Fiscal Year:	FY 2008	**Task Last Updated:**	FY 01/12/2009
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		
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Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:			
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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:	NOTE: Received NCE to 08/23/2009 per J. Dardano/JSC (8/08)		
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)		
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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:	In the past 12 months we have completed three of four specific aims. After performing 160 vestibular screenings on 100 young (age 21+) and 60 elderly (age 60+) subjects we were able to select a group of younger and older subjects with normal and impaired otolith function. From these screenings we have found two major findings. First, there were significant levels of vestibular impairment even in younger individuals, which became worse as individuals became older. Second, the rate of decline of otolith function in females was double to that seen in males. In addition, we found a strong relationship between sway parameters and otolith function. Thus, individuals with the worst otolith function tended to show the greatest sway. These increased levels of sway suggested they were also at greater risk for falls. Thus, elderly individuals with impaired vestibular function may be at even greater risk for falls. Testing a group of elderly subjects with normal and impaired vestibular function found that the group with impaired function demonstrated a significantly greater drop in brain blood flow when upright. In addition this greater drop only occurred when they were blindfolded and had no visual information. This would suggest that individuals with loss of vestibular function may have problems maintaining brain blood flow when upright. In addition, this impairment only occurs when they are unable to use vision in place of vestibular information to tell them about whether they are upright or not. Finally, we have tested a group of young subjects with and without impairment, but not yet analyzed the data. We have already completed specific aim 2 by performing variable-radius centrifugation on a group of healthy subjects. While rotation on center did not cause any changes in brain blood flow, movement forward, causing the perception of forward tilt, and resulted in a significant decrease in brain blood flow. This decrease in brain blood flow could not be explained by any other physiological responses, indicating that vestibular inputs were likely the cause. To complete Specific Aim 3 we used a combination of dynamic tilt and variable radius centrifugation to separate the roles of otoliths vs canals in the brain blood flow response to vestibular stimulation. Brain blood flow oscillated with the frequency of motion, again suggesting an important role for vestibular inputs in this response. In addition, changes at higher and lower frequencies were similar between tilt and centrifugation. Since centrifugation at low frequencies has minimal canal inputs, these data suggest that the response was primarily driven by otolith inputs. In addition, during the previous year we were able to develop a new method of stimulating the vestibular system to increase performance. In the last year of the grant we plan to test our stimulator to determine if it could be used as a new treatment paradigm for vestibular loss with the intention of working towards a countermeasure.
Bibliography Type:	Description: (Last Updated: 10/31/2019)
Abstracts for Journals and Proceedings	Serrador JM, Gopalakrishnan GS, Black FO, Lipsitz LA, Wood SJ. "Effect of vestibular impairment on cerebral blood flow response to dynamic roll tilt." International Autonomic Neuroscience Meeting, Vienna, Austria. 2007. International Autonomic Neuroscience Meeting, Vienna, Austria. 2007. , Oct-2007
Articles in Peer-reviewed Journals	Serrador JM, Lipsitz LA, Gopalakrishnan GS, Black FO, Wood SJ. "Loss of Otolith Function with Age is associated with Increased Postural Sway Measures." Neuroscience Letters (in review), January 2009. , Jan-2009
Articles in Peer-reviewed Journals	Serrador JM, Schlegel TT, Black FO, Wood SJ. "Vestibular effects on Cerebral Blood Flow." BMC Neuroscience (in review), January 2009. , Jan-2009