

# EVALUATION OF INTRANASAL SCOPOLAMINE FOR THE PREVENTION OF WAVE MOTION INDUCED MOTION SICKNESS WHILE MAINTAINING PERFORMANCE ON OPERATIONALLY RELEVANT TASKS

S. J. Wood<sup>1</sup>, N. E. Beltran<sup>2</sup>, A. M. Bollinger<sup>2</sup>, T. R. Macaulay<sup>2</sup>, V. R. Daniels<sup>2</sup>, and Z. Wang<sup>2</sup>

<sup>1</sup>NASA Johnson Space Center, Houston, TX, and <sup>2</sup>KBR, Houston, TX

Motion sickness represents one of the greatest clinical challenges impacting crew activities during and following g-transitions. Our overall goal is to characterize the effectiveness of motion sickness countermeasures during controlled laboratory experiments using capsule wave motion simulation and during field testing in operational environments. This laboratory study focused on 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 symptom score of  $\geq 8$  points using the Pensacola Diagnostic Index [1]. The bioavailability of scopolamine for each session was estimated from plasma concentrations obtained every 15 min [2]. 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. The plasma concentration remained near-peak levels throughout the 45 min motion sickness testing for most subjects. The percentile ranking on the Motion Sickness Susceptibility Questionnaire [MSSQ, 3] 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  $4.4 \pm 18.4$  min, mean  $\pm$  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) of symptoms following g-transitions as one of the key advantages of this formulation is self-administration in a suited environment. We will also 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.

References: [1] Golding J.F. (2006) *Pers Individ Differ* 41, 237-248. [2] Swaminathan S.K. et al. (2005) *J Pharm Biomed Anal* 164, 41-46. [3] Graybiel A. et al. (1968) *Aerosp Med* 39, 453-455.

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