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PI Name:	Wood, Scott J. Ph.D.		
Project Title:	Optimizing the Combination of Intranasal Scopolamine and Sensory Augmentation to Mitigate G-Transition Induced Motion Sickness and Enhance Sensorimotor Performance		
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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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Key Personnel Changes/Previous PI:	Dr. Reschke retired. Dr Natacha Chough has been added.		
COI Name (Institution):	Daniels, Vernie M.S. (KBR/NASA Johnson Space Center) Chough, Natacha M.D. (NASA Johnson Space Center)		
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Task Description:	Motion sickness represents one of the greatest clinical challenges impacting crew activities during and following g-transitions. Shorter duration missions involving new commercial vehicles and/or Artemis lunar missions will require continued emphasis on motion sickness countermeasures for early inflight prevention and treatment. The higher incidence of re-entry motion sickness following longer duration spaceflights coupled with the challenges associated with capsule egress during water landings also impose greater risks for crew recovery operations. Our overall goal is to characterize the effectiveness of motion sickness countermeasures to improve inflight and postflight recovery for future space travelers on these various platforms. We are conducting both controlled laboratory experiments of specific countermeasures during capsule wave motion simulation and conducting field testing in operational environments to characterize the incidence of motion sickness during various mission phases, and the efficacy of motion sickness countermeasures, if any, are utilized. The aims of our laboratory studies include evaluation of intranasal scopolamine and sensory augmentation to mitigate motion sickness and enhance crew performance. The intranasal form of scopolamine has the advantage of rapid bioavailability (i.e., therapeutic plasma concentration) with minimal side effects. This formulation allows crewmembers to self-medicate in a suited environment either before or after the onset of symptoms. Water landings may involve provocative wave motion during which crewmembers are deprived of a stable Earth reference inside the crew capsule. Sensory augmentation, e.g., vibrotactile feedback of Earth vertical, has been effective as a spatial awareness and balance aid with vestibular impairment. We hypothesize that both intranasal scopolamine and sensory augmentation of Earth vertical, either administered separately or combined, will be effective to mitigate motion sickness and improve task performance. The initial pilot ground study involved validation of a wave motion stressor to induce sickness, and evaluation of sensory augmentation in this simulated wave motion environment. A multi-degree of freedom platform with the subject seated in an enclosed cabin mockup was utilized to simulate the provocative capsule motion during water landings. Performance on a series of functional tasks (tilt motion tracking with and without a paced auditory serial addition test (PASAT) dual-task, eye-head-hand target acquisition, psychomotor vigilance test) was measured pre, during, after capsule wave motion. The capsule motion consisted of three 15 min periods of combined pseudorandom pitch, roll and heave that continued until the subject reached a motion sickness endpoint representing severe malaise on the Pensacola Diagnostic Index (up to 45 min maximum duration). The first study aim (1a) focused on prevention of motion sickness using intranasal scopolamine using a double-blinded repeated measures design in 30 subjects. Intranasal scopolamine was provided by Defender Pharmaceuticals, Inc. (DPI-386 Nasal Gel, referred to as Inscop) self-administered by a nasal pump (Aptar Pharma) that delivers 0.4 mg dose (0.2 mg / nostril). Motion sickness symptom onset, severity, and recovery were compared across treatment and placebo control sessions counterbalanced across subjects and separated by at least one week. The bioavailability of scopolamine for each session will be estimated from plasma concentrations obtained every 15 min. Cognition (psychomotor vigilance task) and subjective reports of drug side effects were obtained. Based on the pilot study, operational performance was assessed during the capsule wave motion using tilt motion tracking and a tablet-based eye-hand target acquisition task. The second part of this laboratory aim (1b) will be to evaluate sensory augmentation with and without intranasal scopolamine to prevent motion sickness during simulated capsule wave motion. For specific aim 2, a laboratory-based study will be used to evaluate the efficacy of intranasal scopolamine to provide treatment (“rescue”) of symptoms following motion sickness onset during simulated capsule wave motion. We are currently evaluating utilizing the advanced capsule wave motion capabilities of the Disorientation Research Device (aka Kraken) at the Naval Medical Research Unit – Dayton for aim 1B and/or aim 2. Specific aim 3 will evaluate the feasibility and efficacy of administering the intranasal scopolamine in operational field settings using both astronaut and ground-control subjects that are exposed to provocative motion as part of their assigned duties. For the ground-control subjects, these may involve a number of operational environments including motion simulations (e.g., high-g profile simulations during centrifugation), parabolic flights and/or Orion capsule recovery operations at sea. For the astronaut participants, we are recruiting from free-flier missions (e.g., Polaris Dawn), and both Private Astronaut Missions (PAM) and United States Orbital Segment (USOS) crewmembers assigned to the missions to the International Space Station (ISS). Astronaut participants may choose to test Inscop during provocative preflight training exercises (e.g., centrifugation), and can choose to take the medication prophylactically to prevent symptoms or after symptom onset to treat motion sickness during the launch and/or landing mission phases. Both ground-control and astronaut participants will be required to test the medication during a training session to monitor for adverse side effects. Participants will complete a short debrief questionnaire to capture motion sickness symptoms, side effects, and feasibility comments each time they take the medication. We will also include astronaut “control” subjects who do not take Inscop to comment on motion sickness severity within the initial early inflight and postflight periods, what countermeasures they did use and rate their effectiveness. While this study aim is not blinded, the inclusion of both active and control subjects will provide a more complete characterization of the impacts of motion sickness on crew activities during and following g-transitions, and the effectiveness of motion sickness countermeasures to improve inflight and postflight recovery. In addition, we are conducting a retrospective review of medical records from both the Shuttle and ISS programs to include a more comprehensive characterization of the motion sickness risks during missions with different vehicles and mission durations.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Intranasal scopolamine provides crewmembers with the ability to self-administer medication for prevention and/or treatment of motion sickness during critical mission phases, including launch, landing, and recovery operations. The rapid bioavailability, minimal side effects, and ability to self-administer real-time dosage adjustments make this an ideal formulation for other operational environments that involve provocative motion, e.g., military pararescue and emergency medicine, as well as entertainment platforms, e.g., boating and virtual reality. Sensory augmentation using vibrotactile feedback of body position has shown promise as an effective rehabilitation tool for vestibular disorders and piloting aid. The combination of non-pharmaceutical approaches like sensory augmentation with intranasal scopolamine has the benefit to mitigate motion sickness and enhance crew performance over a variety of spaceflight and earth-based motion platforms.

Task Progress:	Aim 1a Lab Study: This laboratory study focused on the prevention of motion sickness using intranasal scopolamine using a double-blinded repeated measures design in 30 subjects (19M, 11F). Intranasal scopolamine was provided by Defender Pharmaceuticals, Inc. (DPI-386 Nasal Gel, referred to as Inscop) self-administered by a nasal pump (Aptar Pharma) that delivers 0.4 mg dose (0.2 mg/nostril). During each session, subjects were exposed to complex wave motion on a six-degree-of-freedom platform that included pitch, roll, and heave at provocative stimulus frequencies (0.1-0.25 Hz) while seated in an illuminated cabin deprived of external visual cues. Motion sickness symptoms were compared across treatment and placebo control sessions counterbalanced across subjects and separated by at least one week. The time-to-motion sickness endpoint was based on severe malaise, defined as a symptom score of = 8 points using the Pensacola Diagnostic Index (Graybiel et al., 1968). We also employed a Subjective Discomfort Rating using a 0-20-point scale (Oman et al., 1986). The bioavailability of scopolamine for each session was estimated from plasma concentrations obtained every 15 min (Swaminathan et al., 2019). Side effects during the treatment session were minimal, and performance was not impaired on a test battery including motion perception tracking, tablet-based eye-hand coordination, and psychomotor vigilance testing. On average, the plasma concentration reached near-peak levels by the start of the testing and remained elevated throughout the 45-min motion sickness testing. The percentile ranking on the Motion Sickness Susceptibility Questionnaire (MSSQ) (Golding, 2006) was moderately correlated with the motion sickness time-to-endpoint during the placebo control session (rho = – 0.3, p=0.056). Seventeen subjects did not reach an endpoint during their placebo session and were eliminated from subsequent analysis. Another subject was excluded due to insufficient plasma concentration during the treatment session. For the remaining 12 subjects, the change in time-to-motion sickness endpoint between placebo and treatment sessions was moderately correlated with plasma concentration (rho =0.48, p = 0.056), improving on average 4.4 ± 18.4 min, mean ± std with Inscop versus placebo. Our results are consistent with previous findings that intranasal delivery of scopolamine can be effective at reducing motion sickness symptoms with minimal cognitive or sedative side effects. Future work is needed to optimize the delivery of Inscop for rescue (treatment, Aim 2) of symptoms following g-transitions as one of the key advantages of this formulation is self-administration in a suited environment (Wood et al., 2024). As described in the Task Description, we plan to explore how the combination of Inscop with non-pharmaceutical sensory aids, e.g., vibrotactile feedback of Earth vertical, may further mitigate motion sickness and improve task performance. Our pilot study (Bollinger et al., 2023) demonstrated that sensory augmentation (SA) alone appeared to delay symptom onset, with no subjects receiving sensory augmentation reaching the endpoint prior to the end of 45 min (PDI after 15 min = 6.0 ± 2.5 in the control group versus 3.4 ± 2.5 in the SA group, mean ±std). Aim 1a and/or Aim 2 may be conducted at the Naval Medical Research Unit – Dayton (NAMRU-D) Disorientation Research Device (aka Kraken) which would include increased heave for simulated wave motion. Aim 3 Field Testing: Notable progress has been made for the Aim 3 measurements to test the feasibility of intranasal scopolamine during spaceflight, and to better characterize the effectiveness of other motion sickness countermeasures (control subjects). Following the successful implementation of Inspiration 4 (Ericson et al., 2022), we are now prepared to continue data collection this next year on additional free-flier missions (3 control and 1 active on SpaceX Polaris Dawn), private astronaut missions to the International Space Station (ISS) (4 control subjects on Axiom 3), and during nominal long duration ISS increments (starting with 1 active and 1 control on Crew 8). Retrospective Data Mining: In addition to our prospective study, we have been summarizing medical reports of both inflight space motion sickness and reentry motion sickness following landing using data from both Shuttle and ISS missions. This data was obtained from the Longitudinal Study of Astronaut Health (LSAH) data archive and was reviewed as part of a SpaceX symposium to prepare the medical teams involved in postflight recovery operations (Wood, 2023). This data set is being used to evaluate different risk factors such as sex, prior flight experience, body mass index, flight duration, and launch/landing vehicles. As part of this retrospective analysis of the flight motion sickness data, we also re-evaluated the data from all nine Skylab crewmembers to determine asymmetry of each astronaut's ocular counter-rolling (OCR) response and their OCR slope from sigmoid fits during static leftward and rightward body tilts, which we then compared with their Coriolis sickness susceptibility index (CSSI) on the ground, their motion sickness symptom scores during 0 g maneuvers in parabolic flight, and the severity of the symptoms of space motion sickness (SMS) they reported during their spaceflights (see Clément et al., Front Physiol, 2023). We arranged the astronauts in rank order for SMS severity based on the SMS symptoms they reported during spaceflight and the amount of anti-motion sickness medication they used. As previously reported, the OCR amplitudes of these astronauts were within the normal range. We determined that the OCR amplitudes were not correlated with SMS severity ranking, CSSI, or motion sickness symptoms experienced during parabolic flight. Indices of asymmetry in the OCR reflex were generally small and poorly correlated with SMS scores; however, the only subject with a high index of asymmetry also ranked highly for SMS. Although OCR slope, CSSI, and motion sickness symptoms induced during parabolic flight were each only moderately correlated with SMS severity ranking (rho = 0.41–0.44), a combined index that included all three parameters with equal weighting was significantly correlated with SMS severity ranking (rho = 0.71, p = 0.015). These results demonstrate the challenge of predicting an individual's susceptibility to SMS by measuring a single test parameter in a terrestrial environment and from a limited sample size.
Bibliography Type:	Description: (Last Updated: 06/03/2025)
Abstracts for Journals and Proceedings	Bollinger AM, Beltran NE, Wood SJ. "Evaluating sensory augmentation as a non-pharmaceutical tool to mitigate motion sickness and enhance sensorimotor task performance: A pilot study using simulated capsule wave motion." 2023 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-9, 2023. Abstracts, 2023 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-9, 2023. , Feb-2023
Abstracts for Journals and Proceedings	Wood SJ. "Motion sickness induced by g-transitions during spaceflight: Research operations perspective." SpaceX Symposium on Space-Related Motion Sickness: From Launch to Landing, Hawthorne, California, April 18, 2023. Presentations. SpaceX Symposium on Space-Related Motion Sickness: From Launch to Landing, Hawthorne, California, April 18, 2023. , Apr-2023
Articles in Peer-reviewed Journals	Clément G, Macaulay TR, Moudy SC, Kuldavletova O, Wood SJ. "Back to the future—Revisiting Skylab data on ocular counter-rolling and motion sickness." Front Physiol. 2023 Nov 21;14:1303938. https://doi.org/10.3389/fphys.2023.1303938 ; PubMed PMID: 38074314; PubMed Central PMCID: PMC10702735 , Nov-2023