Fiscal Year:	FY 2006	**Task Last Updated:**	FY 02/05/2007
PI Name:	Serrador, Jorge Manuel Ph.D.		
Project Title:	Vestibular-Cerebrovascular Interactions and Their Contribution to Post-Spaceflight Orthostatic Intolerance		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Physiology		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2003 Biomedical Research & Countermeasures 03-OBPR-04
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No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	None		
COI Name (Institution):	Black, Owen (Legacy Health System) Lipsitz, Lewis (Hebrew Rehabiliation Center for Aged) Schlegel, Todd (NASA Johnson Space Center) Wood, Scott (Naval Aerospace Medical Research Laboratory)		
Grant/Contract No.:	NNJ04HI13G		
Performance Goal No.:			
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Task Description:	Post-spaceflight orthostatic intolerance, a principal NASA safety concern, is a complex multi-factorial problem that continues to be poorly understood. Recent evidence clearly suggests that the vestibular otolith system, which is directly affected by spaceflight, assists in both autonomic and blood pressure regulation during orthostatic stress. Vestibular activation has also has direct effects on cerebral blood flow suggesting that vestibular inputs also affect the cerebrovascular response to orthostasis. The goal of this research is to examine the role of vestibular inputs in cerebral blood flow regulation and the effect of these inputs on orthostatic tolerance. Our general hypothesis is that otolith mediated vestibular inputs act as a feed forward mechanism causing cerebral vasodilation to compensate for the decrease in cerebral perfusion pressure during the upright posture. This project's four specific aims are to: 1) Determine the effect of tilts in the pitch plane with and without visual feedback on cerebral blood flow and cerebral autoregulation in healthy elderly with and without vestibular hypofunction and healthy young subjects.; 2) Determine the effect of otolith vs otolith and canal stimulation on cerebral blood flow in healthy elderly with and without vestibular hypofunction and healthy young subjects. This aim will be accomplished by varying the radius of rotation of subjects on a short arm centrifuge; 3) Determine the effect of canal vs canal and otolith stimulation on cerebral blood flow in elderly subjects with normal and reduced vestibular function. This aim will be accomplished by using earth vertical axis rotations vs. head tilt while supine or prone; 4) Determine the effect of training subjects to associate otolith input as tilt on cerebral blood flow during orthostatic stress in elderly subjects with intact and impaired vestibular function. This aim will be accomplished by training subjects with tilt or centrifugation to interpret otolith signals as either translation or tilt by providing visual scenes to reinforce this perception. The results of these studies will provide direct evidence on the role of vestibular inputs in cerebrovascular regulation. This work may lead to new methods to diagnose and treat not only post-spaceflight orthostatic intolerance but also the ~500,000 otherwise healthy subjects that are affected by orthostatic intolerance.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Understanding the causes of orthostatic intolerance will directly benefit two groups of individuals. First, elderly individuals have increased risks of falls which are associated with decreased quality of life and increased mortality. Falls are the leading cause of death for older adults. In fact, Almost 11,000 older adults a year, or 30 each day, die from a falls injury. Half of those who survive a fall never return to their prior level of mobility or independence. By reducing the likelihood that an elderly individual will fall due to light headedness, i.e. orthostatic intolerance, we will be able to improve the quality of life and reduce the rate of fall induced mortality in this group, a significant advance for the aging population. In addition, almost 500,000 Americans suffer from orthostatic intolerance, often with poor treatment outcomes. Currently a possible vestibular role for orthostatic intolerance is not considered. This research could not only highlight a new cause of orthostatic intolerance but lead to new treatments including vestibular rehabilitation, etc.
Task Progress:	To complete testing of the hypothesis laid out in the grant, the PI has had three primary goals during the last year of this grant: 1) Establishing a population of elderly with normal and impaired vestibular function 2) Ensuring testing for the tilt table testing and head rotation experiments could be achieved in year 3 3) Preparing to begin data collection in Portland, Oregon Since this is a first grant for the PI, significant equipment purchases and lab setup time was required. During the first 6 months the PI was able to successfully set up a complete vestibular screening and physiology testing lab. In addition the PI was able to have several custom pieces of equipment designed to meet the screening needs of the studies. Following set-up, the subsequent time has been used to recruit and screen 108 subjects (54% of the total number expected to be enrolled). An important piece of equipment that has been developed is the ocular counterroll chair that allows for assessment of ocular torsion. Since the primary goal of the vestibular screening is to stratify subjects by otolith function, which is the vestibular component primarily affected by spaceflight, measuring ocular torsion is essential to assessing otolith function. Dr. Wood has previously shown that using slow oscillations (+/-20 degrees @ 0.01 Hz) provides an accurate estimate of otolith function as compared to other current assessment techniques (Merfeld et al. J Neurophys 2005; 94: 199-205; Merfeld et al. J Neurophys 2005; 94: 206-218). In a recent study Dr. Wood compared ocular torsion gain during earth horizontal axis (EHA) rotation (i.e. ocular counterroll) and variable radius centrifugation (VRC). Since VRC provides an otolith specific stimulation, torsion produced by this stimulus should be solely of otolith origin. In contrast, during EHA both otolith and canal organs are activated. However, at very low frequencies, response from VRC and EHA are virtually identical. This demonstrates that ocular torsion during ocular counterroll can be used as a good measure of otolith function. In addition with the assistance of Dr. Wood, we have been able to duplicate his ocular torsion analysis system in the PI's lab allowing us to obtain continuous ocular torsion during our screening tilt test (+/-20 degrees @ 0.01 Hz). To address the concern of obtaining an adequate sample of elderly subjects that will allow stratification into impaired and normal vestibular function, recruitment of elderly began within the first 6 months of the grant. Ads were placed in the print publications; Harvard Cooperative Program on Aging and Boston Seniority. Recruitment flyers were also posted at the Harvard Institute for Learning in Retirement. Recruitment has subsequently increased in the past year to 50 subjects, 50% of our target population for elderly subjects. We thus believe we will not have a problem meeting our recruitment goals over the second year of the grant.
Bibliography Type:	Description: (Last Updated: 10/31/2019)
Abstracts for Journals and Proceedings	Devine ER, Milberg WP, Serrador JM. "Does gravity affect functional cerebral blood flow response?" International Cerebral Blood Flow Meeting, Amsterdam, The Netherlands, June, 2005. International Cerebral Blood Flow Meeting, 2005. , Jun-2005
Abstracts for Journals and Proceedings	Devine ER, Serrador JM. "Relationship between stroke volume and cerebral blood flow during pressure changes in humans. " XXXV International Congress of Physiological Sciences, April 2005. FASEB Journal 2005;19(5):A1257. , Apr-2005

Articles in Peer-reviewed Journals	Serrador JM, Wood SJ. "Vasopressin: neurohumoral link between nausea and motion sickness. Author reply." Aviat Space Environ Med. 2005 Aug;76(8):805; author reply 805-6. PMID: 16110700 , Aug-2005
Articles in Peer-reviewed Journals	Serrador JM, Schlegel TT, Black FO, Wood SJ. "Cerebral hypoperfusion precedes nausea during centrifugation." Aviat Space Environ Med. 2005 Feb;76(2):91-6. PMID: 15742822 , Feb-2005