

<b>Fiscal Year:</b>	FY 2015	<b>Task Last Updated:</b>	FY 10/02/2015
<b>PI Name:</b>	Smith, Scott M Ph.D.		
<b>Project Title:</b>	Risk of visual impairment and intracranial hypertension after space flight: Evaluation of the role of polymorphism of enzymes involved in one-carbon metabolism		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>	HUMAN RESEARCH		
<b>Program/Discipline--Element/Subdiscipline:</b>	HUMAN RESEARCH--Biomedical countermeasures		
<b>Joint Agency Name:</b>	<b>TechPort:</b>	No	
<b>Human Research Program Elements:</b>	(1) <b>HHC:</b> Human Health Countermeasures		
<b>Human Research Program Risks:</b>	(1) <b>SANS:</b> Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS)		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Organization Name:</b>	NASA Johnson Space Center		
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<b>Zip Code:</b>	77058-3607	<b>Congressional District:</b>	36
<b>Comments:</b>			
<b>Project Type:</b>	GROUND	<b>Solicitation / Funding Source:</b>	Directed Research
<b>Start Date:</b>	03/15/2012	<b>End Date:</b>	09/30/2015
<b>No. of Post Docs:</b>	<b>No. of PhD Degrees:</b>		
<b>No. of PhD Candidates:</b>	<b>No. of Master' Degrees:</b>		
<b>No. of Master's Candidates:</b>	<b>No. of Bachelor's Degrees:</b>		
<b>No. of Bachelor's Candidates:</b>	<b>Monitoring Center:</b> NASA JSC		
<b>Contact Monitor:</b>	Norsk, Peter	<b>Contact Phone:</b>	
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<b>Flight Program:</b>			
<b>Flight Assignment:</b>	NOTE: End date changed to 09/30/2015 per PI (Ed., 10/9/14) NOTE: End date changed to 10/01/2014 per PI (Ed., 04/10/2014) NOTE: End date is 3/31/2014 per PI (Ed., 12/26/13) NOTE: End date changed to 1/31/2014 per 6/27/13 HRP MTL information (Ed., 10/21/13)		
<b>Key Personnel Changes/Previous PI:</b>	None		
<b>COI Name (Institution):</b>	Zwart, Sara ( USRA/NASA Johnson Space Center ) Gregory, Jesse ( University of Florida ) Ploutz-Snyder, Robert ( USRA )		
<b>Grant/Contract No.:</b>	Directed Research		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>			

Task Description:	<p>The occurrence of long-term or permanent changes in vision of International Space Station crew members during and after flight has been described as “the most significant clinical issue to date” for the U.S. space program. NASA has conducted 2 workshops in which the clinical issues were characterized as the presence of choroidal folds and occurrence of papilledema, significantly elevated opening pressures after lumbar puncture, and MRI (magnetic resonance imaging) visualization showing optic nerve swelling. A primary forward focus has been evaluation of intracranial hypertension and fluid shifts.</p> <p>In evaluating data collected from the Nutritional Status Assessment Supplemental Medical Objective (SMO), we have identified elevations in 4 metabolites of the one-carbon metabolism pathway in affected crew members studied to date. These elevations and related data strongly suggest that polymorphism(s) of one or more of the enzymes in this pathway exist(s) in the affected crew members. The incidence of such polymorphisms in the general population is relatively high, and they have been associated on Earth with increased risk of stroke and other cardiovascular, and specifically cerebrovascular, events. Therefore it is within the realm of plausibility, given the number and ethnic background of the affected astronauts, that these polymorphisms could be causing the cerebrovascular and optical medical issues in astronauts. This evidence demands follow-up to more clearly define this relationship. The proposed study will accomplish this. We expect that, at a minimum, the results of the proposed effort will provide a guiding path for other research to be conducted that would allow this problem to be defined and resolved.</p>
Rationale for HRP Directed Research:	<p>This research is directed because it contains highly constrained research, which requires focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal.</p>
Research Impact/Earth Benefits:	<p>We expect to find evidence of a relationship between polymorphism incidence, biochemical analytes, and vision and optic examination results in affected crew members. These results will guide the path for further research to define a clinical treatment plan for individuals developing symptoms during flight. The results of this effort may also have significant Earth-based applications, and may inform the understanding and treatment of idiopathic intracranial hypertension, migraine headaches, and other cerebrovascular issues.</p>
Task Progress:	<p>Seventy-four past, present, and future International Space Station (ISS) crewmembers were recruited to provide blood samples for biochemical, enzymatic, and limited genotype/polymorphism analyses. Genomic DNA prepared from peripheral leukocytes was analyzed for the existence of 5 single-nucleotide polymorphisms in the one-carbon metabolism pathway: 5,10-methylenetetrahydrofolate reductase (MTHFR) 677C-&gt;T, MTHFR 1298A-&gt;T, serine hydroxymethyltransferase 1 (SHMT1) 1420C-&gt;T, cystathionine <math>\beta</math>-synthase (CBS) 844ins68, and 5-methyltetrahydrofolate homocysteine methyltransferase reductase (MTRR) 66A-&gt;G. Data from vision and related eye exams was obtained, and we sought to relate those findings to the data from our study.</p> <p>Study has been completed, results published – E-published in August 2015; expected final publication January 2016.</p> <p>These findings document a genetic predisposition for some astronauts to develop VIIP (Vision Impairment and Intracranial Pressure) issues during flight. We have proposed a series of follow-on experiments to clarify and extend these findings. The implications of this research for one of NASA’s highest priority crew health risks are significant, along with the implications for a better understanding of the role of one-carbon metabolism in the health of the general population.</p>
Bibliography Type:	Description: (Last Updated: 05/24/2023)
Abstracts for Journals and Proceedings	<p>Smith SM, Gregory JF, Zeisel SH, Ueland P, Gibson CR, Mader T, Kinchen JM, Ploutz-Snyder R, Zwart SR. "Vision issues and space flight: evaluation of one-carbon metabolism polymorphisms." Experimental Biology 2015, Boston, MA, March 28-April 1, 2015.</p> <p>FASEB Journal. 2015 Apr;29(1 Suppl):134.1 See also <a href="http://www.fasebj.org/content/29/1_Supplement.toc">http://www.fasebj.org/content/29/1_Supplement.toc</a> for searching. , Apr-2015</p>
Articles in Peer-reviewed Journals	<p>Zwart SR, Gregory JF, Zeisel SH, Gibson CR, Mader TH, Kinchen J, Ueland P, Ploutz-Snyder R, Heer M, Smith SM. "Genotype, B-vitamin status and androgens affect spaceflight-induced ophthalmic changes." FASEB J. 2016 Jan;30(1):141-8. Epub 2015 Aug 27. <a href="http://dx.doi.org/10.1096/fj.15-278457">http://dx.doi.org/10.1096/fj.15-278457</a> ; PubMed PMID: 26316272; PubMed Central PMCID: PMC4684521 , Jan-2016</p>
Books/Book Chapters	<p>Zwart SR, Gibson CR, Smith SM. "Space Flight Ophthalmic Changes, Diet, and Vitamin Metabolism." in "Handbook of Nutrition, Diet, and the Eye." Ed. V.R. Preedy. Waltham, MA : Academic Press, 2014. p. 393-399. ISBN: 978-0-12-401717-7. <a href="http://dx.doi.org/10.1016/B978-0-12-401717-7.00040-X">http://dx.doi.org/10.1016/B978-0-12-401717-7.00040-X</a> , Apr-2014</p>
Journal/Magazine covers	<p>Zwart SR, Gregory JF, Zeisel SH, Gibson CR, Mader TH, Kinchen J, Ueland P, Ploutz-Snyder R, Heer M, Smith SM. "Cover to be published issue in January 2016 for 'Genotype, B-vitamin status and androgens affect spaceflight-induced ophthalmic changes.' " FASEB J. 2015 Aug 27. [Epub ahead of print] <a href="http://dx.doi.org/10.1096/fj.15-278457">http://dx.doi.org/10.1096/fj.15-278457</a> ; PubMed PMID: 26316272; PubMed Central PMCID: PMC4684521 , Jan-2016</p>
NASA Technical Documents	<p>Smith SM, Zwart SR, Heer MA. "Human Adaptation to Spaceflight: The Role of Nutrition (NP-2014-10-018-JSC)." Houston, TX: National Aeronautics and Space Administration Lyndon B. Johnson Space Center, 2014. (NP-2014-10-018-JSC) (ISBN 978-0-16-092629-7). Available through open access at: <a href="http://www.nasa.gov/hhp/education">http://www.nasa.gov/hhp/education</a> and <a href="http://www.nasa.gov/sites/default/files/human-adaptation-to-spaceflight-the-role-of-nutrition.pdf">http://www.nasa.gov/sites/default/files/human-adaptation-to-spaceflight-the-role-of-nutrition.pdf</a> ; accessed 10/02/15. , Nov-2014</p>
NASA Technical Documents	<p>Smith SM, Zwart SR, Douglas GL, Heer M. "Human adaptation to spaceflight: The role of food and nutrition. Second edition." Houston, TX: NASA Lyndon B. Johnson Space Center, 2021. 255 p. NP-2021-03-003-JSC. <a href="https://www.nasa.gov/sites/default/files/atoms/files/human_adaptation_2021_final.pdf">https://www.nasa.gov/sites/default/files/atoms/files/human_adaptation_2021_final.pdf</a> , Apr-2021</p>