### Project Details

**Fiscal Year:** FY 2005  
**Task Last Updated:** FY 06/22/2005

**PI Name:** Ray, Chester A. Ph.D.  
**Project Title:** Effect of Simulated Microgravity on the Vestibulosympathetic Reflex in Humans  
**Division Name:** Human Research  
**Program/Discipline:** NSBRI Teams  
**Program/Discipline--Element/Subdiscipline:** NSBRI Teams--Cardiovascular Alterations Team

- **Joint Agency Name:** No
- **TechPort:** No
- **Human Research Program Elements:** None
- **Human Research Program Risks:** None
- **Space Biology Element:** None
- **Space Biology Cross-Element Discipline:** None
- **Space Biology Special Category:** None

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**City:** Hershey  
**State:** PA  
**Zip Code:** 17033-2390  
**Congressional District:** 17

**Comments:**

**Project Type:** GROUND  
**Solicitation:** NSBRI  
**Start Date:** 05/01/2001  
**End Date:** 08/31/2005

- **No. of Post Docs:** 2  
- **No. of PhD Degrees:** 1  
- **No. of PhD Candidates:** 1  
- **No. of Master’s Degrees:** 2  
- **No. of Master’s Candidates:** 2  
- **No. of Bachelor’s Degrees:** 0  
- **No. of Bachelor’s Candidates:** 0

**Contact Monitor:**  
**Contact Phone:**  
**Contact Email:**  
**Flight Program:**  
**Flight Assignment:**  
**Key Personnel Changes/Previous PI:**

**COI Name (Institution):** Sinoway, Lawrence (The Pennsylvania State University)  
**Grant/Contract No.:** NCC 9-58-CA00207

**Performance Goal No.:**

**Performance Goal Text:**

1. **Original Aims**

   1. To determine MSNA responses to head-down neck flexion (HDNF) before and after 1 and 7 days of HDBR. HDNF has been used in our laboratory to activate the vestibular system (i.e., otolith organs) in humans. We have shown that HDNF elicits increases in MSNA. We hypothesize that MSNA responses to HDNF will be attenuated after HDBR and that the attenuation of MSNA will increase as a function of HDBR duration. If the hypothesis is true, this would be the first evidence that vestibular system may participate in the regulation of MSNA after simulated microgravity (i.e., HDBR) and possibly spaceflight.

2. To determine MSNA responses to HDNF during lower-body negative pressure before and after HDBR. We have shown that MSNA is augmented by HDNF during lower-body negative pressure. Thus in healthy adults, the vestibulosympathetic reflex can help defend against orthostatic challenges by increasing MSNA. We hypothesize that...
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<td>HDNF after HDBR will not increase MSNA during lower-body negative pressure. Additionally, we hypothesize that there will be an inhibitory interaction between the vestibulosympathetic reflex and baroreflexes. Therefore, after HDBR the vestibulosympathetic reflex will be impaired and not be able to help defend against an orthostatic challenge by increasing MSNA. This finding would give credence to the concept that alterations in the vestibulosympathetic reflex may participate importantly in post-spaceflight OI.</td>
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### 2. Key Findings

During this granting period our laboratory has made significant contributions in the area of the vestibulosympathetic reflex in humans and orthostatic intolerance. We have published 25 papers in top ranked scientific journals with additional manuscripts in preparation. We summarize a selection of these results below.

- **Effect of Short-Term Microgravity and Long-Term Hindlimb Unloading on Rat Cardiac Mass and Function**: These data suggest that cardiac atrophy does not occur following short-term exposure to microgravity, and that neither short- nor long-term simulated microgravity alter cardiac mass or function.

- **Effect of Age on the Vestibulosympathetic Reflex**: These data indicate that aging attenuates the vestibulosympathetic reflex in humans and may contribute to the increased prevalence of orthostatic hypotension with age.

- **The Vestibulosympathetic Reflex During Orthostatic Challenge in Aging Humans**: These data provide experimental support for the concept that age-related impairments in the vestibulosympathetic reflex persist during orthostatic challenge in older adults. Furthermore, these findings are consistent with the concept that age-related alterations in vestibular function might contribute to altered orthostatic blood pressure regulation with age in humans.

- **Attenuated Sympathetic Nerve Responses After 24 Hours of Bed Rest**: These findings suggest that 24 h of bed rest reduces sympathetic nerve responses to LBNP.

- **Melatonin Attenuates Sympathetic Nerve Responses to Orthostatic Stress in Humans**: These findings indicate that high concentration of melatonin can attenuate reflex sympathetic increases to orthostatic stress in humans. These alterations appear to be mediated by melatonin-induced changes to the baroreflexes.

- **Interaction of the Vestibulosympathetic and Arterial Chemoreflexes**: These findings indicate an additive neural interaction between the vestibulosympathetic reflex and arterial chemoreflex for MSNA, but an inhibitory interaction on mean arterial pressure and heart rate. Therefore, no central modulation exists between these two reflexes with regards to MSNA output in humans.

- **Limb Neurovascular Control During Activation of the Vestibulosympathetic Reflex**: These results indicate that there is not differential control of MSNA in the arm and leg during altered feedback from otolith organs in humans, but that greater vasoconstriction occurs in the calf than the forearm. These findings indicate that vasodilation occurs in other vascular bed(s) to account for the lack of increase in arterial blood pressure during HDR.

- **Effect of Vestibular Activation on Respiration**: These data indicate that semicircular canals, but not otolith organs or neck afferents, mediate an increased respiratory rate in humans and support the concept that vestibular activation alters respiration in humans.

- **Aging Attenuates the Vestibulorespiratory Reflex in Humans**: The results of this study indicate that the vestibulorespiratory reflex is attenuated in older humans, with greater vestibular stimulation needed to activate the reflex.

- **Vestibulosympathetic Reflex During Mental Stress**: We conclude that the interaction for MSNA and arterial pressure is additive during combined vestibular and mental stimulation. Therefore, vestibular- and stress-mediated increases of MSNA appear to occur independently in humans.

- **Aging, Opioid Receptor Agonists and Antagonists, and the Vestibulosympathetic Reflex in Humans**: These data do not provide experimental support for the concept that opioids modulate the vestibulosympathetic reflex in humans. Moreover, endogenous opioids do not appear to contribute to the age-associated impairment of the vestibulosympathetic reflex.

### 3. Major Impact

During this funding period we found that aging may serve as an excellent model for determining the effect of microgravity on the vestibulosympathetic reflex.

### 4. Upcoming year plan

- **Testing a countermeasure to bed rest induced orthostatic intolerance by the activation of the vestibulosympathetic reflex**.

### Rationale for HRP Directed Research:

Our studies may provide a new mechanism responsible to orthostatic intolerance in humans. Also, our results provide a rationale for developing a new treatment of orthostatic intolerance in humans via the activation of the vestibulosympathetic reflex.

### Research Impact/Earth Benefits:

We completed our third year by publishing 12 papers. Major new areas of development were our studies examining the interaction of the vestibulosympathetic reflex with thermal stress and mental stress. Both of these factors can contribute to orthostatic intolerance in humans and are particularly relevant to spaceflight. We found in both cases that the neural interaction of the vestibulosympathetic reflex with these two factors were additive. Thus, the vestibulosympathetic reflex is a robust independent activator of muscle sympathetic nerve activity.

### Bibliography Type:

Description: (Last Updated: 01/26/2007)
| Articles in Peer-reviewed Journals | Monahan, K. D., and C. A. RA Y "Cyclooxygenase inhibition and baroreflex sensitivity in humans American Journal of Physiology: Heart and Circulatory Physiology" Jan-2005 |
| Articles in Peer-reviewed Journals | Monahan, K. D., and C. A. RA Y "Gender affects calf venous compliance at rest and during baroreceptor unloading in humans American Journal of Physiology: Heart and Circulatory Physiology" Jan-2005 |
| Articles in Peer-reviewed Journals | Monahan, K. D., T. E. Wilson and C. A. RA Y "Omega-3 fatty acid supplementation augments sympathetic nerve activity responses to physiological stressors in humans Hypertension" 732-738 , Jan-2005 |
| Articles in Peer-reviewed Journals | Wilson, T. E., N. T. Kuipers, E. A. Mc Hugh, S. Newton, and C. A. RA Y "Vestibular activation does not influence skin sympathetic responses during whole-body heating Journal of Applied Physiology" 540-544 , Jan-2005 |
| Presentation | Wilson, T. E., N. T. Kuipers, E. A. Mc Hugh, S. Newton, C. A. RA Y "Is vestibular activation nonthermal modulator of skin blood flow or sweating? " Jun-2004 |
| Presentation | Kuipers, N. T., C. L. Sauder, and C. A. RA Y "Increased sensitivity of the vestibulosympathetic reflex in the upright posture in humans " Nov-2003 |
| Presentation | Monahan, K. D., and C. A. RA Y "Prostaglandin inhibition does not impair baroreflex sensitivity in humans " Apr-2004 |
| Presentation | RA Y, C. A. "Sympathetic and cardiopulmonary regulation by vestibular reflexes " Oct-2004 |