible to the motion stressor (i.e., did not reach an endpoint in the control condition). While the time to endpoint, or number of head movements, did not significantly vary across the three GVR conditions in the remaining subjects, the symptom levels were significantly delayed during the Prevention session when GVR was on throughout the testing. Initiating GVR following symptom onset did not appear to alter the symptom progression nor time to motion sickness endpoint. Based on the joystick measures, GVR significantly modified the perceived roll and pitch sensation during head movements, reducing the amplitude of tilt in most subjects. It is important to note that comparable levels of GVR did not impair performance on the functional test battery including mobility, balance, and oculometric tasks. DISCUSSION: Our findings suggest GVR may be useful in reducing disorienting roll and pitch illusions and delaying the onset of motion sickness. Further enhancements will be required to individualize the stimulation amplitude and optimize the waveform delivery. Adapting this non-pharmaceutical countermeasure approach to allow self-administered titration of current amplitude during recovery would enable transfer to post-flight treatment, perhaps combined with a pharmaceutical approach to mitigate G-transitional induced motion sickness. REFERENCES: Graybiel A, Wood CD, Miller EF et al. (1968) Diagnostic criteria for grading the severity of acute motion sickness. Aerosp Med 39:453-455. Oman CM, Lichtenberg BK, Money KE et al. (1986) M.I.T./Canadian vestibular experiments on the Spacelab-1 mission: 4. Space motion sickness: symptoms, stimuli, and predictability. Exp Brain Res 64:316-334. Pradhan GN, Hagen KM, Cevette MJ et al. (2022) Oculo-Cognitive Addition Test: Quantifying cognitive performance during variable cognitive workload through eye movement features. In: 2022 IEEE 10th International Conference on Healthcare Informatics (ICHI), June 11-14, 2022. pp 422-430. doi:10.1109/ICHI54592.2022.00064
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