NASA-CR-205327

Progress Report and Statement of Work

for Continuation of the Cooperative Agreement entitled

EXERCISE WITHIN LBNP TO PRODUCE ARTIFICIAL GRAVITY

between

NASA Ames Research Center
Moffett Field, CA 94035-1000

and

The Regents of the University of California
University of California at San Diego
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NCC2-852 #4

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10/18/95

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OFFICIAL AUTHORIZED TO SIGN FOR INSTITUTION:

10/17/95

Roger D. Meyer, Associate Dean for Administration — **Date**

PROGRESS REPORT

a. Lower body negative pressure exercise during bed rest maintains orthostatic tolerance.

Recent results:

Integrated physiologic countermeasures are needed to maintain orthostatic tolerance after spaceflight or bed rest. We hypothesized that supine exercise during LBNP would prevent bed rest-induced loss of orthostatic tolerance by preventing hemoconcentration. In a study conducted jointly with NASA Johnson Space Center and the Unversity of Texas Medical Branch, Galveston, TX, fifteen male subjects underwent 5 days of 6° head-down bed rest: 5 control subjects did not exercise, and 10 performed 30 min/day of supine interval treadmill exercise at intensities up to 90% VO_{2peak}. One body weight of footward force was generated by 55 ± 3 mm Hg LBNP during supine exercise on a vertical treadmill. Pre- and post-bed rest orthostatic tolerance was assessed as time to presyncope during 80° head-up tilt (30 min max). Heart rate and arterial blood pressure were measured by standard methods during head-up tilt. Hematocrit quantified hemoconcentration. Mean head-up tilt tolerance was unchanged in the subjects who performed 30 min/day LBNP exercise during bed rest (pre: 25.9 ± 2.8 min, $\bar{X}$ ± SE; post: 28.2 ± 1.8 min; NSD). In contrast, tilt tolerance time in control subjects decreased from 27.3 ± 2.7 min to 22.4 ± 4.0 min ($p < 0.05$). Hematocrit increased from 41.8 ± 1.1 to 45.0 ± 1.0% in the control group during 5 days of bed rest, indicating substantial hemoconcentration. Hematocrit did not increase significantly in the group performing LBNP exercise (42.8 ± 0.8 vs. 43.5 ± 0.8%; NSD). The two groups exhibited similar mean heart rates and arterial blood pressures during orthostasis after bed rest.

Significance:

These results indicate that LBNP exercise during bed rest prevents hemoconcentration, which in turn, may help maintain orthostatic tolerance.

b. A daily, 30-minute bout of interval treadmill exercise with lower body negative pressure does not maintain exercise capacity during bed rest.

Recent results:

We have shown previously that supine exercise during lower body negative pressure (LBNP) can produce similar footward forces and heart rate responses as upright exercise. In this study, we evaluated the effectiveness of a high intensity, interval exercise treadmill protocol to maintain peak oxygen uptake (VO_{2peak}) during 5 days of 6° head-down bed rest. The 30-minute exercise protocol (40 to 90% VO_{2peak}) was performed once daily while subjects ran in the supine position against LBNP adjusted to produce one body weight (55 ± 3 mm Hg). VO_{2peak} was determined using a graded upright treadmill test before and immediately after bed rest in 7 control subjects (no exercise training) and 10 exercise subjects (daily exercise). For the control group, VO_{2peak} decreased for 6 out of 7 subjects (45.6 ± 2.0, mean ± S.E. to 42.6 ± 1.4 ml/kg/min). For the exercise group, VO_{2peak} decreased for 8 out of 10 subjects (48.7 ± 2.0 to 45.8 ± 2.3 ml/kg/min). Both VO_{2peak} values ($P = 0.29$) and the heart rate response to the graded exercise levels ($P = 0.81$) did not differ between groups.

Significance:

Our results suggest that a longer and/or more intense treadmill LBNP exercise protocol will be necessary to maintain aerobic capacity during bed rest and space flight.

c. Supine exercise with lower body negative pressure maintains upright exercise responses after bed rest.

Recent Results:

We hypothesized that daily supine exercise with LBNP would be as effective as upright exercise in maintaining upright exercise responses after 5 days of 6° head-down tilt bed rest. Twenty-four healthy men were randomly assigned to one of three groups (n=8). The control group did not exercise, the upright group performed a daily, 30-minute interval exercise protocol on a treadmill, and the LBNPEx group performed the same protocol while supine in an LBNP device (51.3 ± 0.4 mm Hg). All subjects completed a graded upright treadmill test before and immediately after bed rest at three exercise levels with measurements of heart rate, respiratory exchange ratio, and ventilaton. After bed rest, only the control group had significant ($p < 0.05$) increases in heart rate (176 ± 3 pre vs. 185 ± 2 post), respiratory exchange ratio (1.03 ± 0.02 pre vs. 1.12 ± 0.03 post), and ventilaton (90 ± 5 pre vs. 103 ± 5 post) by exercise level three (VO_2 = 41 ± 1 ml/kg/min).

Significance:

This investigation suggests that supine exercise with LBNP is as effective as upright exercise in maintaining upright exercise responses during bed rest, and should be considered as a possible countermeasure to help sustain egress capability after space flight.

Sections a. - c. above collectively indicate that 30 minutes of supine LBNP exercise per day at 1.0 body weight footward force during bed rest maintain orthostatic tolerance, but not aerobic fitness. Greenleaf (1989) found that 30 min/day of supine cycle ergometry maintained *supine* exercise capacity, but not orthostatic tolerance. He did not measure upright exercise capacity.

Therefore, in this proposal we have increased daily exercise load to 1.2 body weights and exercise duration to 40 minutes to protect upright exercise capacity during bed rest. Preservation of bone properties constitutes additional reason for increasing exercise load and duration. Because bone is more responsive to load magnitude than to load frequency (Whalen et al., 1988), we believe 40 min is a reasonable duration of daily activity. In addition to the potential musculoskeletal and cardiovascular benefits, treadmill exercise within LBNP may activate the same neuromuscular systems as normal ambulation, which should help prevent loss of neuromuscular coordination following bed rest and space flight (Cohen et al., 1986; Dupui et al., 1992; Homick et al., 1977; Young et al., 1984). Exercise within a LBNP chamber in space may provide a safe (no Coriolis effects), inexpensive, energy efficient, and compact alternative to centrifugation during long-duration existence in microgravity.

d. Recent Publications Relevant to Cooperative Agreement

<u>Articles</u>

1. Parazynski SE, AR Hargens, B Tucker, M Aratow, J Styf, and A Crenshaw. Transcapillary fluid shifts in tissues of the head and neck during and after simulated microgravity. Journal of Applied Physiology 71:2469-2475, 1991.
2. Hargens AR, RT Whalen, DE Watenpaugh, DF Schwandt, and LP Krock. Lower body negative pressure to provide load bearing in space. Aviation, Space, and Environmental Medicine 62:934-937, 1991.
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17. Parazynski SE, BJ Tucker, M Aratow, A Crenshaw, and AR Hargens. Direct measurement of capillary blood pressure in the human lip. Journal of Applied Physiology 74:946-950, 1993.
18. Breit GA, DE Watenpaugh RE Ballard, G Murthy, and AR Hargens. Regional cutaneous microvascular flow responses during gravitational and LBNP stresses. Physiologist 36:S110-S111, 1993.
19. Aratow M, RE Ballard, AG Crenshaw, J Styf, DE Watenpaugh, NJ Kahan, and AR Hargens. Intramuscular pressure and electromyography as indexes of force during isokinetic exercise. Journal of Applied Physiology 74:2634-2640, 1993.
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34. Stout MS, DE Watenpaugh, GA Breit, and AR Hargens. Simulated microgravity increases cutaneous microcirculatory blood flow in the head and leg of humans. Aviation, Space, and Environmental Medicine 66:872-875, 1995.
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36. Watenpaugh, DE and AR Hargens. The Cardiovascular System in Microgravity. In: Handbook of Physiology, Section 4: Adaptation to the Environment. Edited by MJ Fregly and CM Blatteis, Part 4: The Gravitational Environment, Chapter 30. New York: Oxford University Press, in press, 1995.
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41. Lillywhite HB, R Ballard, and AR Hargens. Tolerance of snakes to hypergravity. Physiological Zoology, accepted, 1995.
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<u>Patents</u>

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2. Watenpaugh DE. Self-Generated Oscillating Pressure Exercise Device. (U.S. Patent 5,356,361 issued October 1994).

Abstracts

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12. Kahan NJ, M Aratow, DE Watenpaugh, RE Ballard, J Styf, A Crenshaw, and AR Hargens. Surface EMG versus intramuscular EMG: correlations with joint torque during isometric, concentric, and eccentric exercise. FASEB Annual Meeting, FASEB Journal 6:A1237 (1737), 1992.
13. Murthy G, DE Watenpaugh, RE Ballard, RT Whalen, and AR Hargens. Footward forces and intramuscular pressures generated during exercise in supine lower body negative pressure versus upright posture. FASEB Annual Meeting, FASEB Journal 6:A1770 (4823), 1992.
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STATEMENT OF WORK

Bed rest studies to test efficacy of LBNP exercise concept for preventing musculoskeletal and cardiovascular deconditioning

We will undertake two 14 day bed-rest studies (6° head-down tilt bed rest, HDT) to investigate the mechanism of action and efficacy of our partial vacuum exerciser concept. These 14 day bed rest studies were chosen to simulate current microgravity exposures for Space Shuttle crew members. All human research proposed for this cooperative agreement continuation will be performed at NASA Ames Research Center, Moffett Field, CA. The Ames Human Research Facility (HRF) can accommodate 8 subjects comfortably. We will attempt to examine the same 8 subjects in both 14 day bed rest studies, randomly assigning four subjects to 40 minutes of supine running exercise per day at 1.2 body weight of footward force (60-70 mm Hg LBNP), while the remaining four subjects will constitute the nonexercise "control" group. The rationale for selection of 40 minutes of exercise per day is that aerobic fitness (ACSM Position Paper, 1990) and bone material properties (Goldstein et al., 1988; Whalen et al., 1988) should be maintained. Therefore, our interval exercise protocol will be similar to that employed by Greenleaf et al. (1989), but longer and more intense: 7 min warm-up at 40% peak oxygen uptake, followed by 3 min at 60%, 2 min at 40%, 3 min at 70%, 2 min at 50%, 3 min at 80%, 2 min at 60%, 3 min at 80%, 2 min at 50%, 3 min at 70%, 2 min at 40%, 3 min at 60%, and 5 min cool-down at 40% peak oxygen uptake (40 min total).

Four months after the first 14 day HDT study, the two groups will be reversed so that the previous nonexercise group will receive the same 40 min of supine jogging per day at 1.2 body weight (60-70 mm Hg LBNP) while the previously-exercised group will not exercise during the 14 days of HDT. This paired experimental design, where each subject is his own control, will allow for more powerful statistical comparisons. Also, if one or two subjects drop out of the studies, we will still have a total of 6-7 subjects with paired comparisons possible for each physiologic test. Besides having the subjects act as their own control, both HDT sessions will include a three day ambulatory control period to provide baseline data and a two day recovery period to monitor return of physiologic function. If important parameters such as muscle strength, urinary markers of collagen breakdown, or gait have not returned to their normal baseline values after two days, a longer period of recovery testing will be undertaken.

In the two weeks prior to the baseline control period, activity logs will be maintained on each subject, and ambulatory levels of urinary collagen breakdown markers will be established. All physiologic tests and exercise bouts will take place at the same time of day for a given subject. These tests and exercise bouts will be staggered so that sufficient time is allowed to complete the procedure. While the subjects live at the HRF, their diet will be controlled (approximately 2500-3000 kcal per day, depending on exercise level) and their body weight, fluid intake and urine outputs will be monitored. We expect that subjects will maintain a neutral or positive fluid balance, and that they will not lose weight, when performing LBNP exercise during 14 d HDT. During the entire period of bed rest, all subjects will remain in 6° HDT except during periods for showers and exercise (0.5-1.5 h/day), when they will be horizontal (0°).

On the day before HDT bed rest, all subjects will be tested for orthostatic tolerance and upright peak oxygen uptake. Other tests on this day will include cerebral blood flow, plasma volume, leg muscle strength, and urine and gait analyses. During the recovery period, these tests will be repeated within 4 h of return to upright posture and every other day thereafter until results are within 5% of their control, baseline value. Subjects will be staggered with respect to time of HDT initiation and return to upright posture to facilitate testing. Time of day of exercise bouts and physiologic testing will be held constant for a given subject.

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Budget for Continuation Costs

DETAILED BUDGET FOR 12-MONTH CONTINUATION		FROM Dec. 1, 1995		THROUGH Nov. 30, 1996	
		DOLLAR AMOUNT REQUESTED			
PERSONNEL					
NAME	TITLE	EFFORT ON PROJECT	SALARY	FRINGE BENEFITS	TOTALS
D.E. Watenpaugh	Lab Manager	100%	54,111	13,257	67,368
R.E. Ballard	Research Associate	100%	34,065	8,346	42,411
G. Murthy	Research Associate	67%	27,074	6,633	33,707
K.J. Hutchinson	Exp. Data Assistant	100%	30,195	7,397	37,592
	SUBTOTALS →		$145,445	$35,633	$181,078
EQUIPMENT	2 IBM compatible Pentium-based computers			4,000	
	PowerMac computer			4,000	
	Color printer			500	
	IBM compatible laser printer			500	9,000
SUPPLIES	Medical supplies			3,000	
	Gastro-intestinal function study supplies			1,215	
	Page charges			1,000	
	Reproduction services			750	
	Video and film services			750	6,715
TRAVEL	3 investigators to 1 scientific meeting each			2,808	2,808
NON-EQUIPMENT DIRECT COSTS					190,601
INDIRECT COSTS					49,556
EQUIPMENT COSTS					9,000
TOTAL COSTS FOR 12-MONTH CONTINUATION					$249,157

Budget Justification

a. Personnel

Salary support and benefits are required for ongoing employment of laboratory personnel (Ballard, Hutchinson, Murthy and Watenpaugh) and the addition of a lab assistant.

b. Equipment

A recent upgrade in the software necessary to run the Lido dynamometer requires a Pentium-based IBM compatible computer ($2,000) and printer ($500). The Lido dynamometer is necessary for studies of leg muscle strength and endurance. An additional Pentium-based computer is necessary to support general data acquisition needs of the laboratory. Specifically, the orthostatic tolerance test station will require simultaneous monitoring and recording of 11 variables. A PowerMac ($4,000) and color printer will be used to support graphic software upgrades and integrate Mac and IBM data reduction and analysis tasks.

c. Supplies

Supplies include sterile and non-sterile medical supplies (tape, Op-site, electrodes, gauze, catheter introducers, saline, syringes, Lidocaine, gloves, drapes, needles, razors, Betadine swabs, Benzoin, hydrogen peroxide, pressure tubing, 2- and 4-way stopcocks, Evan's blue dye, mouthpieces for oxygen consumption measurement, disposable temperature sensor probes, urinals, Alconox detergent, Cidex disinfectant, etc.), reproduction and film processing services, and support for journal page charges and reprint costs.

d. Travel

Travel support is requested for attendance of one scientific meeting by each of three investigators to present results from the studies proposed in this continuation. The dates and locations of the meetings to be attended are not yet known, because abstracts have not yet been submitted and accepted. However, past experience indicates that the cost for one investigator to attend a typical 4-day meeting equals approximately $936 ($333 airfare, $105 registration, $62/day hotel, $31/day food, and $33/day ground transportation). Therefore, the total cost for three investigators to attend one scientific meeting each is $2,808.

e. Indirect Costs

Indirect costs of this Cooperative Agreement (26%) apply to all non-equipment line items, and are included.