Efficacy of Countermeasures to Cardiovascular Deconditioning in Men and Women During Simulated Moon and Mars Explorations

16th Annual Kentucky EPSCoR Conference
Louisville, KY

May 26, 2011
Team Members

- **University of Kentucky**  
  J Evans, M Meng, S Wang, V Kostas, V Ayanampudi, M Howarth, R Schneider, R Moore, L Mohney, L Krompak, M Haaga, D Irwin, R Shapiro, D Randall, A Patwardhan, C Knapp

- **University of Louisville**  
  K Sharp, G Pantalos

- **Vanderbilt University**  
  A Diedrich

- **NASA Ames Research Center**  
  J Smith, F Moore

- **Johnson Space Center**  
  P Norsk, S Platts, T Schlegel, M Stenger, T Matz

- **Alter-G Corp, Menlo Park CA**  
  F Moore
Space explorations present new challenges to physiological systems. Therefore, we must review, rethink and prepare for such missions.
Cardiovascular Deconditioning: Zero G (Simulated by bedrest or drug administration)

- **Earth’s Gravity (1G)**
  - Normal Volume

- **Zero G**
  - Volume Shifts to Chest and Head

- **Return to Earth’s Gravity**
  - Volume is Low and Now Shifts from Head to Legs
  - Possibility of Fainting!

- **Adaptation to Zero G**
  - Volume is Low and Still Shifted to Chest and Head
To date no single countermeasure to cardiovascular deconditioning is sufficiently effective for mission acceptance, we are studying two that show promise.

In addition, mission requirements have changed:
- Living and working in lunar (1/6 G) and Mars (3/8 G) gravities has been added to the 0 G of space flight and asteroid missions.
- Artificial gravity training as a countermeasure to cardiovascular deconditioning has been added to the latest NASA human research program guidelines.
Mission Objectives

- Simulate space flight-induced cardiovascular deconditioning in a more cost effective way than with head down bedrest.

- Develop a countermeasure more uniquely designed for extended lunar and Mars missions where eventually more time will be spent than in the 0 G environment.

- Simulate activity in lunar and Mars gravity environments for testing proposed countermeasures.

- Test countermeasures for reducing orthostatic intolerance upon return to earth following space missions.
1. Employ a more cost effective human model of space flight-induced cardiovascular deconditioning using a hypovolemia protocol.
Develop a model of space flight-induced cardiovascular deconditioning using a hypovolemia protocol

(More cost effective protocol than head down bedrest)

- A single Lasix® (furosemide) infusion (0.5 mg/kg) followed by a few hours of a very low sodium diet (10 mEq/day) will induce a plasma volume loss similar to that of spaceflight.
NASA JSC Hypovolemia Results

- In 33 volunteers, the plasma volume decrease of 15.8 +/- 1.7% with furosemide equaled the loss during 60 days bedrest, 16.6 +/- 1.4%.

- In 9 astronauts, the JSC laboratory reported that the protocol reproduced exactly the plasma volume loss and presyncopal (symptoms of fainting) responses seen on landing day. Waters, W.W., M.G. Ziegler, and J.V. Meck, *Furosemide plus low salt diet models post-spaceflight plasma volume loss and orthostatic hypotension*. The FASEB Journal, 2004. 18.
Research Goals

1. Employ a more cost effective human model of space flight-induced cardiovascular deconditioning using a hypovolemia protocol.

2. Test the efficacy of a compression garment with spatially distributed pressure as a countermeasure to cardiovascular deconditioning.
JSC Human Study 1

- Determine effectiveness of compression garments to reduce orthostatic intolerance in men and women undergoing a dehydration model of space flight
Test efficacy of a compression garment with spatially distributed pressure as a countermeasure to cardiovascular deconditioning.

- **Adaptation to Zero G (Drug model)**
- **Earth’s Gravity (1G) Normal Volume**
- **Return to Earth’s Gravity (simulated by tilt test) Possibility of Fainting!**
- **Forces produced by spatially distributed elastic garment**

Ultrasonic imaging during tilt test
Results: Effect of Compression Garments on Orthostatic Tolerance

Probability that deconditioned subjects remain standing during head-up tilt with (HYPO W/CM) and without (HYPO W/O CM) the compression garment countermeasure. **Use of Breast-high Compression Garments significantly increased stand time during hypovolemic tilts**
1. Employ a more cost effective human model of space flight-induced cardiovascular deconditioning using a hypovolemia protocol.

2. Test the efficacy of a compression garment with spatially distributed pressure as a countermeasure to cardiovascular deconditioning.

3. Develop a model of deconditioned men’s and women’s cardiovascular responses to the first day of activity in lunar and Mars gravity environments.
Develop a model of the deconditioned cardiovascular response to the first day of lunar and Mars activity

Alter-G reduced gravity trainer
Alter-G Corp, Menlo Park CA
Alter-G Study Procedures

G-Trainer in the Biodynamics Laboratory, Center for Biomedical Engineering, U of KY, Left: Detail of subject chamber interface. Center: Subject standing in G-Trainer positioned between cardiovascular data acquisition cart (UK CBME) and ultrasound unit (NASA JSC). Right: Instrumented subject standing in G-Trainer during acquisition of subclavian ultrasound images.

Seal and support pants
Treadmill
Positive Pressure Chamber
Ultrasound Doppler Measurements
Ultrasound images of blood flow across the aortic valve when supine and during passive standing at different body weights.
Results: Cardiovascular Values

- **Heart Rate**: Heart Rate (Mean ± S.E.M.)
  - 20,40,100 > 0 (p<0.05); 100 > 20,40 (p<0.0001)

- **Stroke Volume**: Stroke Volume Stand Data (Mean ± S.E.M.)
  - 0 > 20,40,100 (p<0.005); 20,40 > 100 (p<0.0001)

- **TPR: Total Peripheral Resistance**: TPR Stand Data (Mean ± S.E.M.)
  - 20,40 > 0 (p<0.05)

- **Systolic Blood Pressure**: Figure 3a: Systolic Blood Pressure (Mean ± S.E.M.)
  - 20,40 > 0 (P<0.001); 20,40 > 100 (p<0.001)

Mean heart rate (HR), stroke volume (SV), peripheral resistance (TPR) and Blood pressure (BP) of 7 men and 7 women standing at different body weights.
RESEARCH GOALS

1. Employ a more cost effective human model of space flight-induced cardiovascular deconditioning using a hypovolemia protocol.

2. Test the efficacy of a compression garment with spatially distributed pressure as a countermeasure to cardiovascular deconditioning.

3. Develop a model of the deconditioned cardiovascular response to the first day of lunar activity and Mars gravity environments.

4. Test the orthostatic tolerance limit of deconditioned men and women following a short exposure to artificial gravity on NASA Ames’ Human Performance Centrifuge.
NASA Ames Human Performance Centrifuge

Currently being modified to accommodate KY NASA EPSCoR 2012 study
Predicted effect of a short exposure to Artificial Gravity on deconditioned orthostatic tolerance (NASA Ames’ Human Performance Centrifuge).

Results of previous AG study conducted at NASA JSC in deconditioned men

Control
AG Countermeasure
P=0.012 (Kaplan Meier)
2008-2012 Study Summary

- **JSC Study (Study 1)**
  Compression garments improved orthostatic tolerance of men and women undergoing a dehydration model of space flight.

- **UK Studies (Studies 2 and 3)**
  G-Trainer model of Lunar and Mars cardiovascular responses similar to tilt model for nonvolemic men and women plus allows for activity. Summer 2011 study will determine deconditioned responses of men and women.

- **NASA Ames Study (Study 4)**
  Effectiveness of a short bout of artificial gravity to maintain deconditioned men and women’s orthostatic tolerance to be determined in 2012.
1. Employ a more cost effective human model of space flight-induced cardiovascular deconditioning using a hypovolemia protocol.

2. Test the efficacy of a compression garment with spatially distributed pressure as a countermeasure to cardiovascular deconditioning.

3. Develop a model of the deconditioned cardiovascular response to the first day of lunar activity and Mars gravity environments.

4. Test the orthostatic tolerance limit of deconditioned men and women following a short exposure to artificial gravity on NASA Ames’ Human Performance Centrifuge.

5. Outreach: Use EPSCoR developed techniques to identify autonomic cardiovascular neuropathy in diabetic patients.
Autonomic Neuropathy, a serious complication of diabetes that destroys nerve pathways to the heart and blood vessels, is difficult to diagnose.

Patients with clear peripheral neuropathy (damages sensory / motor pathways) were studied.

Indexes of autonomic activity, developed in earlier EPSCoR studies, were applied to these patients in an attempt to noninvasively classify their level of autonomic neuropathy.
Outreach: Magnitude of blood pressure and heart rate oscillations between .003 and 0.5 Hz (2-333 sec).

Able Bodied

Autonomic neuropathy

Blood Pressure oscillations

Heart Rate oscillations
Diabetics with definite autonomic neuropathy demonstrate:

- significant loss of sympathetic control of peripheral vasomotion
- significant loss of parasympathetic control of heart rate
- significant loss of the arterial baroreflex
Supported by

Kentucky NASA EPSCoR Grant
WKURF 516204-08-01

NASA Ames Gravitational Research Branch

NASA JSC Cardiovascular Laboratory

NIH R01N539774 and UK GCRC USPHS #
M01RR02602
Thank You
Ultrasound images of the right subclavian vein during passive standing in earth gravity (top left) and simulated lunar gravity (lower left). Images taken while the subject was walking are shown on the right side of the figure. Note increase of cross sectional area of the subclavian vein during reduced BW.
Cardiovascular data from a typical subject supine (left panel), standing at 100%, 40%, and 20% body weight (middle panel) and walking at 3.4 miles per hour (right panel) at 100%, 40% and 20% body weight. Note shift of fluid from Thorax to lower body.
EFFECTIVENESS OF COMPRESSION GARMENT TO REDUCE CARDIOVASCULAR DECONDITIONING IN MEN AND WOMEN UNDERGOING A MODEL OF SPACE FLIGHT FOLLOWED BY FIRST DAY LUNAR ACTIVITY

Space suit with compression stockings

Alter-G reduced gravity trainer
Develop a model of the deconditioned cardiovascular response to the first day of lunar activity

Astronaut would wear a compression garment

Alter-G reduced gravity trainer
Alter-G Corp, Menlo Park CA
(Unit purchased by UK’s Ctr. for Biomedical Engr.)
(tests will include subjects at 1/6 body weight with and without compression garments)
Summary

- **JSC study (Study 1)**
  EFFECTIVENESS OF COMPRESSION GARMENTS TO REDUCE CARDIOVASCULAR DECONDITIONING IN MEN AND WOMEN UNDERGOING A DEHYDRATION MODEL OF SPACE FLIGHT

- **JSC study (Study 2)**
  EFFECTIVENESS OF COMPRESSION GARMENT TO REDUCE CARDIOVASCULAR DECONDITIONING IN MEN AND WOMEN UNDERGOING A MODEL OF SPACE FLIGHT FOLLOWED BY FIRST DAY LUNAR ACTIVITY

- **NASA Ames study (Study 3)**
  EFFECTIVENESS OF COMPRESSION GARMENTS TO MAINTAIN BLOOD PRESSURE IN MEN AND WOMEN UNDERGOING A SIMULATION OF A LUNAR MISSION G PROFILE
Outreach: response to head-up tilt (able bodied and diabetic men and women)

Typical heart rate/blood pressure response to 30 min Head-up Tilt (HUT). Note ability of able bodied to increase blood pressure and heart rate (Decrease RR interval) during tilt.
Summary of Results

Compared to able bodied, we determined that diabetic neuropathy is characterized by:
1) Decreased control of peripheral vasomotion by the sympathetic nervous system
2) Decreased control of heart rate by the parasympathetic nervous system
3) Decreased baroreflex slope
4) Increased number of blood pressure ramps and
5) Decreased number of baroreflex sequences with the result that neuropathy
6) Decreased baroreflex effectiveness in regulating blood pressure.

Conclusions

Diabetic neuropathy can be noninvasively diagnosed and classified from continuous blood pressure data acquired from resting subjects.
Outreach: Baroreflex function at four levels of diabetic autonomic neuropathy

Numbers of blood pressure ramps, numbers of baroreflex sequences and baroreflex effectiveness in blood pressure regulation at rest and first 3 min HUT in able bodied (blue), diabetics without neuropathy (pink), diabetics with possible neuropathy (red) and diabetics with definite neuropathy (brown).

Neuropathy increased the number if blood pressure ramps but decreased the number of baroreflex sequences with the result that neuropathy decreased baroreflex effectiveness in regulating blood pressure.
The footward shift of thoracic fluid in response to standing on Earth can be reduced to simulate that of standing in Mars or Moon gravities by the use of Alter-G LBPP.

Cardiovascular responses to standing on Earth (increased heart rate, indexes of sympathetic drive to the heart and periphery, decreased baroreflex slope, etc) are smaller when standing in simulated Moon and Mars gravities.

This summer (Study 3) we will determine deconditioned subjects’ cardiovascular responses to reduced gravity.