Mechanistic Studies on Reduced Exercise Performance and Cardiac Deconditioning with Simulated Zero Gravity

(NASA-NAG 2-392)

Charles M. Tipton, Ph.D.

Department of Exercise and Sport Sciences

University of Arizona

Tucson, Arizona 85721

Part I: Current Activities

A. Introduction

As indicated by the title, the primary purpose of this sponsored research is to study the physiological mechanisms associated with the exercise performance of rats subjected to conditions of simulated weightlessness. A secondary purpose is to study related physiological changes associated with other systems. To facilitate these goals, a rodent suspension model was developed (Overton-Tipton) and a $\dot{V}O_2$ max testing procedure was perfected.

Three methodological developments have occurred during this past year deserving of mention. The first was the refinement of the tail suspension model so that (a) the heat dissipation functions of the caudal artery can be better utilized and (b) the blood flow distribution to the tail would have less external constriction (Figure 1). The second was the development on a one-leg weight bearing model for use in simulated weightlessness studies (Figure 2) concerned with change in muscle mass, muscle enzyme activity and hindlimb blood flow.

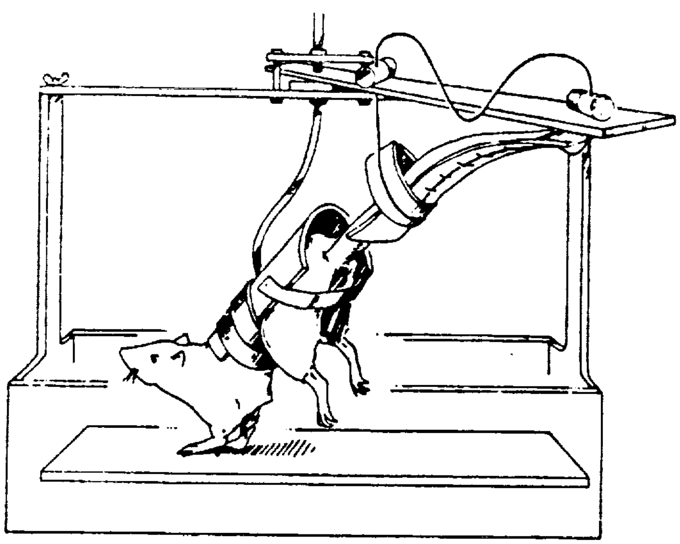


Figure 1

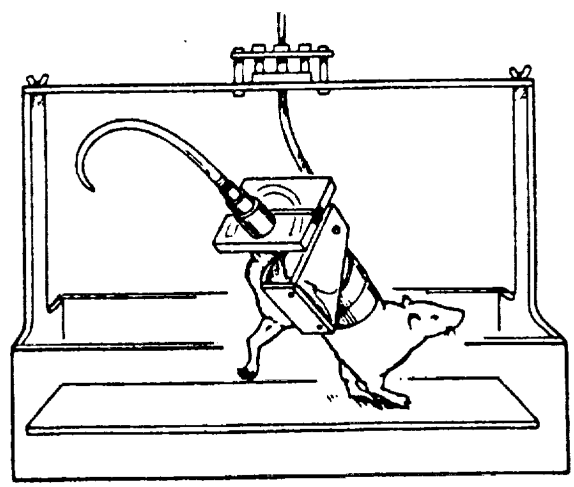


Figure 2

With the assistance of a visiting Professor, Dr. Roger Coomes and Mr. Craig Stump, a NASA Pre-Doctoral Fellow, the chemical body composition of 30 rats was determined and used to develop a prediction equation for percent fat using underwater weighing procedures to measure carcass specific gravity and to calculate body density, body fat and fat free mass. The mathematical least square equation that had the best fit was $Z = a/x + bY + c$ where: $a = -2136.4$, x = specific gravity -1.00000 (10^5), $b = 0.05555$, y = body mass in grams and $c = -10.09180$. The correlation coefficient between the measured fat percentage and the predicted fat percentage was 0.834.

1. A comparative study on the effects of two suspension methods on select anatomical, biochemical and physiological variables.

   a. We wanted to determine if exercise performance results were different depending upon the method selected.

   b. Select results ($\bar{X}$,* intergroup statistical significance) from controls between the Morey-Holton and the Overton-Tipton models were as follows:

Group	N	% Change in Plasma NE (2 Days)	% Change in Plasma NE (9 Days)	% Change in Body Mass (14 Days)	% Change in $\dot{V}O_2$ max (14 Days)	% Change in Run Time (14 Days)
Cage Control	3-10	11	5	3	5	16
Morey-Holton	6-10	53*	47*	-5	-7	-26*
Overton-Tipton	7-9	71*	212*	-14*	0	-19*

2. Relevant findings from the one-leg weight (4) bearing model were:

   a. The decrease in soleus muscle mass with suspension can be minimized or prevented by having one hindlimb support the mass of the animal.

   b. The decrease in the activity of acrobic enzymes of the soleus muscle with suspension can not be prevented by having one hindlimb support the body mass of the animal.

   c. The increase in resting blood pressure observed with a one-leg hindlimb suspension model may be associated with the integration of the afferent inputs by the medulla.

3. Conclusions:

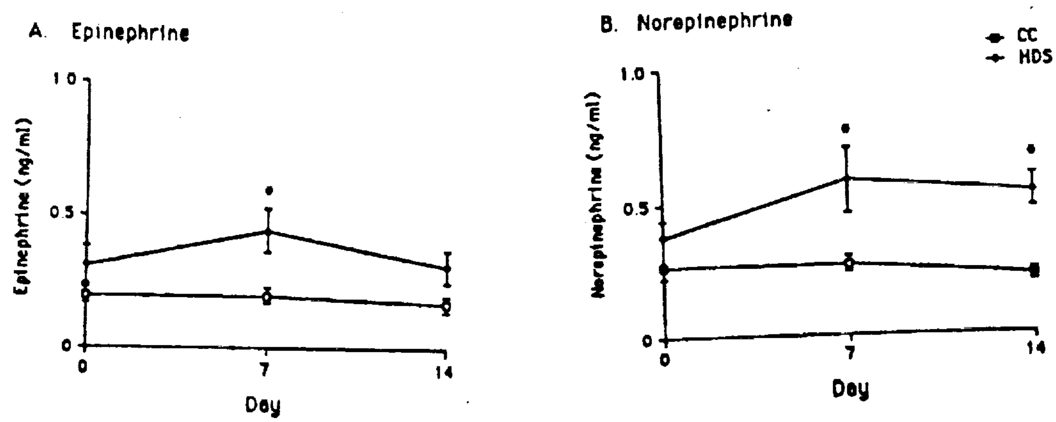
   a. We now have suspension techniques suitable to measure the effects of posture and weight bearing on a variety of physiological, biochemical, and anatomical parameters.

   b. We can now better estimate the body compositional changes with simulated weightlessness.

B. <u>The Influence of Sympathetic Nervous System</u>

1. Time course of changes in catecholamines.

   a. To determine the changes in the Overton-Tipton model before initiating sympathectomy studies, a study with 10 control and 11 suspended rats was conducted. The results are listed in Figure 3 ($\bar{X}$,SE,* intergroup and intragroup difference that was statistically significant).



2. The effects of chemical sympathectomy and simulated weightlessness on exercise performance.

   a. To determine whether exercise performance would be altered after the "removal" of the sympathetic nervous system.

   b. Select $\dot{V}O_2$ max results with saline or quanethidine sulfate injections in male or female rats ($\bar{X}$,SE,* intragroup, ⊗ intergroup statistical significance, $ml \cdot mm^{-1} \cdot kg^{-1}$ or $ml \cdot min^{-1} \cdot kg\ FFM^{-1}$).

Group	N	Pre-Suspension	After 7 Days	After 14 Days	After 14 Days (FFM)
SHAM (males)					
Cage Control	6	84±3	86±3	85±2	102±6
Suspended	6	84±2	87±1	80±2*	94±6
SYMX (males)					
Cage Control	6	81±1	82±2	77±2	88±4
Suspended	8	86±2	98±2*⊗	94±1*⊗	108±6*
SHAM (females)					
Cage Control	8	83±2	85±2	78±2	92±2
Suspended	7	89±1	84±2	88±2⊗	94±3
SYMX (females)					
Cage Control	6	88±4	89±3	88±3	104±3
Suspended	7	85±2	95±4*	94±4⊗	109±4

4. The combined influences of sympathectomy, adrenal demedullation and simulated weightlessness on exercise performance.

   a. Although the results are in the analysis stage, the data (presented) are in form for publication.

   b. Trends suggest that absolute $\dot{V}O_2$ max is significantly decreased when demedullation is coupled with sympathectomy. Changes in relative $\dot{V}O_2$ max are not as apparent.

5. Conclusions: The presence of circulating epinephrine (and its receptors) appears to be essential to avoid the marked decrease in $\dot{V}O_2$ max that occurs with weightlessness.

C. <u>Effects of Simulated Weightlessness for 28 Days on Performance and Fat-free Mass</u>

1. To determine whether longer durations would affect both exercise performance and fat-free mass.

   a. Select results ($\bar{X}$,SE,* intragroup, ⊗ intergroup statistical significance) pertaining to % fat, $\dot{V}O_2$ max ($ml \cdot min^{-1} \cdot kg^{-1}$ or FFM^{-1}) or run time (min) of female rats.

			$\dot{V}O_2$ max			Run Time	
Group	N	% Fat	Start	End	End (FFM)	Start	End
Cage Control	9	12±1	99±3	92±2*	109±8	15±.6	13±.7*
Suspended	8	7±2*	96±3*	90±4	102±8	15±.8	10±.5*⊗

2. Conclusions: Simulated weightlessness causes more of a change in fat mass than in fat-free mass. Consequently, the decline in $\dot{V}O_2$ max is due to other mechanisms than a decrease in the active muscle mass.

D. <u>The Effect of Prior Endurance Training on Exercise Performance of Rats Exposed to Conditions of Simulated Weightlessness for 28 Days</u>

1. To determine whether trained rats would exhibit greater decreases in exercise performance than nontrained rats with suspension.

2. Results are after 6 weeks of training ($\bar{X}$,SE,⊗ intergroup statistical significance).

	N	Body Mass (g)	$\dot{V}O_2$ max ($ml \cdot min^{-1} \cdot kg^{-1}$)	Run Time (Minutes)
Nontrained	12	344±16	82±2	12±.4
Trained	10	330±10	98±1⊗	16±.4*

3. The influence of simulated weightlessness for 28 days on the exercise performance of nontrained and trained animals.

   a. Rational was the same as listed in above.

b. Results are ($\bar{X}$SE,* intragroup, ⊗ intergroup statistical significance) for body mass (gram), $\dot{V}O_2$ max ($ml \cdot min^{-1} kg^{-1}$) and run time (min).

Group	N	Body Mass		$\dot{V}O_2$ max		Run Time	
		Start	End	Start	End	Start	End
NT-Cage Control	12	344±16	431±11*	82±2	75±4	12±.4	11±.4
NT-Suspended	9	341±16	309±16*	81±4	77±3	12±.5	8±.2*⊗
T-Cage Control & Detraining	10	330±10	419±11*	91±1	84±3	16±.4	15±.5
T-Suspended	10	344±7	285±15*⊗	95±2	81±3*	16±3	10±1.1*⊗

4. Conclusions: Prior exercise training is associated with a faster decline in performance measures than nontrained rats during this time period. It is unknown whether the same trends would continue longer durations.

E. Published Results on the Effects of Simulated Weightlessness on Select Physiological Parameters.

1. Baroreflex control of heart rate (LBNP; sympathominetric agents) was not significantly altered by 9 days of simulated weightlessness (3).

2. Suspended rats exhibited a reduced pressor response to phenylephrine injections than cage control rats. Also with this finding was a significant elevation in mesenteric vascular resistance (3).

3. Suspended rats had greater decreases, but not statistically, in plasma volume than nonsuspended rats (3).

4. Blood flow results obtained from Doppler probes indicated that:

   a. Suspension was associated with an increase in iliac and mesenteric vascular resistance during exercise (3).
   b. Iliac blood flow was significantly decreased after 48 hours suspension (4).
   c. The decrease in iliac blood flow with suspension was prevented by having one hindlimb support the weight of the animal (4).

5. The effects of simulated weightlessness on the rise in core temperature with a gradual heat challenge indicated that the suspended rats reached 40.5°C sooner than their nonsuspended controls. We speculate that these results occur because of a reduction in hindlimb blood flow and a decline in plasma volume.

Part II: Future Projects and Their Relevance to Current or Future NASA Projects

A. The influence of 42-56 days of simulated weightlessness on exercise performance as evaluated by $\dot{V}O_2$ max, run time and mechanical efficiency.

B. The influence of 42-56 days of simulated weightlessness on resting and exercise cardiac hemodynamics, plasma volume, blood gas changes, and baroreflexes.

C. The influence of an elevated plasma volume on the prevention of $\dot{V}O_2$ max changes with short (14 day) and long (42-56) durations of simulated weightlessness.

D. The influence of short (14 days) and long (42-56) durations of simulated weightlessness on tissue norepinephrine turnover rates.

E. The influence of front leg exercise training by suspended rats on their whole body $\dot{V}O_2$ max values.

F. The influence of short (14 days) and long durations (42-56 days) of simulated weightlessness on the exercise performance of hypophysectomized rats.

Part III. Publications Associated Directly or Indirectly with NASA-NAG 2-392

A. Manuscripts Published in 1990

1) Kregel, K.C., D.G. Johnson, C.M. Tipton, and D.R. Seals. Arterial baroreceptor reflex modulation of sympathetic cardiovascular adjustments to heat stress. Hypertension 15:497-504, 1990.

2) Kregel, K.C., C.M. Tipton, D.R. Seals. Thermal adjustments to nonexertional heat stress in mature and senescent Fisher 344 rats. J. Appl. Phys. 68:1337-1342, 1990.

3) Overton, J.M. and C.M. Tipton. Effect of hindlimb suspension on cardiovascular responses to sympathectomized and lower body negative pressure. J. Appl. Physiol. 68:355-362, 1990.

4) Stump, C.S., J.M. Overton, and C.M. Tipton. Influence of a single hindlimb support during simulated weightlessness in the rat. J. Appl. Physiol. 68:627-634, 1990.

B. Abstracts Published in 1990

5) Coomes, R.K., L.A. Sebastian, C.S. Stump, P.K. Edwards, and C.M. Tipton. Influence of two methods of head-down suspension (HDS) on the stress response of rats: Preliminary Results. ASGSB Bulletin. 4(1) 73, 1990.

6) Kregel, K.C., J.M. Overton, D.G. Johnson, C.M. Tipton, and D.R. Seals. Cardiovascular sympathoadrenal and thermal adjustments to nonexertional heat stress in the conscious rat. FASEB J. 4(3):A889, 1990.

7) Stump, C.S., C.R. Woodman, and C.M. Tipton. Exercise induced glycogen depletion in select rat hindlimb muscles after two weeks of hindlimb suspension. Med. Sci. Sports Exerc. 22(2):S52, 1990.

8) Woodman, C.R., K.C. Kregel, and C.M. Tipton. Thermal responses to non-exertional heat stress following simulated weightlessness in the conscious rat. FASEB J. 4(3):A569, 1990.

9) Woodman, C.R., C.S. Stump, L.A. Sebastian, and C.M. Tipton. Influences of 28 days of hindlimb suspension on the $\dot{V}O_2$ max of trained and nontrained rats. ASGSB Bulletin, 4(1):65, 1990.