NASA/CR 97-

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Final

Grant Title:	Baroreflex Function in Rats after Simulated Microgravity
Report Type:	Summary of Research
Investigator:	Eileen M. Hasser, Ph.D.
Report Period:	April 1, 1996 through March 31, 1997
Recipient:	The Curators of the University of Missouri 310 Jesse Hall Columbia, MO 65211
Grant Number:	NAGW-4991

FY96 Data Update Form
Life and Biomedical Sciences and Applications Division
PI Index: Task Description/Bibliography Database

DIRECTIONS: Please provide or update the information contained on the form below. Please do not leave any fields blank

1. COMPLETE TASK TITLE

Baroreflex function in rats after simulated microgravity

2. PRINCIPAL INVESTIGATOR

Last Name: Hasser
First Name or Initial: Eileen
Middle Name or Initial: M.
Prefix Title *(Mr., Dr., Prof., etc.)*: Dr. **Suffix Title** *(Ph.D., Sc.D., M.D., etc.)*: Ph.D.
Affiliation: University of Missouri, Columbia

3. INVESTIGATOR CONTACT INFORMATION

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Mail Code (if any)
Institution
Street
City, State, Zip Code

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Department of Veterinary Biomedical Sciences
E102 Veterinary Medicine
University of Missouri, Columbia
Columbia, MO 65211

Congressional District: 65251

4. CO-INVESTIGATOR INFORMATION

Co-Investigator Name(s) and Degree(s)	Co-Investigator Affiliation(s)
1. James C. Schadt, Ph.D.	University of Missouri
2. M. Harold Laughlin, Ph.D.	University of Missouri
3.	
4.	
5.	
6.	

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Eileen M. Hasser; University of Missouri, Columbia

5. TASK INFORMATION

Solicitation *(NRA, AO, e.g., 93-OLMSA-07)*: 95-OLMSA-01

Task Type *(Flight/Ground)*: Ground

Task Identification Number: 199-14-17-17

Grant Number: NAGW-4991

Joint Agency Participation *(NIH, NIST, DoD, etc.)*:

Discipline Name *Please choose ONE (and only one) of the disciplines listed below that best describes this task.*

- ☒ Cardiopulmonary
- ☐ Hematology/Immunology
- ☐ Endocrinology/Metabolism
- ☐ Pharmacology
- ☐ Musculoskeletal/Connective Tissue
- ☐ Neuroscience
- ☐ Toxicology
- ☐ Barophysiology
- ☐ Microbiology
- ☐ Advanced Hormone, pH, or Electrolyte Sensors
- ☐ Methods for Storing Biological Samples
- ☐ Advanced Displays and Controls Dev.
- ☐ Human-Machine Function Allocation
- ☐ Interaction Among Intelligent Agents
- ☐ IVA & EVA
- ☐ Analog Studies
- ☐ Situational Awareness
- ☐ Human Communication
- ☐ Human Engineering Methodologies
- ☐ Space Workstations
- ☐ Telescience, Training, and Maintenance
- ☐ Strength Decrements
- ☐ Air Revitalization
- ☐ Water Recovery
- ☐ Solid Waste Processing
- ☐ Plant Production
- ☐ Food Processing and Storage
- ☐ Thermal Control Systems
- ☐ Monitoring & Control
- ☐ EVA
- ☐ Technology to Improve EVA Garments
- ☐ Environmental Monitors and Sensors

6. FUNDING

Period of Performance from *(mo/yr)*: 04/96 **to** *(mo/yr)*: 04/97

Yearly Funding *(FY1996)*: $120,707 Direct
$170,333 Total

Students Affiliated with Task:

Level	Number
Pre-college	
Undergraduate	
Graduate	1
Post Docs	
TOTALS	

7. FLIGHT INFORMATION (FLIGHT INVESTIGATORS ONLY)

Monitoring NASA Center *(HQ, ARC, JSC, KSC)*: HQ

Flight Hardware *(BRIC, AEM, STL, etc.)*:

Current Flight Assignment *(STS-89-Neurolab, etc.)*:

Reflight History *(STS-9, STS-54, etc.)*:

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FY96 TASK ABSTRACT

Dr. Eileen M. Hasser, Ph.D. 199-14-17-17 Ground

Baroreflex function in rats after simulated microgravity

Directions: Update to reflect any changes in the direction of the task. However, please limit the length of the text. Significant alterations, additions, or deletions should preferably be submitted in both hard copy and electronic form.

Prolonged exposure of humans to decreased gravitational forces during spaceflight results in a number of adverse cardiovascular consequences, often referred to as cardiovascular deconditioning. Prominent among these negative cardiovascular effects are orthostatic intolerance and decreased exercise capacity. Rat hindlimb unweighting is an animal model which simulates weightlessness, and results in similar cardiovascular consequences. Cardiovascular reflexes, including arterial and cardiopulmonary baroreflexes, are required for normal adjustment to both orthostatic challenges and exercise. Therefore, the orthostatic intolerance and decreased exercise capacity associated with exposure to microgravity may be due to cardiovascular reflex dysfunction. The proposed studies will test the general hypothesis that hindlimb unweighting in rats results in impaired autonomic reflex control of the sympathetic nervous system. Specifically, we hypothesize that the ability to reflexly increase sympathetic nerve activity in response to decreases in arterial pressure or blood volume will be blunted due to hindlimb unweighting. There are 3 specific aims: 1) To evaluate arterial and cardiopulmonary baroreflex control of renal and lumbar sympathetic nerve activity in conscious rats subjected to 14 days of hindlimb unweighting; 2) To examine the interaction between arterial and cardiopulmonary baroreflex control of sympathetic nerve activity in conscious hindlimb unweighted rats; 3) to evaluate changes in afferent and/or central nervous system mechanisms in baroreflex regulation of the sympathetic nervous system. These experiments will provide information related to potential mechanisms for orthostatic and exercise intolerance due to microgravity.

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FY96 TASK PROGRESS

Dr. Eileen M. Hasser, Ph.D. 199-14-17-17 Ground

Baroreflex function in rats after simulated microgravity

Directions: Task progress should include a brief but meaningful paragraph about the status of the task. Answers to the following questions should help to formulate an appropriate statement of progress: What has been accomplished thus far? What questions have been answered? What new questions have arisen? How does this year's progress affect future work on this task? Please note that the taskbook is tied to the fiscal cycle, which may not coincide with the funding cycle of individual tasks. However, even tasks for which funding began in he middle of FY96 should report progress for the partial year. Please submit this text in both hard copy and electronic form.

ATTENUATED BAROREFLEX CONTROL OF SYMPATHETIC NERVE ACTIVITY IN HINDLIMB UNWEIGHTED RATS. (Manuscript to be submitted to Am. J. Physiol.)

This study tested the hypothesis that hindlimb unweighting in rats, an animal model of microgravity, results in attenuated baroreflex control of sympathetic nerve activity. A corollary hypothesis was that reflex control of sympathetic nerve activity to the viscera and to skeletal muscle would be impaired in a differential manner. Rats were either hindlimb unweighted by attachment of a tail harness, or served as cage controls. Following 13 days of HU or normal cage activity, rats were implanted with femoral catheters and electrodes for recording either renal sympathetic nerve activity (RSNA) or lumbar sympathetic nerve activity (LSNA) and allowed to recover 24 hours. Thus, there were four groups of rats: control RSNA(n = 8), HU RSNA (n = 8), control LSNA (n = 8)and HU LSNA (n = 8). Reflex changes in RSNA or LSNA and heart rate (HR) were recorded in response to changes in arterial pressure. Mean arterial pressure (MAP) was increased or decreased by ramp infusions of phenylephrine and nitroprusside, respectively. Data relating RSNA or LSNA and HR to MAP were fit to a sigmoid logistic function, and curve parameters generated. Resting MAP was not altered by HU, while HR was significantly increased (HU: 423.8±10.5, C: 365.4±7.3). Maximal RSNA in response to decreases in MAP (HU: 249 ± 12 % control, C: 455 ± 34% control) and gain of baroreflex control of RSNA (HU: -5.1 ± 0.2, C: -15.0 ± 4.0) were significantly reduced. In addition, maximal LSNA in response to decreases in MAP (HU: 204 ± 12 % control, C: 342 ± 31% control) and gain of baroreflex control of LSNA (HU: -4.0 ± 0.6, C: -7.8 ± 1.3) were also significantly reduced. Baroreflex control of HR was not different between groups. Thus, HU attenuated baroreflex control of both RSNA and LSNA. These data are consistent with the concept that impaired baroreflex function could be a contributing factor to orthostatic intolerance following exposure to microgravity.

EFFECTS OF HINDLIMB UNWEIGHTING ON BARORECEPTOR AFFERENT SIGNALING. **(Abstract at Experimental Biology 97 - Study in Progress)**

Previous studies utilizing the hindlimb unweighting (HU) model of microgravity indicate a significant attenuation in baroreflex control of sympathetic nerve activity. This experiment tested the hypothesis that the difference in baroreflex function is due to altered central processing of baroreceptor information, and not to an impairment of baroreceptor afferent responses to changes in pressure. Rats were either hindlimb unweighted (n=4) by attachment of a tail harness, or served as cage controls (n=4). Following 13 days of HU or control activity, rats were anesthetized with Inactin, and implanted with arterial and venous femoral catheters. Electrodes placed on the aortic depressor nerve (ADN) and on a branch of the renal nerve for recording renal sympathetic nerve activity (RSNA). Changes in ADN activity and RSNA were recorded in response to increases and decreases in mean arterial pressure (MAP) due to ramp infusions of phenylephrine and nitroprusside,

Dr. Eileen M. Hasser, Ph.D. 199-14-17-17 Ground

Baroreflex function in rats after simulated microgravity

Directions: Answers to the following questions should help to formulate an appropriate statement of Earth benefits: Does this research seek to understand a disease or malady that affects humans on Earth and/or in space? Does this research seek to develop new therapeutics or protocols for alleviating symptoms of a disease or malady on Earth? Will this research yield a new understanding of basic biological processes? What relationship does this task posit between processes on Earth and in space? What impact could the results of this research have on the common man? What benefits are foreseen by the development of this new technology? Please submit this text in both hard copy and electronic form.

respectively. Data relating RSNA to MAP were used to assess overall baroreflex function; data relating ADN activity to MAP were used to assess baroreceptor afferent function; and data relating RSNA to ADN activity were used to assess central processing of baroreceptor afferent information. All data were fit to a sigmoid logistic function. Curve parameters were generated for each animal and averaged. As in the previous study, HU reduced the maximum activation of RSNA in response to a decrease in arterial pressure. Hindlimb unweighting did not significantly alter the ADN activity in response to changes in arterial pressure. The efferent RSNA response to changes in afferent activity was reduced by HU. Thus, the attenuation of baroreflex control of sympathetic nerve activity does not appear to accounted for by changes in afferent signaling, thus indicating a possible central mechanism in this dysfunction.

EFFECTS OF HINDLIMB UNWEIGHTING ON THE RESPONSE TO HEMORRHAGE
(Study in Progress)

Initial studies indicated that baroreflex mediated activation of the sympathetic nervous system in response to a hypotensive challenge was attenuated by hindlimb unweighting. This preliminary study has begun to evaluate the functional significance of this alteration in reflex function by testing the hypothesis that hindlimb unweighting reduces the ability of an animal to defend arterial pressure against blood loss. Rats were either hindlimb unweighted (HU) (n = 3) by attachment of a tail harness, or served as cage controls (n = 3). Following 13 days of HU or normal cage activity, rats were implanted with femoral catheters and electrodes for recording lumbar sympathetic nerve activity (LSNA), and allowed to recover 48 hours. Control and hindlimb unweighted animals were then subjected to hemorrhage at a rate of blood removal of 1 ml/min, and hemodynamic responses monitored. Preliminary data suggest that the reflex increase in LSNA and the blood loss required to reduce arterial pressure to 50 mmHg is less in HU rats compared to controls. These data are consistent with the concept that impaired baroreflex function in HU rats is functionally relevant.