RESEARCH REPORT

Title: Cardiovascular Dynamics During Space Sickness and Deconditioning
(NAG 2-514)

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I. INTRODUCTION

We are currently funded by NASA for the project, "Cardiovascular Dynamics During Space Sickness and Deconditioning" (#NAG2-514). NASA has given priority to the investigation of two problems encountered in the long-term space flights currently being planned: 1) space motion sickness and, 2) cardiovascular deconditioning. We have proposed to use spectral and nonlinear dynamical analysis of heart rate data to quantify the presence of these problems and to evaluate countermeasures against them.

We recently reported the first evidence that space motion sickness may be associated with very low frequency oscillations in heart rate which can be easily detected using frequency analysis of Holter monitor data (Fig. 1). These oscillations were not appreciated in earlier studies, which confined their analysis to alterations of mean heart rate and not to dynamic beat-to-beat fluctuations. These heart rate oscillations probably reflect altered autonomic nervous function and are of potential practical importance because they may 1) serve as the first objective non-invasive way of assessing susceptibility to space motion sickness in flight, 2) help monitor the efficacy of preventive and therapeutic measures and, 3) permit comparison with the dynamics of conventional terrestrial motion sickness.

We also reported the use of spectral analysis in detecting a loss of normal heart rate variability in healthy athletic men subjected to 7-10 days of head-down bed rest, a model for cardiovascular deconditioning during space flight (Goldberger AL, et al. Atropine unmasks bed rest deconditioning effect in healthy men: a spectral analysis of cardiac interbeat intervals. J. Appl. Physiol. 61:1843-1848, 1986). Similar analysis may be of practical use in assessing the efficacy of countermeasures, such as intermittent centrifugal acceleration or time-varying lower body negative pressure.

The goals of this project, in concert with colleagues at NASA-Ames and JSC are:

1) To compile digitized databases of continuous ECG recordings a) from crew members of previous and future flights and b) from previous studies of induced motion sickness in ground-based simulations.

2) To correlate the low frequency ($\leq$ .01 Hz) heart rate oscillations observed during space flight with a) subjective motion sickness symptoms, b) activity level, and c) a respiratory signal derived from the Holter ECG.

3) To determine whether heart rate dynamics during terrestrial motion sickness (rotating chair test) are equivalent to those observed in space flight.

4) To develop a physiological model of heart rate variability that explicitly includes gravitational forces and that can be used to simulate the oscillations observed in space and to test the role of autonomic perturbations in their pathogenesis.

5) To quantitate the loss of heart rate variability associated with bedrest deconditioning; to determine whether countermeasures (e.g. intermittent acceleration) prevent this deconditioning effect; and to determine whether bedrest deconditioning induces changes in heart rate dynamics comparable to those actually observed during space flight.

II. RECENT ACCOMPLISHMENTS

A. Analysis of Ground-Based Motion Sickness Tests

In collaboration with Pat Cowings, Ph.D. and her associates at NASA-Ames, we have performed detailed spectral and time series analysis of data from 20 healthy volunteers studied during a rotating chair protocol designed to simulate ground-based motion sickness. Analysis of the relatively short (<5 min) data segments obtained at successive stages of the protocol did not reveal heart rate patterns or changes that were predictive of susceptibility to terrestrial motion sickness. However, the short data segments available from the study preclude any conclusions about lower frequency fluctuations (eg., $\leq$ .05 Hz) that may be of importance. For example, in our preliminary analyses of space flight data, the oscillations we detected were $\leq$ .01 Hz. Similarly, pathologic heart rate oscillations we have observed in other settings (eg., heart failure) were also usually $\leq$ .04 Hz.

B. Analysis of In-Flight Data

Apart from the Holter records that we have analyzed previously (Fig. 1 from: Goldberger AL et al. Low frequency heart rate oscillations in space shuttle astronauts: a potential new marker of susceptibility to space motion sickness. Space Life Science Symposium. Three Decades of Life Science Research in Space. Washington, D.C. 1987:78-80), the only existing records of in-flight heart rate variability are found in the records acquired by Dr. Cowings and on echocardiograms given to us by Dr. Charles of NASA Johnson. Release of in-flight data from Dr. Cowing's laboratory is still pending administrative clarification from NASA Headquarters and NASA-Ames. We have developed image processing software to help extract the heart-rate data from Dr. Charles' video tapes. However, preliminary analysis of these data show that they do not provide a consistent recording of <u>continuous</u> heartbeat cycles since the echocardiographic transducer is not in one locus for sustained periods. Also, the recordings contain frequent interruptions due to change from M-mode to 2D images. Therefore, analysis of continuous in-flight data remains of critical importance.

C. Analysis of Other Heart Rate Data

In collaboration with Lewis Lipsitz, M.D. of the Gerontology Division at Beth Israel Hospital and Harvard Medical School, we analyzed spectral characteristics of heart rate variability before and during postural tilt in young and old subjects. We found that young, healthy subjects with syncope had a significant increase in low frequency heart rate variability during tilt compared to those without vasovagal syncope. On the other hand, elderly subjects did not develop syncope and showed reduced supine heart rate

variability, as well as absent or attenuated low frequency activation during tilt. Our findings may provide a marker for susceptibility to vasovagal syncope and may provide a physiologic explanation for resistance to vasovagal syncope in old age.

D. Mathematical Modeling and Nonlinear Analysis

Interpretation of the observed heart rate variability is being made with the aid of mathematical models of the cardiovascular system. We have devised a preliminary nonlinear model of heart rate control that under different parameter values yields erratic fluctuations, sustained oscillations and abrupt changes of the type we have observed under a variety of physiologic and pathologic conditions (Fig. 2).

We have also analyzed the nonlinear dynamics of normal heart rate variability in healthy subjects. To test the hypothesis that physiologic beat-to-beat variability in sinus rhythm represents nonlinear "chaos" -- a non-random type of erratic behavior generated by deterministic processes -- we computed Lyapunov exponents for heart rate time series (10,240 consecutive data points over 1 1/2 hours) of subjects under basal conditions, after filtering with singular value decomposition. All data sets had a positive Lyapunov exponent (.02-.04) consistent with an underlying nonlinear chaotic mechanism. This novel finding will be presented at the 1990 National American Heart Association Meeting.

A flow chart of our ECG data analysis protocol is given in Fig. 3.

III. FUTURE PLANS

A. In-Flight Data Analysis

Analysis of in-flight data (with suitable pre- and post-flight controls) remains a high priority. We have arranged with Dr. M. Bungo and Dr. J. Charles of JSC to collaborate in the analysis of Holter monitor data to be provided by the Soviets from ongoing and future flights. We have participated extensively in discussion and briefings with Dr. Bungo and colleagues by telephone and in person during a May 1990 invited visit to JSC, to review the technical aspects of data collection and data analysis. During that visit Dr. Goldberger and Dr. Rigney presented a seminar on Cardiac Dynamics and met with members of the JSC cardiovascular research team.

Based on conversations with Dr. J. Stoklosa of NASA Headquarters, we anticipate the imminent release of data from Dr. Cowings' laboratory with recordings of in-flight and post-flight data from several U.S. astronauts.

B. Bedrest Studies

During our May 1990 visit to JSC we met with Suzanne Fortney, Ph.D. and made plans to collaborate in the analysis of heart rate data obtained from healthy subjects during a bedrest protocol. We have begun to perform analysis on the first subjects in this session to test the hypothesis that bedrest

deconditioning alters heart rate variability, particularly with an attenuation of higher frequency components due to vagal tone (Fig. 4).

C. Management Distribution and Archiving of Physiological Signals

We have been informed that essentially all the computer tapes with heart rate data from earlier missions (Mercury, Gemini, Apollo and Skylab) have already been discarded because of lack of storage space at NASA/Johnson and incompatibility of the tapes with current equipment. Given the great expense of these missions and the uniqueness of the data, a centralized, accessible and comprehensive library of these kinds of records is of critical importance. It should be emphasized that these heart rate data are not only of value to groups such as ours interested specifically in space sickness and cardiovascular deconditioning. They are also an invaluable resource for investigators in other areas, such as studies of circadian rhythms.

Details related to archiving and distribution of the ECG data needs to be decided in collaboration with NASA. In particular, the possibility of distributing these data after de-identification in the form of compact discs should be explored. We have practical experience with this novel form of inexpensive ($3.00/disc) data archiving and distribution. Other important issues relating to the contents of the database, authorization for its use, and so forth, will also require collaboration with NASA during the definition phase of the project. This new archiving and retrieval system using compact discs would greatly simplify information and storage by Life Science Investigators.

Discussion with NASA is also required concerning the protocol for recording and archiving of heart rate data from future flights. Careful analysis of existing data will help guide the formulation of protocols for data acquisition on future missions. Should heart rate data be acquired throughout the flights or just at selected times? What control data should be acquired pre-flight and post-flight? What equipment should be used to record these data?

IV. PUBLICATIONS AND PREPRINTS SUPPORTED BY PRESENT GRANT

1. Goldberger AL, Rigney DR. On the non-linear motions of the heart: fractals, chaos and cardiac dynamics. In A Goldbeter, ed. Cell to cell signalling: from experiments to theoretical models, Academic Press, San Diego, 1989, pp 541-549.

2. Rigney DR, Goldberger AL. Nonlinear dynamics of the heart's swinging during pericardial effusion. Am J Physiol. 257:(Heart Circ Physiol 26): H1292-1305, 1989.

3. Goldberger AL, Rigney DR, West BJ. Chaos and fractals in human physiology. Sci American. 262:42-49, 1990.

4. Goldberger AL. Nonlinear dynamics, fractals and chaos: Application to cardiac electrophysiology. Ann Biomed Eng. 18:195-198, 1990.

5. Goldberger AL. Fractal electrodynamics of the heartbeat, Ann NY Acad Sci. 591:402-409, 1990.

6. Lipsitz LA, Mietus J, Moody GB, Goldberger AL. Spectral characteristics of heart rate variability before and during postural tilt. Relations to aging and risk of syncope. Circulation 81:1803-1810, 1990.

7. Goldberger AL. Fractal mechanisms in cardiac electrophysiology. In S. Sideman, A Kleber, eds. Cardiac electrophysiology and transport, Kluwer Academic Publishers, Norwell, MA, in press.

8. Goldberger AL. Fractals and the heart. Proc Royal Dutch Acad Sci, in Press.

9. Rigney DR, Mietus J, Goldberger AL. Is normal sinus rhythm "chaotic"? Measurement of Lyapunov exponents. Circulation. 82(Suppl III): 236, 1990.

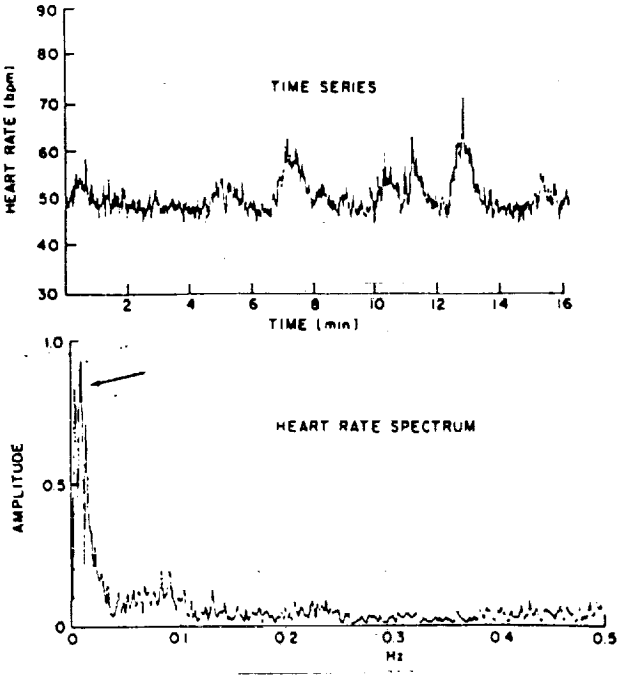


Figure 1. Heart rate time series and corresponding frequency spectrum from an astronaut with space motion sickness (SMS). Upper panel: During SMS, the astronaut's heart rate is seen to exhibit a series of large amplitude oscillations, not seen under normal conditions, that might be used as a marker of the syndrome's presence. Lower panel: This is the Fourier spectrum of the above heart rate time series, showing the range of frequencies over which the oscillations occur. They are found in the band centered around 0.01 Hz that is indicated by the arrow.

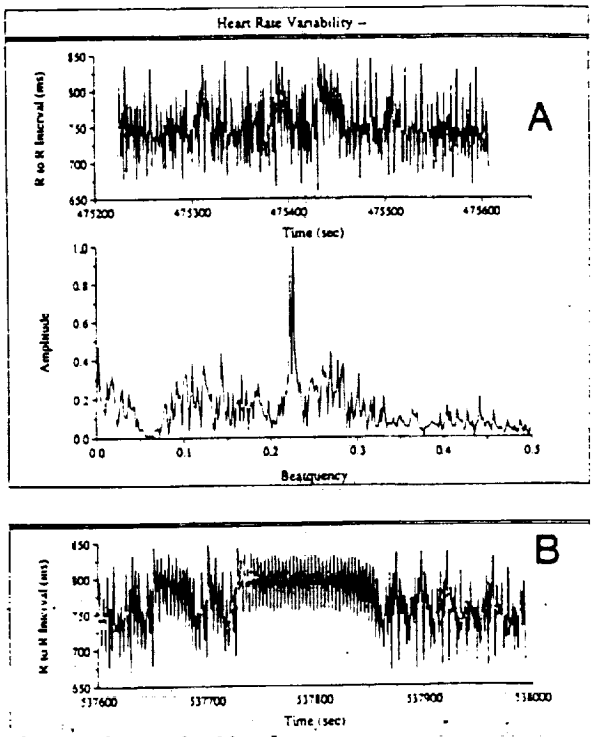
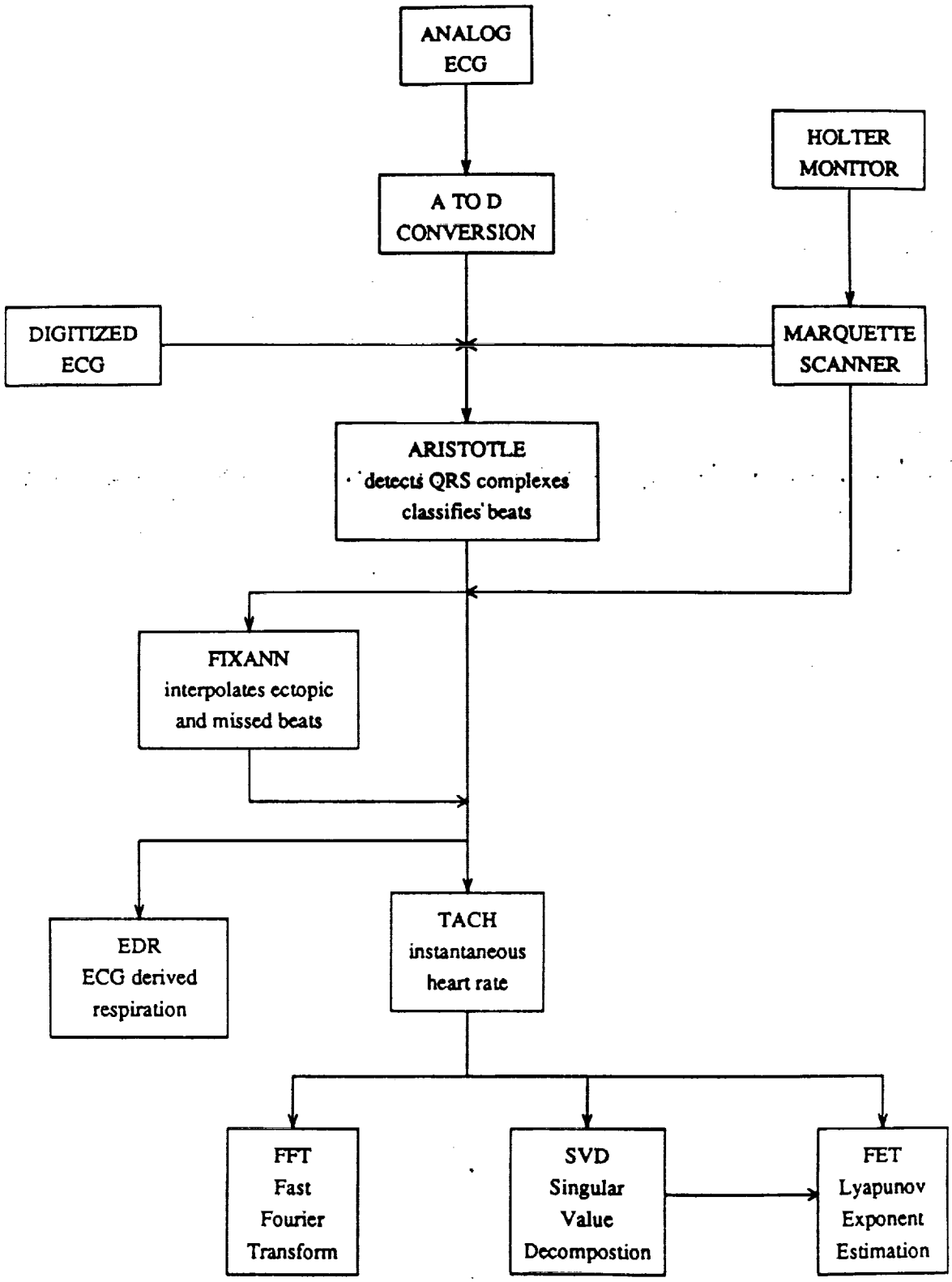
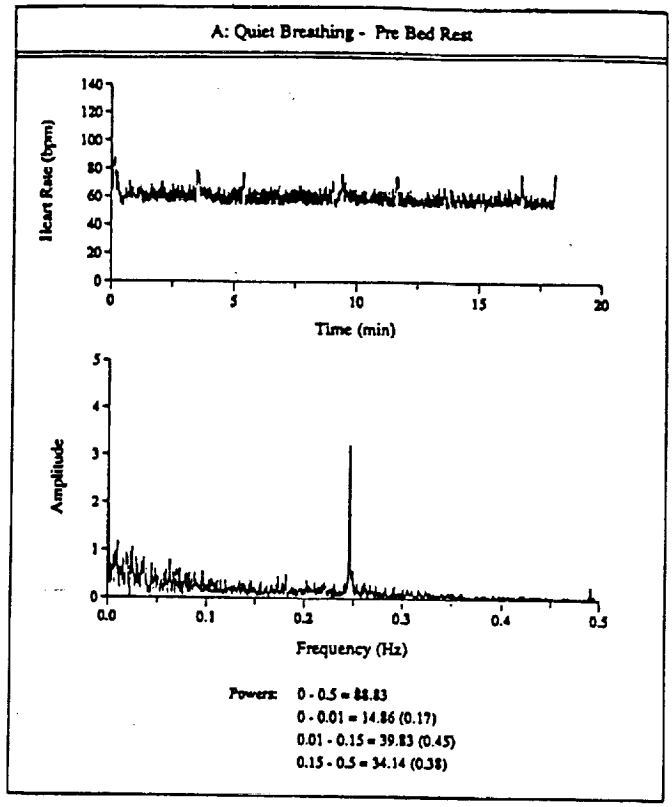
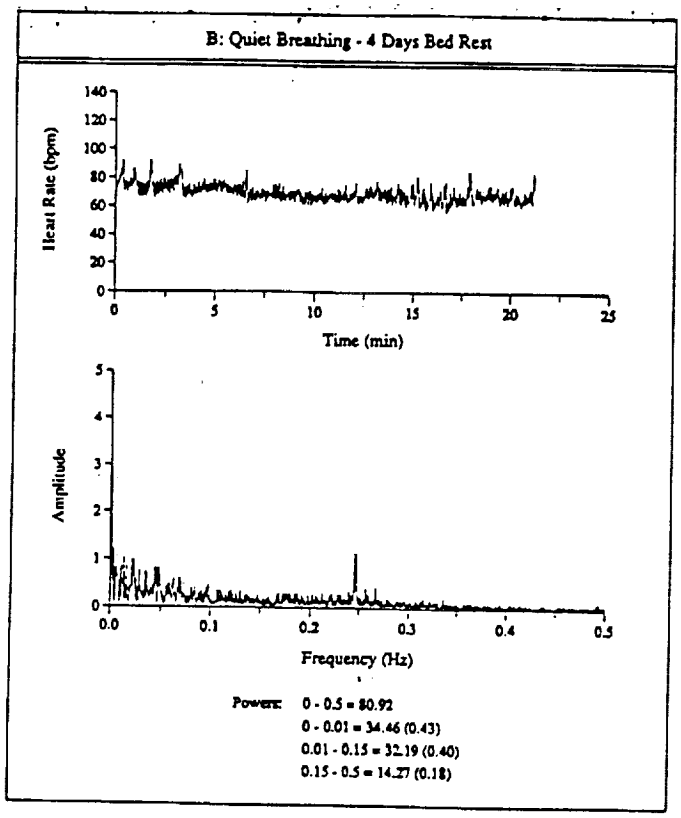


Figure 2. Erratic and periodic heart rate data in a totally deterministic, nonlinear model of cardiovascular control. A. For certain parameter values, the heart rate fluctuates deterministically for thousands of beats. The peak at 0.225 beat^{-1} is due to baroreflex. B. The continuation of the simulation in (A) demonstrating intermittency that starts and stops abruptly.

Figure 3. Flow chart for electrocardiographic data analysis in our laboratory.







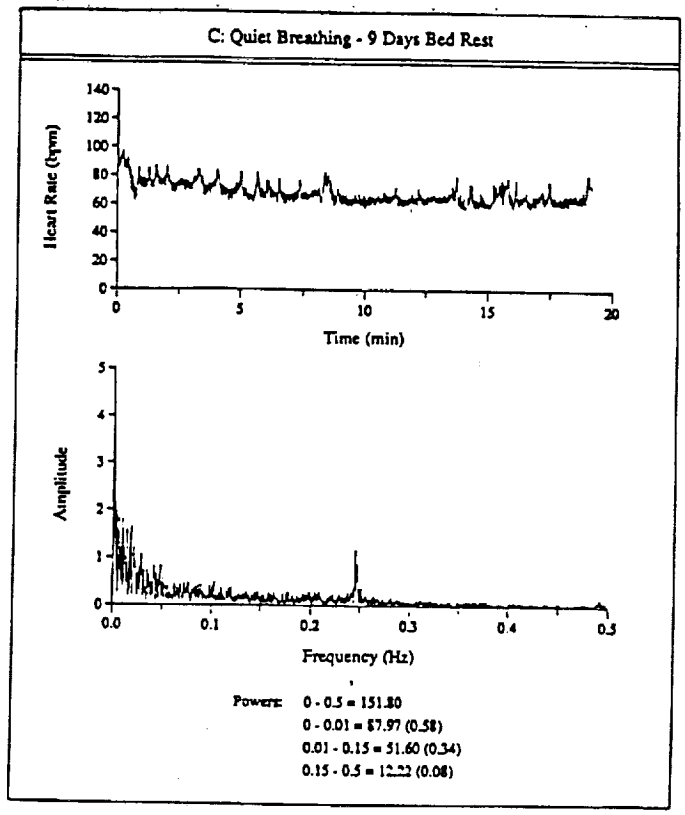


Figure 4. Heart rate time series and spectra from a young healthy adult female before and during bedrest study. Note the prominent, vagally-mediated high frequency peak in panel A associated with metronomic breathing at .25 Hz. During bedrest (B, C) there is attenuation of this peak, consistent with a loss of vagal tone associated with deconditioning. Average heart rate is also increased. Data are from the study being conducted by Dr. Suzanne Fortney, JSC. Spectral power for different bands is shown below each data set. Numbers in parentheses indicate percentage of total power in each band.