Acronym: Integrated Cardiovascular

Title: Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capability and Risk for Cardiac Arrhythmias

Principal Investigator(s):
Benjamin D. Levine, M.D., Institute for Exercise and Environmental Medicine, Presbyterian Hospital and University of Texas Southwestern Medical Center at Dallas, Dallas, TX
Michael W. Bungo, M.D., University of Texas Medical School, Houston, TX

Co-Investigator(s):
Steven H. Platts, Ph.D. Johnson Space Center, Houston, TX
Douglas R. Hamilton, M.D., Ph.D., Wyle Laboratories, Houston, TX
Smith L. Johnston, M.D., Johnson, Space Center, Houston, TX

Contact(s):
PI - Benjamin D. Levine, BenjaminLevine@TexasHealth.org, (214) 345-4620
PI - Michael W. Bungo, Michael.W.Bungo@uth.tmc.edu, (713) 500-5532
Primary - John Love, john.e.love@nasa.gov, (281) 483-7713
Secondary - Cathy Modica, catherine.g.modica@lmco.com, (281) 218-3303

Mailing Address:
Dr. Benjamin D. Levine
Institute for Exercise and Environmental Medicine
Presbyterian Hospital of Dallas
University of Texas – Southwestern
7232 Greenville Ave., Ste. 435
Dallas, TX 75231

Dr. Michael W. Bungo
University of Texas Medical School
6431 Fannin St., MSB #1.242
Houston, TX 77030

Developer(s): Johnson Space Center, Human Research Program, Houston, TX

Sponsoring Agency: National Aeronautics and Space Administration (NASA)

Increment(s) Assigned: 19, 20

Mission Assigned: N/A

Brief Research Summary (PAO): Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capability and Risk for Cardiac Arrhythmias (Integrated Cardiovascular) will quantify the extent of long-duration space flight-associated cardiac atrophy (deterioration) on the International Space Station crewmembers.

Research Summary:

- Atrophy (a decrease) in the size of the heart muscle appears to develop during space flight and its ground-based analogues (i.e., bedrest) which could lead to impaired functioning of the heart and low blood pressure or fainting upon return to gravity on the Earth, the moon or Mars.

- Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capability and Risk for Cardiac Arrhythmias (Integrated Cardiovascular) will determine how much cardiac atrophy occurs during space flight, how fast and, whether this atrophy causes problems with the heart's pumping or electrical function, and how both the atrophy and any associated changes develop.

- The effects of this atrophy on how the heart fills, how blood pressure responds to the lack of and reintroduction to gravity (Earth, the moon and Mars), a crewmember's ability to exercise, and the likelihood of developing unusual heart rhythms will also be determined, both in space on the International Space Station, and following return to Earth.

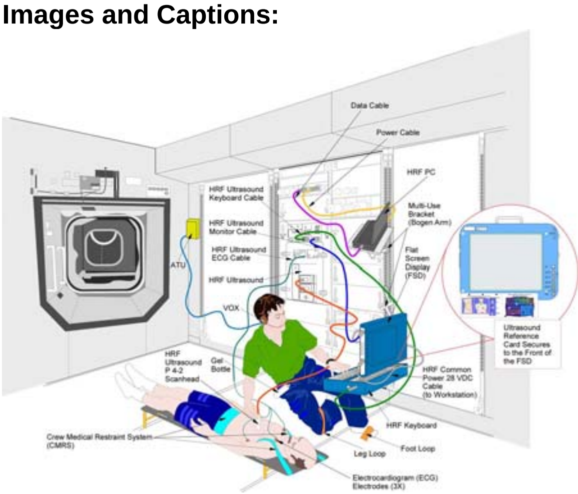
- Results from this investigation will ensure crew health on future long-duration exploration missions and will help in the development of any needed countermeasures for the effects of space flight on the cardiovascular system.

Detailed Research Description: Cardiac atrophy (decrease) appears to develop during space flight or its ground-based analogues, i.e., bedrest, leading to diastolic dysfunction (abnormal left ventricle in the heart) and orthostatic hypotension, a condition where the blood pressure drops when an individual stands up. Such atrophy also may be a potential mechanism for the cardiac arrhythmias (irregular heartbeat) recently identified in some crewmembers after long-duration exposure to microgravity aboard the *Mir* space station. Recent studies has suggested that cardiac atrophy may be progressive, without a clear plateau over at least 12 weeks of bedrest, and thus may be a significant limiting factor for extended duration space exploration missions. Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capability and Risk for Cardiac Arrhythmias (Integrated Cardiovascular) will quantify the extent, time course and clinical significance of cardiac atrophy and identify its mechanisms. The functional consequences of this atrophy also will be determined for cardiac filling dynamics, orthostatic tolerance at gravity on Earth and fractional gravity (Mars and the moon) conditions, exercise tolerance, and arrhythmia susceptibility, both in space on the International Space Station (ISS), and following return to Earth.

Integrated Cardiovascular will determine the magnitude of the left and right ventricular atrophy associated with long-duration space flight (using magnetic resonance imaging,MRI) and relate this atrophy to measures of physical activity and cardiac work inflight, determine the time course and pattern of the progression of cardiac atrophy inflight using cardiac ultrasound, determine the functional importance of cardiac atrophy for cardiac diastolic function and the regulation of stroke volume (volume of blood pumped by the right/left ventricle of the heart in one contraction) during gravitational transitions, and identify changes in ventricular conduction, depolarization and repolarization during and after long-duration space flight and relate these to changes in heart mass and morphology (shape and form).

Project Type: Payload

Images and Captions:



Computer generated diagram of the Integrated Cardiovascular investigation onboard the ISS. Image courtesy of the Johnson Space Center, Human Research Program.

Operations Location: ISS Inflight

Brief Research Operations:

- Inflight operations include:
  - Resting echocardiograms (ECG), using the HRF Ultrasound, are performed four times during flight. An exercise ECG is performed before and after exercise one time during the expedition.
  - An ambulatory blood pressure, holter, activity monitoring occurs for 24-hours either before or after each resting and exercise ECG session. The data is downloaded and downlinked from all hardware to the HRF personal computer (PC) following the completion of each set of ECG sessions.
  - Logging of inflight exercise and medication will be obtained through data sharingwith other activities.

- Preflight and postflight operations include:
  - Resting ECG before and after flight. An exercise ECG will occur once before and twice after flight.
  - An ambulatory blood pressure, holter, activity monitoring occurs for 48-hours two times before and one time (for 24 hours) after flight. A cardiac MRI, with magnetic resonance spectroscopy and gadolinium enhancement) once before and twice after flight are also required.
  - Graded tilt test with ECG once before and once after flight; exercise and medication logs will be obtained via data sharing.

Operational Requirements: A total of twelve subjects are required for this investigation. Inflight scanning sessions are planned on flight day 14 (FD14) +/- 4-days, FD30 +/-5 days, FD75 +/-5 days, FD135 +/-5 days, and R-15 +/-4 days. Ambulatory blood pressure, holter, activity monitoring is required within one week (preferably three days) of each session. The total number of sessions required is dependent on mission length. Both an operator and a subject are required for the ultrasound scans along with real-time video downlink to enable remote guidance by ground experts.

Operational Protocols: Inflight, resting ECG, using the HRF Ultrasound will be performed on FD14, FD30, FD135, and return plus 15-days (R+15) using real-time remote guidance. On FD75, an exercise ECG session will be performed with measurements taken before and after exercise. Both the resting and exercise sessions will be preceded or followed by 24-hours of ambulatory blood pressure, holter, activity monitoring. For these sessions, subjects will apply electrodes and then don the HRF Holter Monitor, ESA Cardiopres, and two Actiwatches (one at the waist and one at the ankle). These devices will be worn for 24-hours after which the devices will be doffed and the data from all experiment hardware will be downloaded to the HRF PC and downlinked to the ground. Inflight exercise and medication logs will be obtained through data sharing.

On the ground, resting ECG will be obtained between launch minus 21-days (L-21) and L-7 and again at return plus 7-days (R+7). Exercise ECG will be performed between L-75 and L-60 and again at R+4 and R+14. Preflight, ambulatory blood pressure,holter, activity monitoring for 48-hours will be conducted between L-75 and L-60 and again between L-21 and L-7.

Postflight, ambulatory blood pressure, holter, activity monitoring for 24-hours will be conducted on R+0. Cardiac MRI (with Magnetic Resonance Spectroscopy and gadolinium enhancement) will be obtained between L-75 and L-60 (a repeat between L-75 and launch in Russia will be required if a Russian landing is planned) and again at R+3 and between R+22 and R+30. Graded tilt tests with ECG will be performed between L-75 and L-60 and again on R+0. Exercise and medication logs will be obtained both before and after flight, preferably via data sharing.

Category: Human Research and Countermeasure Development for Exploration

Subcategory: Cardiovascular & Respiratory Systems in Space

Space Applications: Once the magnitude, time course, and inciting factors for cardiac atrophy have been determined, effective countermeasures currently being developed by the investigators in parallel ground-based experiments may be applied, focused on normalizing cardiac work and volume during long-duration space flight. Upon completion of these experiments, a number of important risks for long-duration space flight, such as cardiac function and arrhythmia risk may either be deemed manageable by current preventive measures, or clearly defined for future countermeasure research.

Earth Applications: The information obtained from these space flight experiments also may be relevant for patients after prolonged confinement to bedrest, or chronic reduction in physical activity, as well as for patients with disease processes that alter cardiac stiffness such as congestive heart failure, ischemic heart disease, and normal ageing.

Manifest Status: Planned

Supporting Organization: Exploration Systems Mission Directorate (ESMD)

Previous Missions: The investigators have extensive previous experience with cardiovascular investigations performed on Space Shuttle and *Mir*; however, this is a new experiment.

Results: N/A

Results Publications: N/A

Related Publications

Dorfman TA, Rosen BD, Perhonen MA, Tillery T, McColl R, Peshock RM, **Levine BD**. Diastolic Suction is Impaired by Bed Rest: MRI Tagging Studies of Diastolic Untwisting Journal of Applied Physiology. 2008; 104(4):1037-1044.

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Cox JF, Tahvanainen K, Kuusela TA, **Levine BD**, Cooke WH, Mano T, Iwase S, Saito M, Sugiyama Y, Ertl AC, Biaggioni I, Diedrich A, Robertson RM, Zuckerman JH, Layne LD, Ray CA, White RJ, Pawelczyk JA, Buckey JC, Baisch FJ, Blomqvist CG, Robertson D, and Eckberg DL. Influence of microgravity on astronaut's sympathetic and vagal responses to Valsalva's manoeuvre. The Journal of Physiology. 2002 ;538:309-320.

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Web Sites:
ISS Medical Project
https://hrf.jsc.nasa.gov/science/default.asp?e_id=101

Institute for Exercise and Environmental Medicine
www.ieemphd.org

Related Payload(s): None