

Fiscal Year:	FY 2022	Task Last Updated:	FY 03/25/2022
PI Name:	Zwart, Sara Ph.D.		
Project Title:	B Complex: A Nutraceutical SANS Countermeasure		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline-- Element/Subdiscipline:			
Joint Agency Name:	TechPort:	No	
Human Research Program Elements:	(1) HHC :Human Health Countermeasures		
Human Research Program Risks:	(1) HHC Food :Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System (IRP Rev J) (2) SANS :Risk of Spaceflight Associated Neuro-ocular Syndrome (IRP Rev I)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	77058-3607	Congressional District:	36
Comments:			
Project Type:	FLIGHT	Solicitation / Funding Source:	Directed Research
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
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	<p>Some astronauts on International Space Station (ISS) missions have experienced ophthalmic pathologies including optic disc edema, part of what is characterized as Spaceflight Associated Neuro-ocular Syndrome (SANS). While the precise cause for the optic disc edema is not known, it is likely that there are multiple contributing factors, including genetic and environmental factors that may affect the response to headward fluid shifts. Biochemical evidence reveals that crewmembers with optic disc edema have higher circulating concentrations of at least 4 metabolites from the one-carbon metabolic pathway before, during, and after flight compared to astronauts that did not develop optic disc edema. B-vitamin status at landing and the presence of specific one-carbon pathway single nucleotide polymorphism (SNP) alleles were significant predictors for the incidence of astronaut ophthalmic pathologies, including optic disc edema, choroidal folds, and cotton wool spots. When looking at the individual SNPs, the G allele of methionine synthase reductase (MTRR, rs1801394) A66G, and the C allele of serine hydroxymethyltransferase-1 (SHMT1, rs1979277) C1420T, were associated with higher incidence of ophthalmic findings after flight compared to those with the A or T alleles.</p> <p>In ground analog studies, end-tidal CO₂, a reflection of arterial CO₂, response to acute head-down tilt (HDT) bed rest and CO₂ exposure was related to G and C alleles of MTRR A66G and SHMT1 C1420T and B-vitamin status. Supportive of this, these same alleles were related to the presence of optic disc edema in different bed rest subjects. Subjects were exposed to strict 6°-HDT bed rest and 0.5% CO₂ for 30 days and 5 out of 11 subjects developed optic disc edema. The number of G and C alleles were found to be associated with the change in total retina thickness (ΔTRT), a quantitative measure of optic disc edema. Based on our data, differences in genetics and altered one-carbon biochemistry before flight support that one-carbon metabolism may be involved.</p> <p>We hypothesize that genetics and B-vitamin status are indispensable elements of this phenomenon, along with other potential factors. Dietary B-vitamin insufficiencies and variants in genes involved in the one-carbon metabolic pathway can contribute to lower B-vitamin status and pathway inefficiency, which can affect numerous outcomes, including nitric oxide (NO) production and endothelial function.</p> <p>To that end, we propose a nutraceutical containing bioactive B-vitamins as a countermeasure to optimize function of the one-carbon pathway and prevent or mitigate optic disc edema during spaceflight.</p> <p>This proposal aims to test the hypotheses that one-carbon pathway genetics can predispose an individual to SANS pathologies during flight, and that this effect may be prevented or mitigated through supplementation of vitamins that can affect one-carbon pathway function.</p> <p>The hypothesis will be tested in the following specific aims:</p> <ol style="list-style-type: none"> 1. Determine whether provision of a daily nutraceutical containing 5-methyltetrahydrofolate (5-MTHF), pyridoxine, methylcobalamin (vitamin B12), and riboflavin prevents or mitigates SANS pathology (significant ΔTRT) compared to astronauts who did not take the supplement in previously flown astronauts with available TRT data. 2. Determine one-carbon pathway SNP profiles in all participating astronauts being supplemented, and assess whether individuals with 3-4 risk alleles for MTRR A66G and SHMT1 C1420T polymorphisms have greater mitigation of ΔTRT during and after spaceflight. 3. Determine whether subjects with 3-4 risk alleles exhibit differences in biomarkers of endothelial function, compared to subjects with 0-2 risk alleles. <p>We propose to provide the nutraceutical countermeasure to all participating crewmembers before and during flight, and we will assess whether the supplement provides greater mitigation of changes in TRT in individuals with 3-4 risk alleles. We will include assessments of ocular health, along with determinants of vascular endothelial function, advanced glycation end products, and nutritional status and one carbon biochemistry. These additional measures will be critical for the further definition of the causes of SANS, and in understanding the effect of the countermeasure. Finally, the supplemented subjects in this study will be compared against TRT data from previously flown astronauts known to have not taken supplements during their missions.</p>
Rationale for HRP Directed Research:	<p>This research is directed because it contains highly constrained research. This project originated as an update to a proposal originally titled "B Complex: 5-Methyltetrahydrofolate, Riboflavin, Pyridoxine, and Methylcobalamin Supplementation as a Non-Mechanical Countermeasure to Mitigate Optic Disc Edema Changes During Strict 6° Head-Down Tilt Bed Rest", which was reviewed and selected from the 80JSC018N0001-SANS NASA Research Announcement. The implementation of this countermeasure during bed rest was not possible given constraints around this type of countermeasure study at the German Aerospace Center's (DLR) :envihab facility. Therefore, this bed rest study was converted to a flight study in order to test this countermeasure in an actual spaceflight environment.</p>
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2022.
Bibliography Type:	Description: (Last Updated:)