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Project Title:	Fluid Shifts		
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Program/Discipline-- Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:	TechPort:	No	
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Human Research Program Risks:	(1) Cardiovascular: Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes (2) SANS: Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS)		
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Space Biology Special Category:	None		
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Task Description:

Editor's Note (7/11/2013): NOTE THIS IS A CONTINUATION OF FUNDING FOR NNX13AB42G (Microgravity Associated Compartmental Equilibration (MACE)) WITH THE SAME PRINCIPAL INVESTIGATOR. Fifty percent of American astronauts have developed ocular refraction change after long duration space flight on the International Space Station (ISS). Recent findings have also included structural changes of the eye (papilledema, globe flattening, choroidal folds) and the optic nerve (sheath dilatation, tortuosity, and kinking), as well as imaging signs and lumbar puncture data indicative of elevated intracranial pressure (ICP). While short duration space flight is also characterized by vision disturbances, these are generally transient and do not appear to have lasting impacts on the structure or function of the eye. Changes in vision, eye, and adnexa morphology, are hypothesized to be the result of space flight-induced cephalad fluid shifts and transiently elevated intracranial pressure. This hypothesis, however, has not been systematically tested. In earlier anecdotal publications, ICP elevation in long-duration space flight has been inferred but without association with structural or functional changes of the eye. Furthermore, while fluid shifts and compartmentalization during short-duration space flight (Space Shuttle missions) have been studied, the fluid distribution patterns and their effects on intracranial pressure or the structure and function of the sensory organs in the course of long-duration space flight are not well known.

Several ISS crewmembers have reported consistent worsening of nasal congestion and associated symptoms in late afternoon hours, necessitating topical and systemic decongestant use. Although several explanations have been entertained, food (salt) and water intake are likely to have provoked these symptoms through postprandial modification of fluid balance or increase in the circulating volume that manifests in the most susceptible individuals.

The purpose of the proposed work is to objectively characterize the changes in fluid distribution, including intra/extracellular and intra/extravascular fluid shifts, by applying advanced non-invasive assessment technologies before, during, and after long duration space flight. Additionally, we will examine the relationship between the type and magnitude of the fluid shift with any effects on eye morphology and vision disturbances, intraocular pressure (IOP), and measures of intracranial pressure. Further, we seek to determine whether the magnitude of fluid shifts during space flight, as well as the above effects of those shifts can be predicted based upon crewmember baseline data and responses to acute head-down tilt tests performed before launch. Finally, we propose to evaluate the effect of lower body negative pressure (LBNP) on the above parameters.

To our knowledge, this is the first attempt to systematically determine the impact of the fluid distribution in microgravity on a comprehensive set of structural and functional measures including, but not limited to, those related to intracranial pressure, vision, morphology of the eye and its adnexa, and the vascular systems of the head and neck, during and after long duration space flight. The study design and methodology are based on the extensive relevant experience of the Investigators, including many successful ground-based, space flight analogue, and space flight projects and investigations.

Primary Hypothesis

Prolonged microgravity-induced, headward volume, and pressure shifts promote elevation of intracranial pressure and result in alterations in crewmembers' vision.

Specific Aims

Specific Aim I: To characterize fluid distribution and compartmentalization before, during, and after long-duration space flight.

Hypothesis 1: Fluid distribution measured by dilution techniques will reflect a headward fluid shift and an intra- to extra-vascular fluid shift during space flight, returning to pre-flight condition after landing.

Hypothesis 2: Regional headward fluid shifts in-flight are documented by increased cephalad venous dimensions (jugular veins) and flow characteristics, skin and soft tissue thickness.

Hypothesis 3: Fluid re-distribution towards the eye (detected in choroid, retina, and optic nerve head using ultrasonography and optical coherence tomography), and in arteries supplying ocular vascular beds, contributes to vision alterations.

Hypothesis 4: Splanchnic venous congestion (detected by portal vein size) contributes to headward volume shift, but is not in communication with the veins of head and neck. Thus, there should be a different level of venous congestion in these two compartments.

Specific Aim II: To correlate in-flight alterations of eye structure, ocular vascular parameters, and vision with headward fluid shifts, vascular dimensions, and flow patterns.

Hypothesis 5: Space flight-induced fluid shifts will have an upregulating effect on ICP and will alter ocular refraction / visual acuity. These changes will vary in magnitude and respectively, in their resolution pattern after space flight.

Hypothesis 6: In-flight ICP-related measures, IOP, venous and arterial morphometric and flow characteristics, vascular resistance of ocular vascular beds, and optic nerve anatomy will trend towards normal-gravity levels temporarily during and residually after fluid sequestration (LBNP) interventions.

Specific Aim III: To determine systemic and ocular factors of individual susceptibility to the development of ICP elevation and/or vision alterations.

Hypothesis 7: Subjects with greater fluid shifts (as measured by the ultrasound method in Aim 1) during pre-flight testing will experience greater fluid shifts in-flight and will be more susceptible to flight-induced vision alterations.

Hypothesis 8: Subjects who are resistant to the reversal of in-flight symptoms and physiological status through the application of LBNP will be more susceptible to persistent flight-induced vision alterations.

Hypothesis 9: Propensity towards more severe changes in-flight and the more indolent postflight resolution pattern will correlate with a range of individual characteristics of the crewmembers, such as anatomical and microanatomical and physiological features and potentially, hitherto unsuspected factors.

NOTE: This study was merged with investigations from Dr. Alan Hargens (Fluid distribution before, during and after prolonged space flight) and Dr. Michael Stenger (Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance) resulting in a comprehensive study titled "Fluid

Shifts Before, During and After Prolonged Space Flight and Their Association with Intracranial Pressure and Visual Impairment” (short title: Fluid Shifts).

Rationale for HRP Directed Research:

Research Impact/Earth Benefits:

Current means of measuring increased intracranial pressure require an invasive monitoring system with skilled medical personnel. The techniques outlined in this proposal, if verified, would provide a rapid, accurate, non-invasive, and scalable solution to measure increases in intracranial pressure for a number of critical medical conditions. These studies will also provide physiological insight to the mechanisms of fluid shifts and their relationship to intracranial pressure. This information could be relevant to terrestrial disorders of intracranial pressure such as idiopathic intracranial hypertension (IIH).

Task Progress:

We have made significant progress over the past year in all dimensions of the Fluid Shifts (FS) experiment. To date the team has performed preflight baseline data collection on five crewmembers, completed three inflight sessions and one postflight session for the two One Year Mission crewmembers, and concomitantly supported training activities for upcoming FS subjects. We have continued to optimize our pre-, in-, and postflight tests to maximize their scientific value and to minimize impacts and risks to ISS crewmembers. Initial analysis (imagery, otoacoustic emission phase shift, etc.) of the majority of data is performed as it becomes available.

Erik Hougland, our International Space Station Medical Projects (ISSMP) flight project manager, continues to coordinate our bi-weekly FS team telecons. Over the past year we have provided inputs to updated versions of the FS Experimental Document (ED), recently revised and under review as of March 2016. The ISSMP team has done an excellent job coordinating crew ICBs, training, and testing as well as coordinating Russian activities. The FS team has collectively responded to changes in circumstances (inflight schedules, Russian travel limitations, etc.) that have required a review of existing experiment requirements. The team has reasoned through multiple such scenarios to solve the dilemma and preserve scientific value.

We have continued to work with the University of Texas Medical Branch (UTMB) Victory Lakes 3T MRI (magnetic resonance imaging) facility to employ scanning protocols that maximize science return while capitalizing on the existing MRID (MED B) sequences. Over the past year Dr. Larry Kramer has been added to the team to assist with data analysis. MRI analysis methods continue to be refined to optimize both collected data as well as analysis resources. Medical Operations has made the decision to use contrast agent during MED B MRI scans as the preferred protocol. Our team has worked closely with the NASA medical community to accommodate this change in protocol to preserve comparability with our existing FS MRI protocol while capitalizing on the use of contrast agent in these scans.

Since Russian and European Space Agency (ESA) crews are also “direct return” to their home countries, they are not available in Houston for immediate postflight testing, requiring reproduction and testing of the imaging procedure and protocol elements at the additional scanning locations in Moscow (Research Center of Neurology) and Cologne (DLR/envihab:). Our team has been especially involved with the process of providing 15-degree foam wedges to both the Russian scanning facility and the ESA scanning facility. Terry Guess (Wyle STE) was once again instrumental in this process, specifically in the rapid construction of a second wedge to ensure that a wedge was available for postflight testing on the Russian One Year Mission crewmember. Thanks to extensive coordination and technical exchanges, the Fluid Shifts 3Tesla MRI protocol was successfully completed on the Russian one-year crewmember on March 10, 2016 in Moscow. Based on prior parabolic flight work, the team developed procedures for “free-floating” use of the OCT device for in-flight measurements. An inflight free-float practice run was successfully completed in April 2015, demonstrating that this approach is feasible and would result in valuable data collected on crewmembers while in Chibis. The team has proceeded to collect six sets of data during the One Year Mission using this technique, which has resulted in similar exam times and data quality when compared to the traditional chinrest method.

Our team has made great advances in the analysis of otoacoustic emission (OAE) data over the past year. Dr. David Kemp (the first to experimentally document OAEs) and Rozela Melgoza (a Johnson Space Center audiology intern) joined the team this past year and have been instrumental in data analysis and interpretation. Dr. Kemp has graciously guided the FS OAE team through development of novel analysis techniques for OAE data, and Ms. Melgoza has performed analysis on all available data, culminating in a poster presentation of the FS OAE data at the 2016 Human Research Program (HRP) Workshop. Of particular interest are the consistent phase shifts of transient evoked OAE (TEOAE) in response to posture change and lower body negative pressure. TEOAE phase shifts are consistent with intracranial pressure changes across a relatively broad frequency range, and appear to be consistent across multiple subjects. Further, TEOAE phase shifts are largely consistent with CCFP results.

The team has coordinated closely with the Twins study to ensure the most efficient and effective data collection for both Fluid Shifts and Twins study. Sessions corresponding with preflight, a single mid-mission inflight, and postflight have been completed on the ground twin.

Our team attended the NASA HRP Investigators’ Workshop in Galveston, TX in February 2016, presenting an overall project poster for Fluid Shifts and participating in many Vision Impairment and Intracranial Pressure (VIIP)-related sessions and discussions, including the VIIP modelling breakout session. Our team also presented an otoacoustic emissions poster based on the data collected for Fluid Shifts.

Presentations (past year):

1) Stenger M, Hargens A, Dulchavsky S, Ebert D, Lee S, Laurie S, Garcia K, Sargsyan A, Martin D, Lui J, Macias B, Arbeille P, Danielson R, Chang D, Gunga H-C, Johnston S, Westby C, Ploutz-Snyder R, Smith S. Fluid Shifts. Presented at 2016 NASA Human Research Program Investigators’ Workshop, Galveston, TX. February 8-11, 2016.

2) Melgoza R, Kemp D, Ebert D, Danielson R, Stenger M, Hargens A, Dulchavsky S. Fluid Shifts: Otoacoustic Emission Changes in Response to Posture and Lower Body Negative Pressure. Presented at 2016 NASA Human Research Program Investigators’ Workshop, Galveston, TX. February 8-11, 2016.

3) Ebert D, Garcia K, Sargsyan A, Young M, Dulchavsky S, Dentinger M. The Hydrostatic Gradient, Individual Responses, and Other Challenges. Presented at 2016 NASA Human Research Program Investigators’ Workshop VIIP Modelling Session, Galveston, TX. February 8-11, 2016.

Bibliography Type:	Description: (Last Updated: 02/23/2023)
Abstracts for Journals and Proceedings	Stenger M, Hargens A, Dulchavsky S, Ebert D, Lee S, Laurie S, Garcia K, Sargsyan A, Martin D, Lui J, Macias B, Arbeille P, Danielson R, Chang D, Gunga H-C, Johnston S, Westby C, Ploutz-Snyder R, Smith S. "Fluid Shifts." Presented at 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX. February 8-11, 2016. 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX. February 8-11, 2016. , Feb-2016
Abstracts for Journals and Proceedings	Melgoza R, Kemp D, Ebert D, Danielson R, Stenger M, Hargens A, Dulchavsky S. "Fluid Shifts: Otoacoustic Emission Changes in Response to Posture and Lower Body Negative Pressure." Presented at 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX. February 8-11, 2016. 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX. February 8-11, 2016. , Feb-2016
Abstracts for Journals and Proceedings	Ebert D, Garcia K, Sargsyan A, Young M, Dulchavsky S, Dentinger M. "The Hydrostatic Gradient, Individual Responses, and Other Challenges." Presented at 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX. February 8-11, 2016. 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX. February 8-11, 2016. , Feb-2016