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RESEARCH AND OPERATIONAL EFFORTS IN SUPPORT OF SKYLAB EXPERIMENT M093

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Final Report

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Contract Background

The use of vectorcardiography during spaceflight was originally proposed by Captain N.W. Allebach at Naval Aerospace Medical Institute and Dr. Allebach was awarded NASA Contract T-23237G to determine the feasibility of using the Frank lead system and VCG analysis under a variety of special environmental conditions. During the subsequent years, an experimental protocol was accepted for the Apollo Applications Program and the experiment was designated M018. Dr. Raphael F. Smith became the Principal Investigator of that experiment. In 1969 Dr. Smith accepted a position on the faculty of Vanderbilt University School of Medicine and continued to serve as Co-Principal Investigator of the vectorcardiogram experiment which had been renamed Skylab Experiment M093. Research and operational efforts by personnel at Vanderbilt University were funded from NASA Contract T-23237G by way of a subcontract from the Naval Aerospace Medical Center, ONR Contract N00014-71-A-0212. Funding by this mechanism involved two naval contracting authorities and to eliminate administrative redundancy, we were advised to request a direct allocation from the National Aeronautics and Space Administration. In July, 1972 Vanderbilt University was awarded contract NAS 9-12889 by Lyndon B. Johnson Space Center. This change was for fiscal administrative purposes only and there was no change in the objectives, personnel, or conduct of the project. Although this document is entitled "Final Report", it concerns the phase of the project funded by the Department of the Navy and should not be considered the final report of contract NAS 9-12889.

Scientific Background

The objectives of Skylab Experiment M093 were to measure electrocardiographic signals during spaceflight, to elucidate the electrophysiological basis for the changes observed, and to assess the effect of the change on the human cardiovascular system. Vectorcardiographic methods were used to quantitate changes, standardize data collection, and to facilitate reduction and statistical analysis of data. Since the Skylab missions provided an unique opportunity to study the effects of prolonged weightlessness on human subjects, an effort was made to construct a data base that contained measurements taken with precision and an adequate number to enable conclusions to be made with a high degree of confidence. Standardized exercise loads were incorporated into the experiment protocol to increase the sensitivity of the electrocardiogram for effects of deconditioning and to detect susceptibility for arrhythmias.

Vectorcardiography provides a comprehensive, three dimensional approach to the analysis of electrocardiographic data which has proven to be useful in both clinical[1,2] and research applications.[3,4] Vectorcardiographic techniques have been utilized to quantitate electrocardiographic changes during bedrest experiments[4] and Keplarian parabola flights.[5] In-flight vectorcardiograms were not obtained during the Mercury, Gemini, or Apollo missions, although preflight and postflight vectorcardiograms were obtained during Apollo 15, 16, and 17.

In this report we will describe the M093 experiment design, the data transmission system, data reduction methods, and the analysis of data from the three Skylab missions. The report will also include clinical applications of the techniques developed for Skylab Experiment M093.

METHODS

Experiment Design

Vectorcardiograms (VCG) were taken at rest, during exercise, and after exercise in each crewman during the preflight, in-flight, and postflight phases of the Skylab missions. Experiment M093 was designed primarily to obtain electrocardiographic data. In a second Skylab experiment, M171 Metabolic Activity, the Frank lead system[6] was applied for the purpose of obtaining electrocardiographic data during more strenuous exertion. In both experiments vectorcardiograms were obtained from the crewmen at rest for five minutes. In experiment M093 the subject exercised on the bicycle ergometer at a work load of 150 watts for two minutes; during M171 the subject exercised on the ergometer at levels equivalent to 25,50, and 75% of his maximum aerobic capacity determined prior to the flight. The subject exercised for five minutes at each work load for a total of 15 minutes. After the single exercise load in experiment M093, vectorcardiograms were obtained for 10 minutes. In experiment M171, postexercise vectorcardiograms were obtained for five minutes. The exercise profiles are depicted in Figure 1 and the ergometer is shown in Figure 2. Mechanical problems in the orbital workshop during the early portion of Skylab 1/2 caused scheduling conflicts which resulted in the deletion of the M093 protocol during the flight. However, the M093 protocol was performed throughout SL3 and SL4.

Instrumentation

Eight electrodes were applied to the crewmen in a modified Frank lead configuration. To lessen muscle noise during exercise, the lead system was modified by transferring the left leg electrode to the left sacral region since the potential difference between the left leg and the

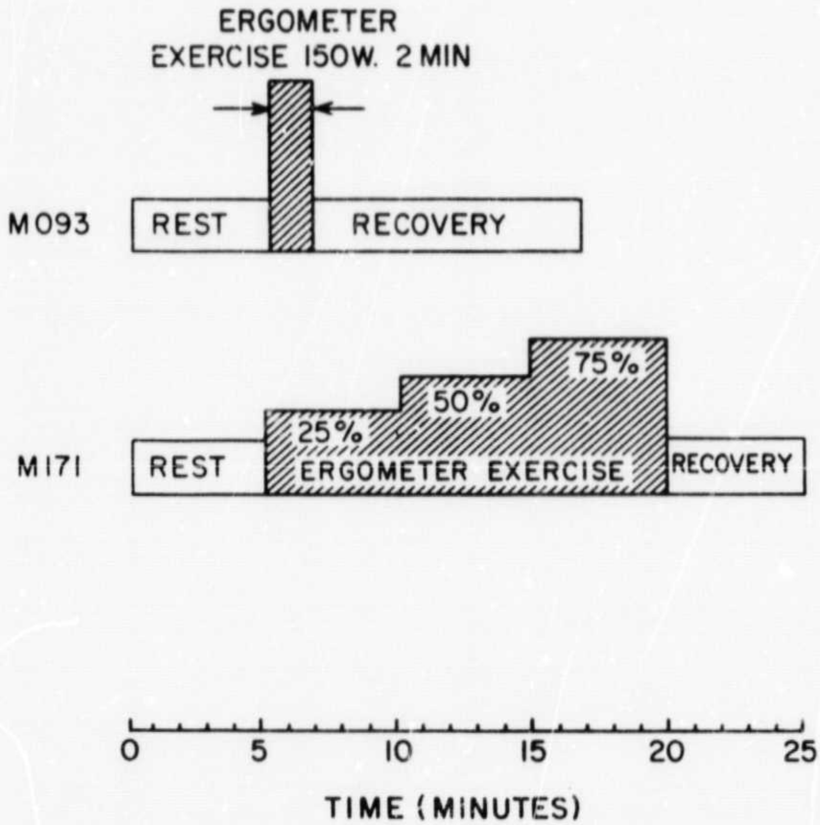


Figure 1. Ergometer exercise profiles for Experiment M093 and Experiment M171. For the M171 protocol, the maximum aerobic capacity of each astronaut was determined prior to the flight and the work levels were 25, 50, and 75 percent of this value.

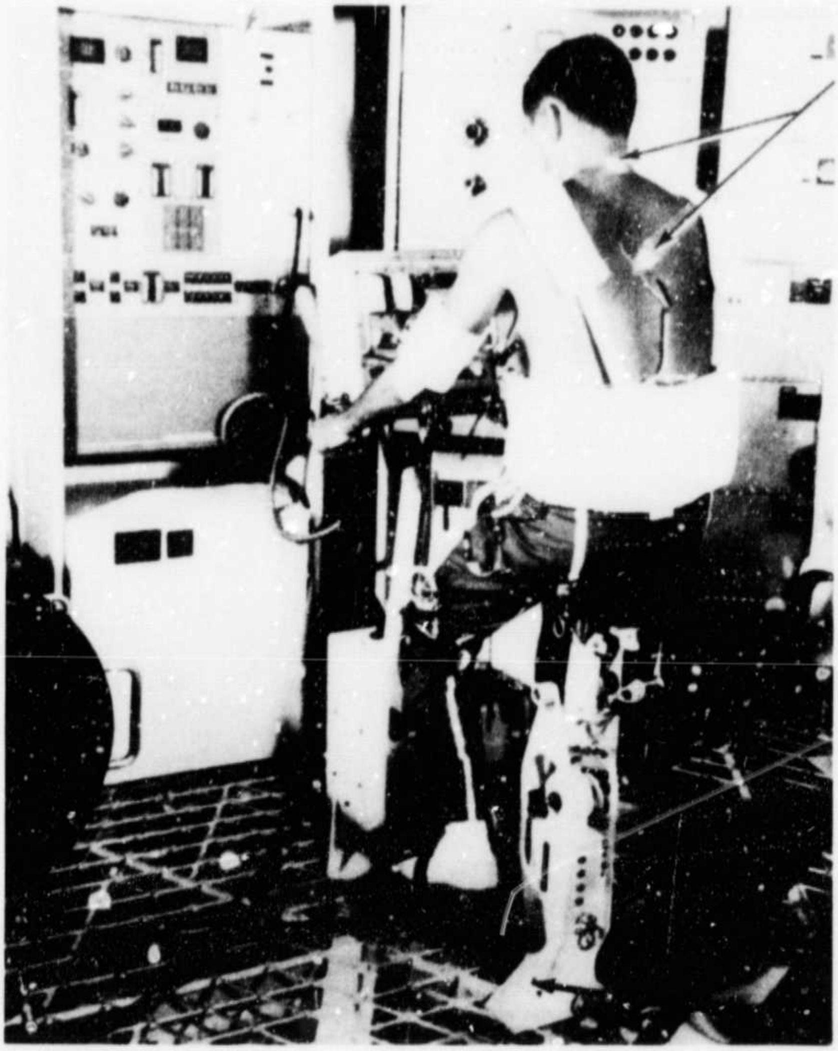


Figure 2. Oribital Workshop bicycle ergometer. The Experiments Support System and VCG subpanel can be seen in the background. The arrows show the positions of two electrodes of the Frank lead system.

left sacrum is negligible. The resistor network proposed by Frank was utilized to correct for the distortion of the cardiac dipole field that results from the shape of the torso and the eccentric location of the heart in the chest. The output of the network is theoretically proportional to the orthogonal components of the cardiac dipole. In the preflight period the electrode sites were marked on each crewman's body by a small tattoo and immediately before the run the electrode site was prepared with zepharin chloride. The electrodes were well-type disks and a sponge impregnated with a conductive electrolyte gel served as an interface between the silver-silver chloride electrode and the skin. After attaching the electrodes to the body, the ground reference electrode was tested to determine if there was proper isolation of the subject from the spacecraft ground, then each electrode was tested in sequence to determine the impedance of the skin-electrode interface. The electrode contact was considered to be satisfactory if the impedance was less than 100,000 ohms. To prevent the electrocardiographic signals from exceeding the dynamic range of the recording system, the proper signal conditioner gain for each crewman was determined prior to the flight and the appropriate switch position selected for the individual at the start of the experiment run.

The signal conditioners had differential input with input impedance greater than 40 megohms. The frequency response of the signal conditioners was flat from 0.14 Hz to 90 Hz; at 0.05 Hz, and at 100 Hz, the frequency response was less than 3 db down from the flat portion of the frequency response curve. The harmonic distortion of the signal conditioners was less than 1% over the frequency range of the unit. The phase angle difference between VCG amplifiers did not exceed one degree over the frequency range of the unit. The three VCG channels were simultaneously calibrated by a 10 Hz square wave. The Experiment Support System conditioned and distributed electrical power to experiment equipment, received experiment data in analog and digital form, displayed heart rate data for the crewmen, and routed analog signals to the Airlock Module telemetry system.

The spacecraft recording and telemetry system consisted of two PCM (pulse code modulation) programmers, a PCM interface box, a data storage and playback system, and remote multiplexers and signal conditioners. This equipment was located primarily in the Airlock Module. The system accepted analog signals from the VCG amplifiers and arranged these data into binary coded words at a rate of 320 samples per second. Tape recorders were used to record data for delayed transmission to Lyndon B. Johnson Space Center. The unit recorded reduced bit rate segments of the PCM outputs from the PCM programmer together with voice data from the crewmen. The recording speed was 1 7/8 inches per second (.048 meters/second) and the tapes were played back at 41 1/4 inches per second (1.05 meters/second) thus allowing four hours of data to be transmitted in less than 11 minutes. Data were transmitted at "greater-than-real time" rates during passes over receiving stations, a procedure referred to as data "dumps". Due to the volume of data from Skylab experiments it was necessary to compress the VCG data and eliminate redundant samples. A zero order predictor algorithm was selected as the data compression technique. In essence, a digital sample of a parameter was tested to determine if it differed from the value of the sample last transmitted. If there was no difference between the current sample and the previous sample, the value was considered to be redundant and not transmitted to L.B. Johnson Space Center.

Computer Analysis Program

The pattern recognition logic of the M093 program is based on a statistical method of identifying components of the vectorcardiogram rather than utilizing empirically derived fiducial values. The program consits of a main program and 10 subprograms that scale and analyze the data. The main program initializes constants, enters identifying information, enters data pertaining to the length of calibration and length of experimental data, generates a digital filter, and serves as a control program for the subroutines. The subroutines compute scale factors from the calibration pulses, apply digital filtering, define the baseline, determine onset and end of waves and segments, and generate a tabular and graphical output of vectorcardiographic items. An optional subroutine derives the 12 conventional ECG's from the three orthogonal vectors leads or derives any lead for which spatial coordinates are given. The following VCG items are measured or calculated:

P, QRS, T duration; start and end time

P, QRS, T maximum voltage X,Y,Z leads; time of occurrence

P, QRS, T vector loop length

P, QRS, T maximum vector magnitude, aximuth, elevation; time of occurrence

P, QRS, T maximum vector velocity; time of occurrence

P, QRS, T, ST area X,Y,Z leads

P, QRS, T, ST spatial vector magnitude, azimuth, elevation

Ventricular gradient magnitude, azimuth, elevation

QRS instantaneous vector magnitude, azimuth, elevation at 10 millisecond intervals

Angle between spatial mean QRS-T vectors

Slope and curvature ST segme t

Heart rate

A program for statistical analysis of intra-experiment data has been used in series with the M093 analysis program. The statistical program provides tabular output and graphic displays of both standard statistical parameters and special statistical metrics for directional measurements.

Data Management

For crew safety during the flights, the electrocardiographic signals from each experiment were examined within 24 hours for changes of clinical importance. Occasionally when the orbital workshop was in communications range and an experiment was in progress, ECG signals were available for immediate analysis. However, due to the gaps in ground station coverage, in most cases the complete data from the experiment were not available until 12 to 24 hours following the run. An analog version of the lead transformation algorithm was available to convert the three orthogonal VCG leads to a conventional 12 lead electrocardiogram. Combinations of electrical resistance were chosen to provide the best match between ECG signals obtained from the standard clinical leads and the derived ECG signals. Circuit boards were constructed for each astronaut and inserted into the synthesizing unit when an experiment was in progress.
Figure 3A is an actual 12 lead ECG from the Commander of SL1/2 and Figure 3B shows the 12 leads that were derived from the VCG signal. Microfilm copies of the computer analysis of experiment data were available within 48 hours after the experiment was performed. These reduced data were reviewed and after inspection of an analog reconstruction, spurious values were deleted from the data base.

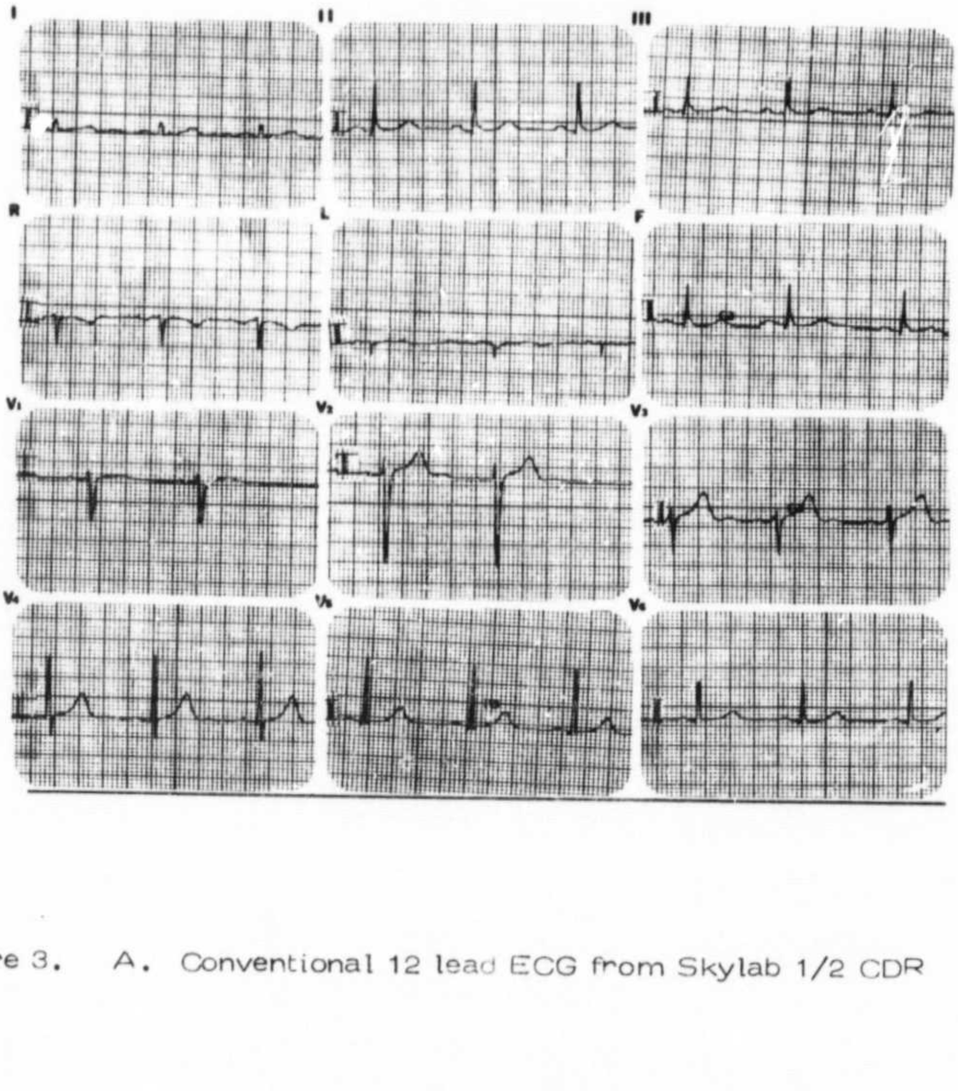
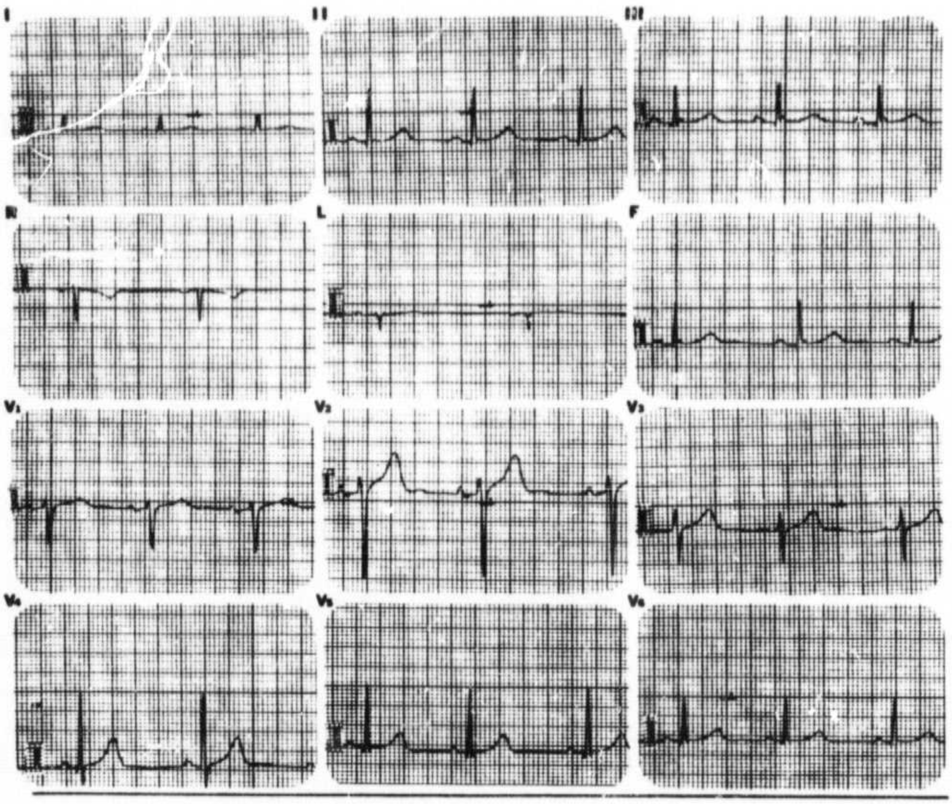


Figure 3. A. Conventional 12 lead ECG from Skylab 1/2 CDR



B. Twelve lead ECG derived from Frank orthogonal leads.

RESULTS

Vectorcardiographic parameters from 131 in-flight tests were analyzed by digital computer and compared to pre- and postflight values. The VCG items examined were heart rate, QRS duration, QRS maximum vector magnitude and direction, T maximum vector magnitude and direction, PR interval, QT interval, area of ST segment X lead, and the spatial angle between QRS and T mean vectors. A statistically significant increase in QRS maximum vector magnitude occurred in six of the nine crewmen. Crew trends plotted as a percentage change from the mean preflight value are shown for the three Skylab missions in Figures 4,5, and 6 respectively. Although crew trends were similar during the three Skylab missions, there were interesting individual differences in the time course of the magnitude changes. For example, in some astronauts the increase in QRS maximum vector magnitude began in the preflight period as depicted in Figures 7 and 8 and in other crewmen the pre-flight was not evident as shown in Figure 9. It should be noted that the data points are spaced equally on the abscissa of Figures 7,8, and 9 although the actual time intervals between the experiments were not equal. The preflight data collection period for Skylab 1/2 was approximately six months; thus, the rate of QRS maximum vector magnitude increase was considerably greater during the flight than in the preflight period. The magnitude of the spatial T vector increased in five of the nine Skylab

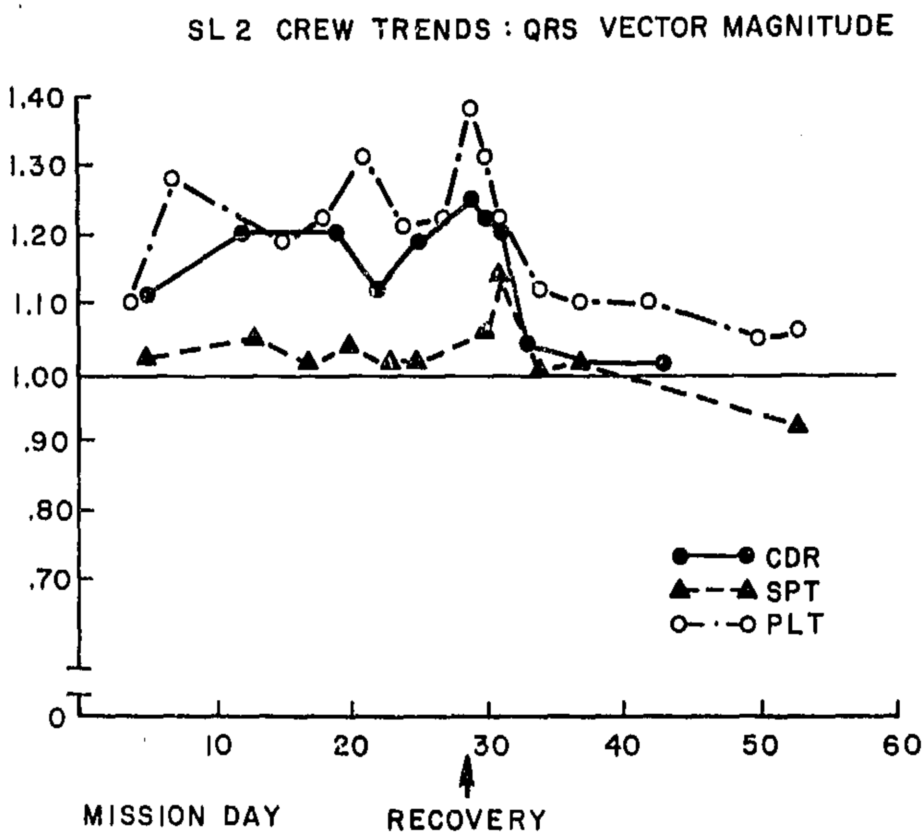


Figure 4. QRS vector magnitude during SL 1/2 mission. Data plotted as percentage change from the mean preflight value.

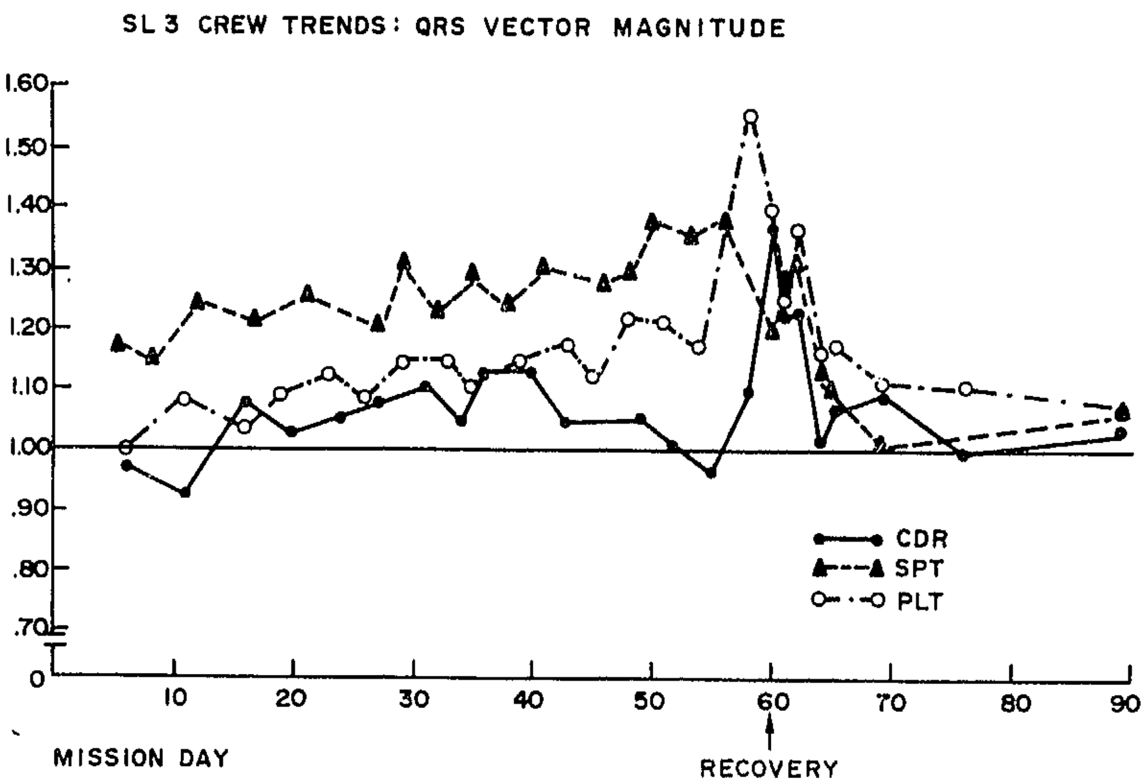


Figure 5. QRS vector magnitude during SL3.

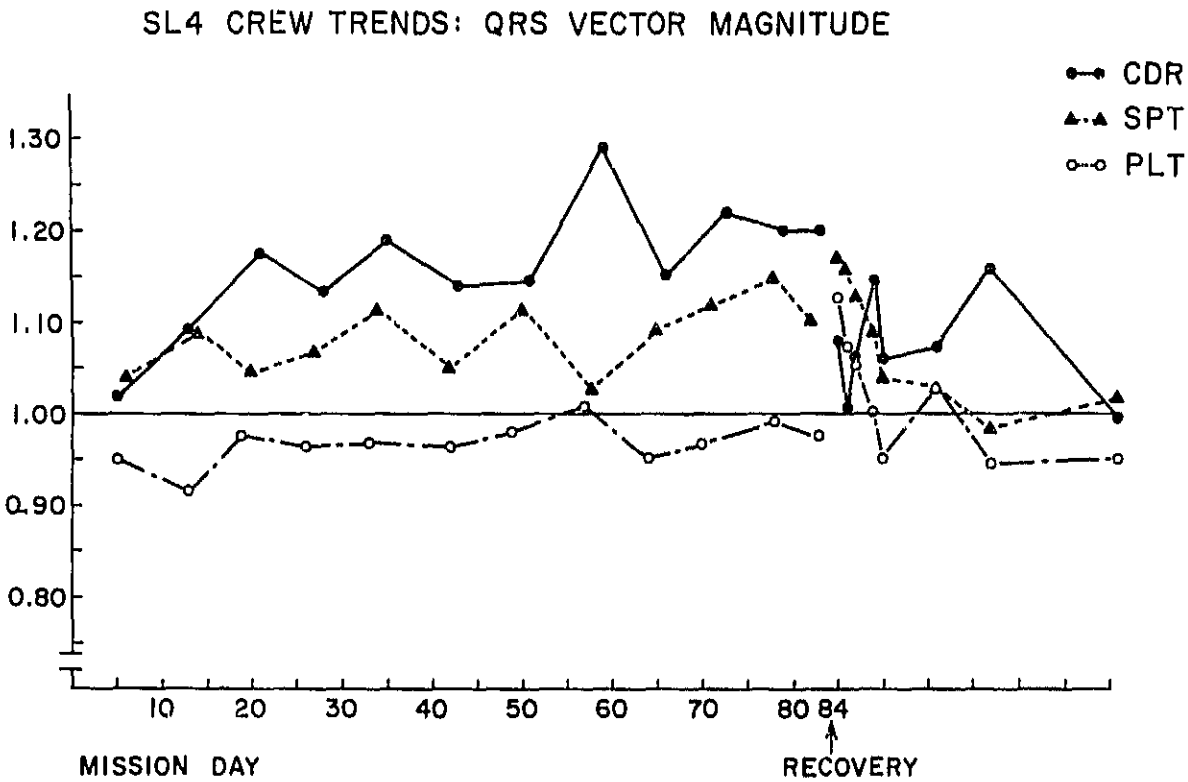


Figure 6. QRS vector magnitude during SL4.

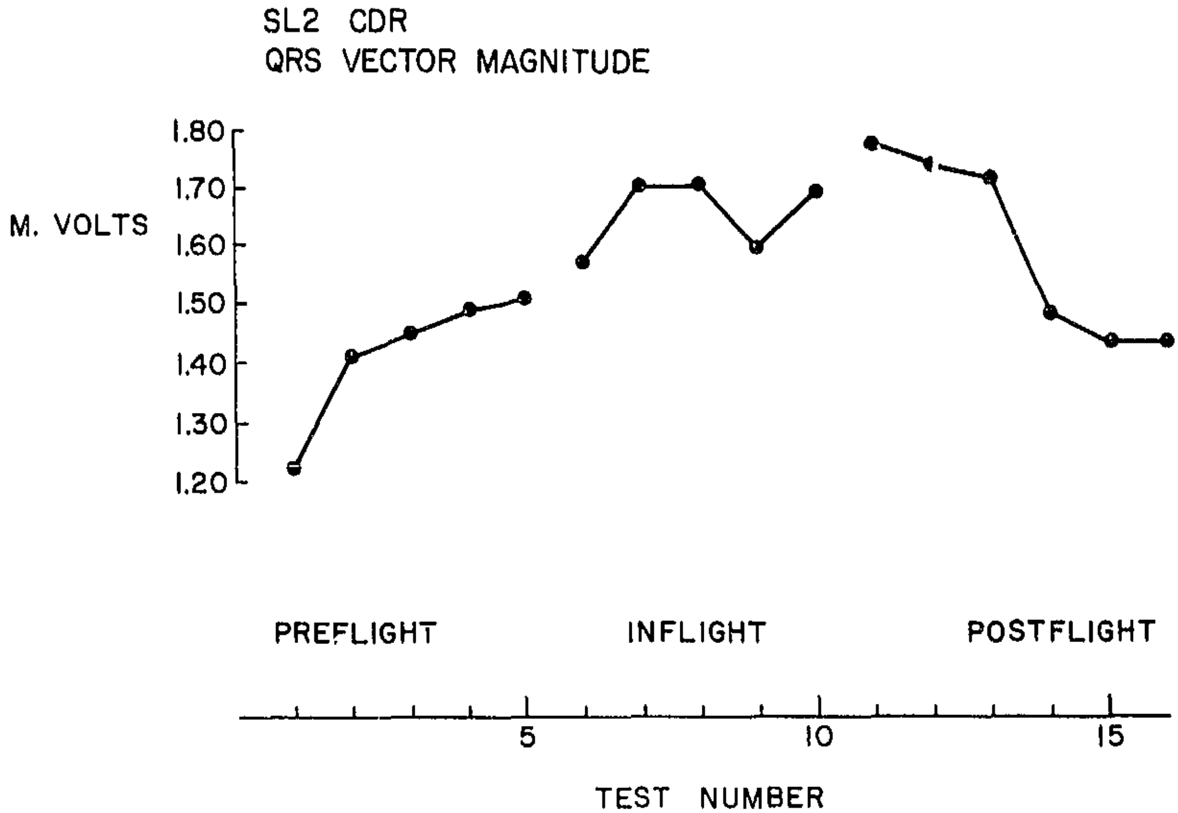


Figure 7. Evolution of QRS vector magnitude change in the CDR SL 1/2. Experiments are spaced equally on abscissa although the time intervals between the experiments were not equal.

crewmen and although the increase was statistically significant, variation in the measurements was large. The angle between the spatial QRS and T mean vectors did not increase significantly in any crewmen during the flights and there were no major changes in QRS, T, or ST vector direction.

The duration of the PR interval measured at rest increased in six of nine crewmen during the three flights and the crew trends for SL3 and SL4 are shown in Figures 10 and 11. However, the average PR interval in-flight did not exceed the clinical standard for the upper limit of normal (0.20 seconds) in any crewman. During exercise the PR interval did not show a significant difference from the PR interval duration for comparable exercise in the preflight period. A significant decrease in the resting heart rate was observed in the SL 1/2 crew during the flight. However, a significant change in resting heart rate was not a crew trend in the later missions. In general, the average heart rate during the third level of exercise, M171 protocol remained the same as preflight or tended to decrease slightly during the flights. In the immediate postflight period there was a marked increase in the resting heart rate and heart rate response to a given exercise load. As an example, the heart rate responses during SL4 are shown in Figures 12 and 13.

The scalar analog reconstructions of the digital VCG signals, the 12 lead ECG's obtained with the transformation circuitry, and instantaneous vector loop displays were reviewed to check the technical

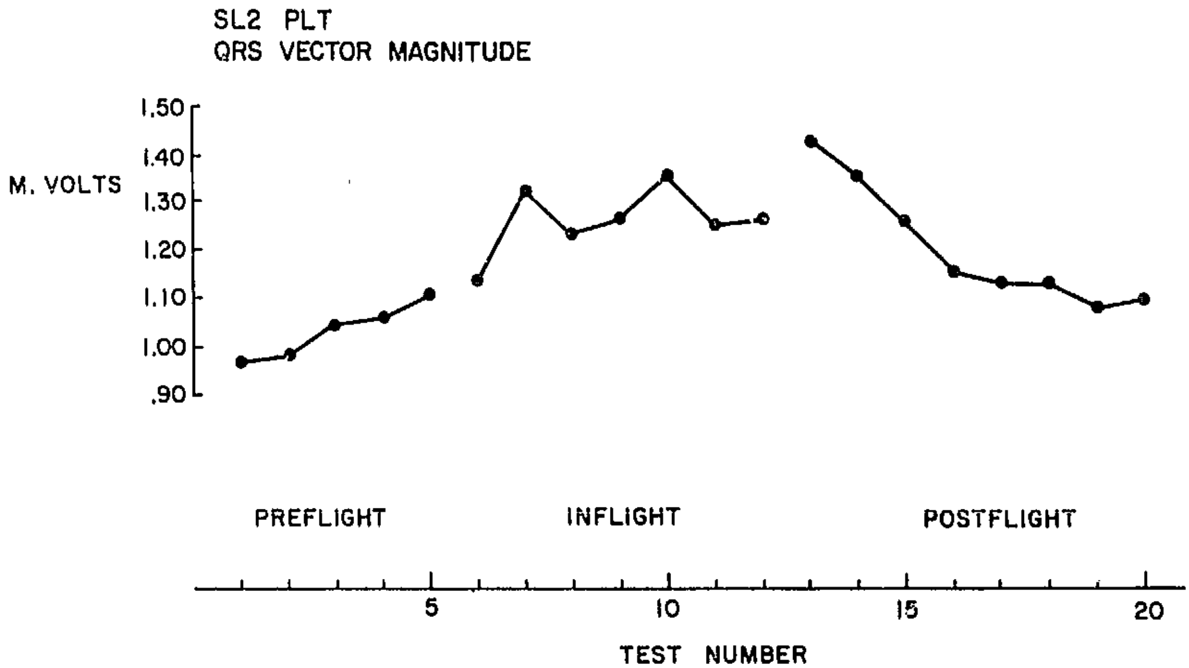


Figure 8. Evolution of QRS vector magnitude change in the PLT SL 1/2.

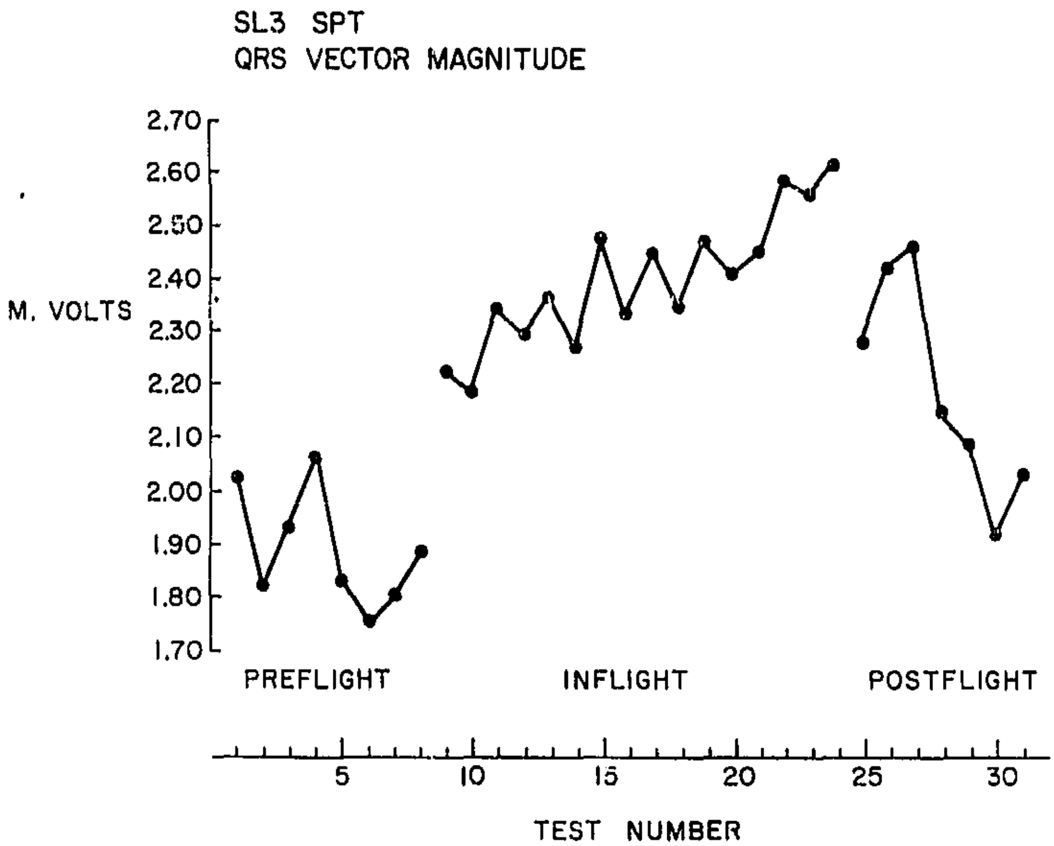


Figure 9. Evolution of QRS vector magnitude change in the SPT SL3.

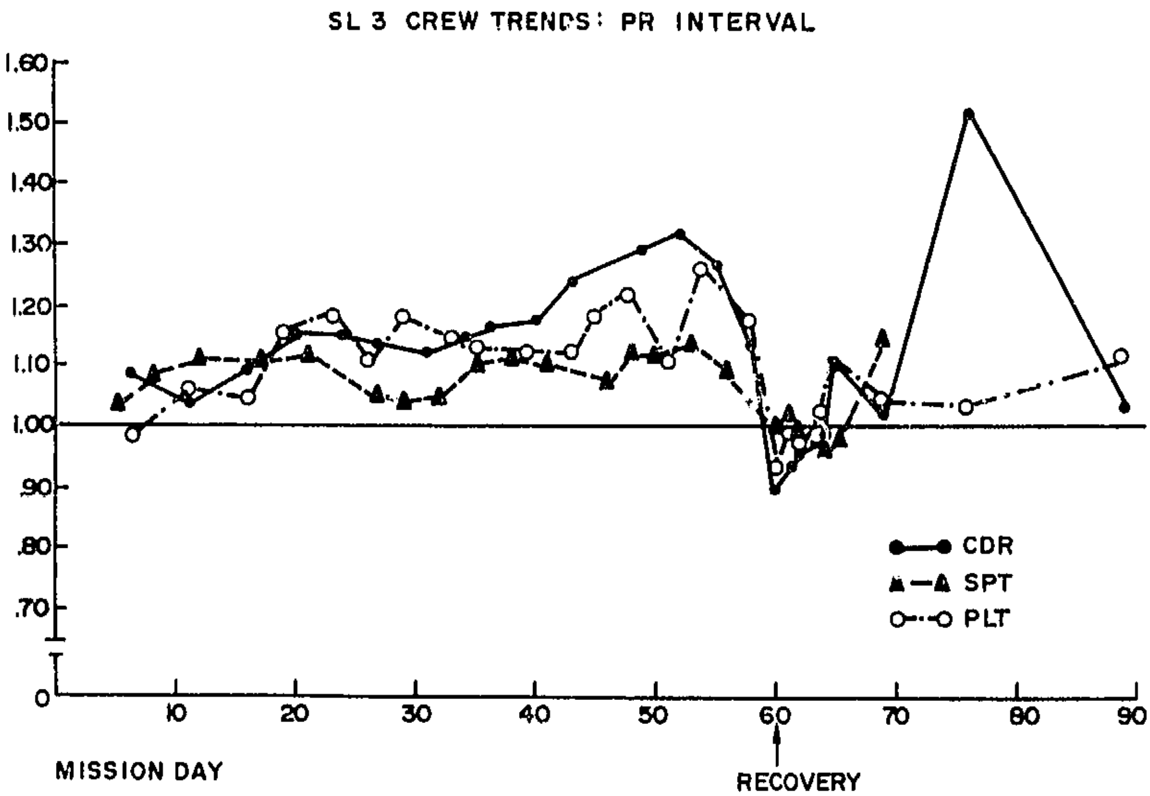


Figure 10. PR interval duration during SL3. Data plotted as percentage change from the mean preflight value.

11d

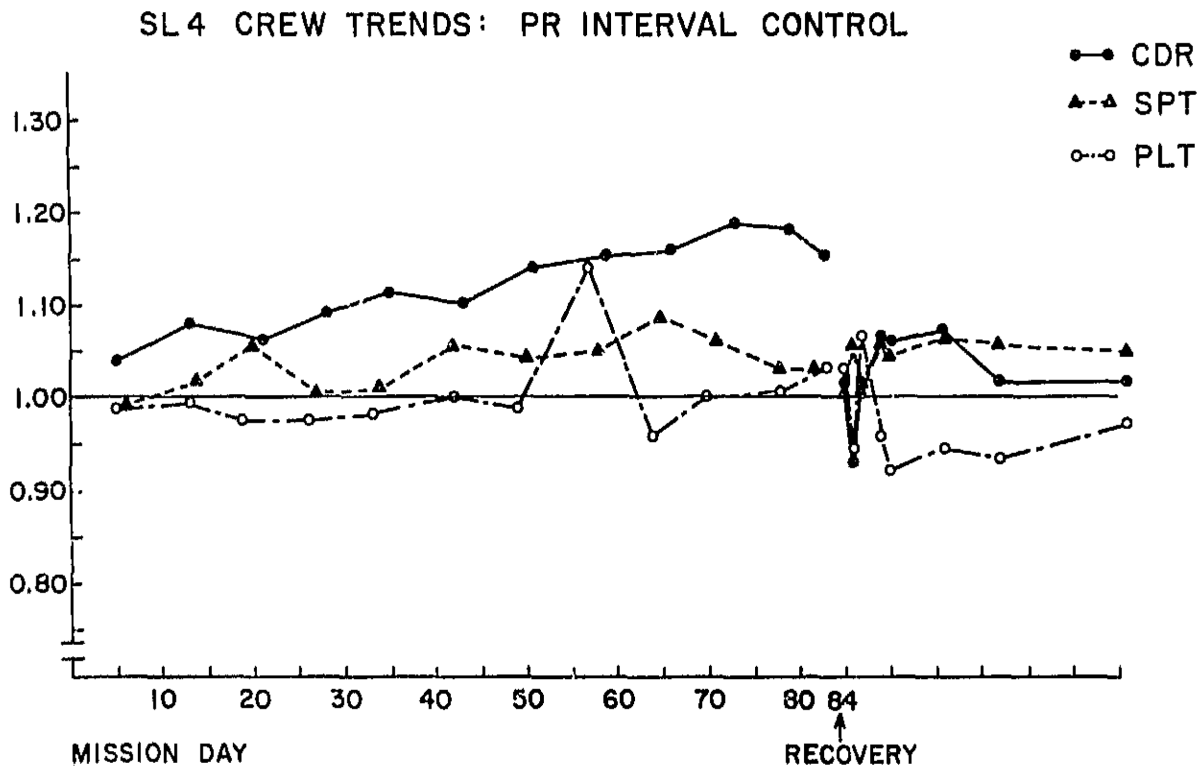


Figure 11. PR interval duration during SL4.

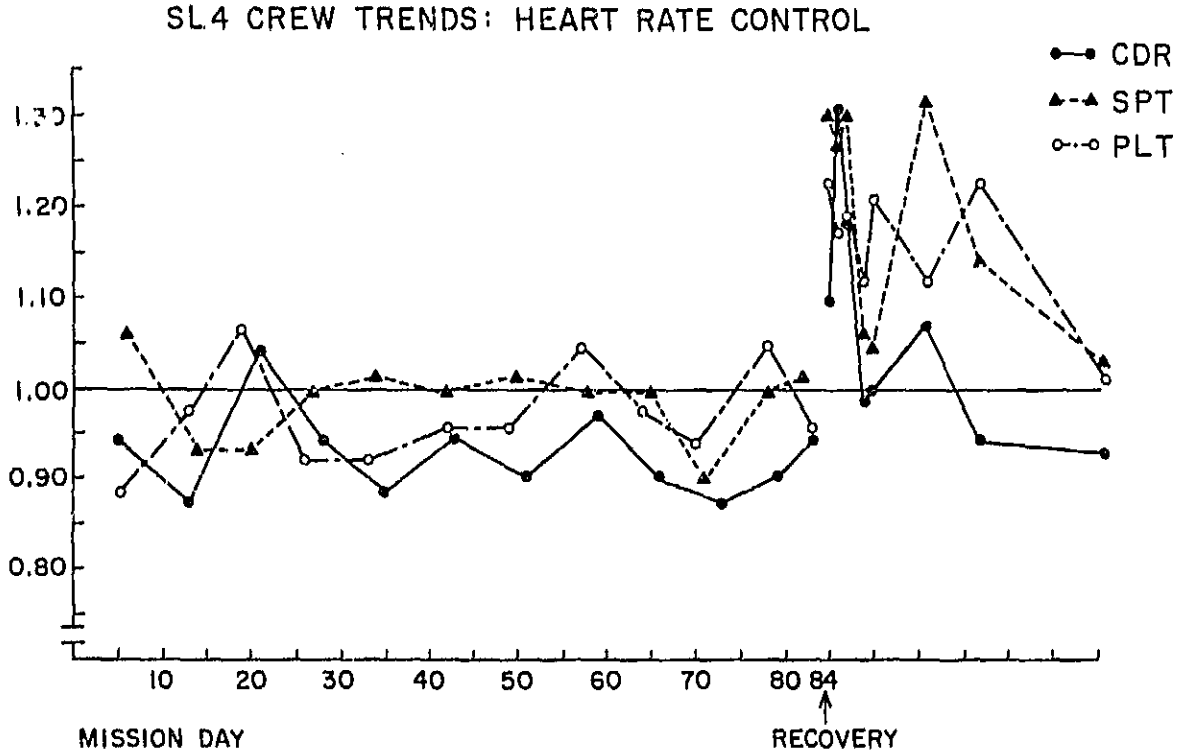


Figure 12. Resting heart rates SL4 crew plotted as a percentage of the mean preflight value.

11f

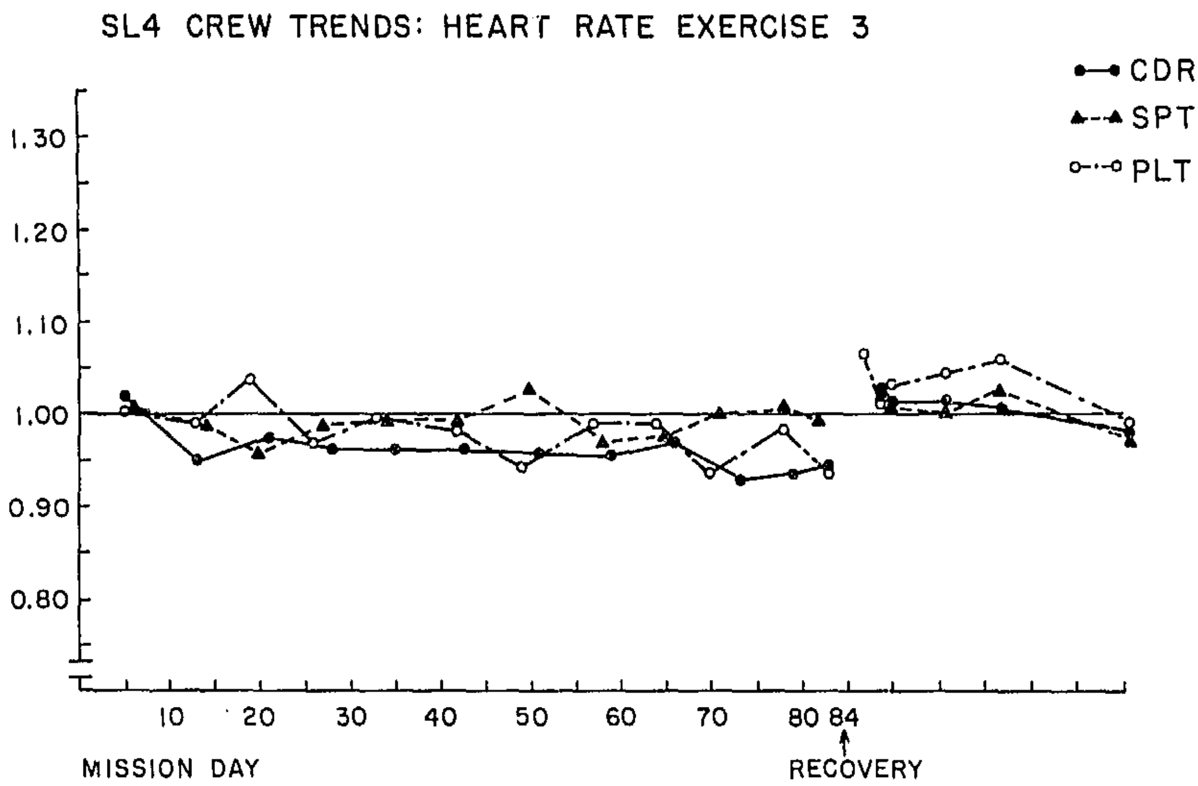


Figure 13. Average heart rate during the highest level of exercise M171 protocol. The data are plotted as a percentage of the mean preflight value. It should be noted that the exercise loads were decreased in the immediate postflight period.

quality of the data and to detect changes of clinical importance. During the three Skylab missions there were no ST segment abnormalities that suggested myocardial ischemia or other changes in the configuration of the ECG waveforms that were considered to be adverse. During the three flights cardiac arrhythmias were occasionally observed. The CDR of SL 1/2 had multiple ventricular ectopic beats during the third level of exercise on the initial in-flight M171 test but no arrhythmias were noted on subsequent tests throughout the remainder of the mission. No arrhythmias were evident in the exercise tests that the PLT of SL 1/2 performed in the preflight period and during the mission. However, during the third level of exercise (M171 protocol) on R+21 he had salvos of ectopic ventricular beats for approximately 1 1/2 minutes. He was monitored for 72 hours, no arrhythmias were detected and he has had no difficulty on subsequent heavy-load exercise tests.

The SPT of SL3 had premature ventricular beats sporadically during the second Skylab mission. On mission day 8 during a long EVA period he was noted to have 80 premature ventricular beats over a 6 1/2 hour period of observation. These ectopic beats were isolated in occurrence and had a configuration suggesting a unifocal origin. This astronaut also had intermittent periods of AV junctional rhythm at rest throughout the flight. On mission day 21 SL3 the CDR had a three-beat run of atrioventricular dissociation presumably due to advanced AV block. The atrial rate was 50 and the junctional escape rate was approximately 39. The episode occurred during the recovery phase of experiment M092 and was not observed in later tests. The crew of SL4 had premature ventricular beats sporadically throughout the mission. On mission day 43 the CDR had two consecutive ectopic ventricular beats during the third level of exercise M171 protocol and on mission day 83 he had three successive ventricular fusion beats during the first exercise level of an M171 test. The PLT of SL4 and AV junctional rhythms at rest and after release of lower body negative pressure. There was no impairment of function during the arrhythmia.

DISCUSSION

Elucidation of the mechanisms that underly the cardiac electrical changes is made difficult by the large number of environmental and physiological variables that were uncontrolled during the Skylab flights. It is known that ECG changes occur when there are shifts in the anatomical position of the heart, with hypokalemia, with perturbations of the autonomic nervous system, with changes in the volume of intracavitary blood, and with physical conditioning and "deconditioning". These factors have either been shown to vary during spaceflight or alterations in these factors would intuitively be expected in a weightless environment.

The increase in the magnitude of the QRS maximum vector is an especially interesting change because this has been a crew trend in each Skylab flight. In the majority of the astronauts the QRS maximum vector magnitude has progressively increased during the flight and in several the upward trend began prior to the flight. The T maximum vector magnitude also tended to increase but variation between measurements was greater. The changes observed during the Skylab flights differ from left ventricular hypertrophy encountered clinically in that the angle between the spatial QRS and T vectors was unchanged or decreased in the astronauts and with pathological left ventricular hypertrophy the angle characteristically increases. The QRS and T magnitude increase and the directional relationship between the QRS and T vectors resemble those changes seen in athletes whose ECG's are followed during a physical conditioning program.[7] Similarly in dogs given heavy exercise loads over a 12 week period, Wyatt and Mitchell observed a decrease in resting heart rate, a decrease in heart rate response to a standard work load, and an increase in QRS spatial vector magnitude.[8]

Increased intracavitary blood due to the centripetal shift of volume during weightlessness may be another mechanism that contributed to the increase in QRS maximum vector magnitude. From a theoretical analysis Brody[9] predicted that an increase in intracavitary blood would augment potentials from radially oriented cardiac dipoles and attenuate those from tangentially oriented dipoles. Since the radially oriented dipoles have the most marked influence on the QRS vector, the net effect of increased diastolic volume would be to increase QRS vector magnitude. Millard, Hodgkin, and Nelson[10] using a series of physiological interventions in experimental animals have confirmed the validity of the Brody effect. Morganroth _et al_[11] determined left ventricular volumes, wall thickness, and mass by echocardiography in 26 actively competing college athletes. Athletes competing in events requiring strenuous isotonic exercise had increased left ventricular volume without increased wall thickness and athletes competing in isometric events had increased wall thickness without increased left ventricular volume. Thus, centripetal shift of fluid and isotonic exercise may have had an additive effect in causing the increased QRS vector magnitude that has been observed during the Skylab flights. Measurement of cardiac diastolic dimensions by echocardiography during the pre- and postflight periods of SL4 suggested that there was a decrease in the transverse cardiac dimension on R+1 in two of the three crewmen.[12] However, after each mission the QRS maximum vector magnitude has remained increased for five to ten days.

An increase in the PR interval duration was a common observation during the three Skylab missions. The PR interval duration is a composite of the conduction time through intra-atrial pathways, the AV node, and the bundle of His. Since conduction in the AV node is longer than in the other components, for clinical purposes the PR interval duration serves as an estimate of AV node conduction. Although drugs such as digitalis, beta-adrenergic blockade, and nodal ischemia can cause prolongation of AV conduction time, an increase in vagal tone is a more likely explanation of the prolongation of the PR intervals seen in the Skylab astronauts. Further support for this explanation comes from the observation that the PR duration during exercise in flight was the same as the PR interval duration measured in the preflight period during comparable exercise. Thus the adrenergic influence of exercise tended to overcome the increased vagal influence observed when the men were at rest.

Ventricular ectopy occurred throughout the three Skylab missions. In general this was sporadic, did not alter hemodynamic function in a detectable manner, and electrocardiographic signs of myocardial ischemia were not associated. On three occasions – first in-flight test M171 protocol SL 1/2, during a long EVA SL3, and during the last in-flight M171 test SL4 – the crewman involved was under extraordinary stress. In the case of the more serious ventricular ectopy observed in the PLT on the 21st postflight day SL 1/2, the relationship of the arrhythmia to the flight is conjectural. He had been in another city on the evening prior to the test and had returned to Houston early on the day of the test.

No arrhythmias were observed during the 72 hours following the test and the exercise protocol has been repeated on multiple occasions and the arrhythmia did not recur during testing.

With the exception of the arrhythmias, no adverse electrocardiographic changes were observed in the Skylab crews that could be attributed to long exposure to a weightless environment or to the other stresses of extended spaceflight. Specifically, there was no evidence of myocardial ischemia or changes in the ECG that would suggest vaso-regulatory abnormalities or the emergence of patterns that have been observed in de-conditioning experiments.[4] The vectorcardiographic techniques utilized in the M093 experiment added both accuracy and precision to the data acquisition and facilitated both scientific investigation and monitoring for crew safety.

Validation of the Quantitative Exercise Stress Methods Used in Experiment M093

Preliminary studies in a highly selected population have revealed that the integral of the T-wave measured after exercise and expressed as a spatial vector provides a specific insensitive means of differentiating patients with coronary disease from normal subjects.[2] In these studies the integral of the total repolarization wave (ST-T) had greater diagnostic power than did the initial fraction of repolarization (ST) which is contrary to the experience with conventional electrocardiographic stress test.

In addition, the best discrimination between normal subjects and coronary disease patients occurred three minutes after exercise. We have attempted to extend this methodology to the study of patients who are referred for evaluation of coronary heart disease. The patients are assigned exercise and electrocardiograms are taken before exercise, during exercise and in a post-exercise recovery period. The electrocardiograms are then analyzed with the M 093 computer program and correlations are made with other independent measures of the disease process such as coronary arteriography. During the two years of ONR sponsorship, 235 exercise tests were carried out using the essential elements of the protocol and the ECG signals were stored on FM magnetic tape. Forty-one of the patients had in the test were also studied with selective coronary arteriography. Our correlative analysis is still in progress and no conclusions conerning the value of this method have been reached.

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