·DAA/AMES

FINAL TECHNICAL REPORT

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University of California, San Diego

Principal Investigator, Ary L. Goldberger, M.D.*

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General Summary:

Over the past year, in collaboration with Dr. Danielle Goldwater of NASA/AMES we have performed spectral analysis of heart rate data from healthy subjects during weightlessness simulation. The purpose of these studies was to test the hypothesis that spectral analysis may provide a sensitive new technique for assessing cardiac function during space flight and in detecting potentially detrimental effects of certain drugs on cardiac reserve. The initial findings detailed in the enclosed reprint and preprints are very promising in this regard.

In particular, the grant has supported the publication of one article (1), the recent completion of another paper (2) which is being submitted to the Journal of Applied Physiology and acceptance of an abstract (3) for presentation at the upcoming 7th International Man in Space Symposium at NASA Johnson Space Center in February, 1986. Copies of all these documents have been included. These documents comprise the Final Technical Report for this Cooperative Agreement.

No patent requests relating to this Cooperative Agreement were submitted.

Publications:

1. Goldberger AL, Goldwater D, Bhargava V. Atropine unmasks bedrest deconditioning effect in healthy men: spectral analysis of cardiac interbeat intervals. Submitted for publication.

2. Goldberger AL, West BJ, Bhargava V. Nonlinear mechanisms in physiology and pathophysiology. Toward a dynamical theory of health and disease. Proceedings of the 11th International Association for Mathematics and Computers in Simulation, World Congress, Oslo, 1985.

3. Goldberger AL, Goldwater D, Bhargava V. Atropine unmasks bedrest deconditioning effect in healthy men. A spectral analysis. (Abst)

Technical Report Document #1

Atropine Unmasks Bedrest Deconditioning Effect in Healthy Men: Spectral Analysis of Cardiac Interbeat Intervals

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ABSTRACT

Bedrest deconditioning is suspected to reduce cardiac function. However, quantitation of subtle decreases in cardiac reserve may be difficult. Normal subjects show considerable variability in heart rate response, reflected by a relatively broadband interbeat interval power spectrum. We hypothesized that the deconditioning effects of bedrest would induce narrowing of this spectrum, reflecting a reduction in the autonomically-modulated variability in heart rate. Ten aerobically conditioned men (average 35-50 years) underwent orthostatic tolerance testing with lower body negative pressure pre-bedrest and after 10 days of bedrest, while on placebo and after intravenous atropine. Spectra were derived by Fourier analysis of 128 interbeat interval data sets from subjects with sufficient numbers of beats during matched periods of the protocol. Root-mean-square (RMS) values ($\bar{X}\pm SD$) for the band encompassing the 2nd to 64th harmonics were computed.

Condition	Placebo RMS (n=6)		Atropine RMS (n=7)	
Pre-bedrest	P=NS	93±33 ms	P<.01	63±24 ms
Bedrest		84±38 ms		40±23 ms

These data suggest that atropine unmasks the deconditioning effect of bedrest in athletic men, evidenced by a reduction in interbeat interval spectral power compared with placebo. Spectral analysis offers a new means of quantitating the effects of bedrest deconditioning and autonomic perturbations on cardiac dynamics.

Index words: bedrest deconditioning; autonomic nervous system; power spectrum analysis; atropine

INTRODUCTION

The physiological effects of prolonged bedrest are of interest from two major perspectives. Historically, the deconditioning effects of bedrest were first studied based on the concern that recumbency itself might further impair the physiological response to a variety of unrelated disease states. Thus, to the extent that it adversely influences adaptive and homeostatic mechanisms, bedrest may actually both compound the negative effects of the primary disease as well as retard recovery (7,24). Because it reduces gravitational effects, bedrest has also been utilized intensively in recent years by investigators in the manned space program as a way of simulating weightlessness (21). There has been considerable interest, therefore, in studying alterations in cardiovascular function as well as in assessing changes in other physiological processes associated with "hypodynamic" environments (12).

The major pieces of evidence cited in support of the hypothesis that bedrest "deconditions" the cardiovascular system are decreased exercise capacity, increased resting pulse rate and decreased tolerance to orthostatic stress (3-5,17,20,21,24). The mechanisms underlying these maladaptive changes, however, are poorly understood. Furthermore, the likely contribution of changes in autonomic nervous system function has received limited appraisal. Animal (15) and human (5,16) studies have suggested altered sympathetic function. The effects of bedrest on parasympathetic function have not been directly addressed.

A central problem in studying bedrest deconditioning has been the development of non-invasive yet sensitive tests for assessing overall

cardiovascular reserve and autonomic function. Studies of functional capacity and orthostatic tolerance have been useful in this regard. However, reduced exercise capacity or intolerance to tilt may reflect a variety of noncardiac changes associated with prolonged bedrest, including diminished muscular tone and reduced circulating blood volume (3,17,21,24).

We hypothesized that prolonged bedrest leads to alterations in autonomic function and that these perturbations will result in a decrease in the physiologic variability in short-term heart rate fluctuations. Furthermore, we speculated that such potentially subtle alterations in neuro-cardiac dynamics might be detected by spectral (frequency) analysis of cardiac interbeat intervals. In particular, a reduction in physiological heart-rate variability should be reflected in a relative narrowing of the interbeat interval power spectrum. This report describes a novel application of this sensitive technique in assessing dynamic changes in cardiovascular reserve.

METHODS AND SUBJECTS

Subjects

Ten aerobically-conditioned men ages 35-50 years underwent serial tests of orthostatic tolerance with lower body negative pressure (LBNP) performed before, during and after bedrest. All men had a history of regular aerobic training and a mean maximum oxygen consumption of 47.5 ml kg^{-1} min. Subjects had to pass a rigorous physical examination which included treadmill electrocardiogram (ECG), exercise testing and echocardiography.

Pre-bedrest and Bedrest Protocol

Subjects were housed in the NASA/Ames Human Research Facility. During a ten-day pre-bedrest phase the subjects were ambulatory. For the next ten days, head down (-6°) bedrest was strictly maintained. The bedrest phase was followed by a two-week ambulatory recovery phase during which the subjects were allowed to leave the facility for sedentary activities at home for six days. Subjects returned to live in the facility for the final week of recovery testing. During the study, subjects ate a nutritionally balanced diet of 2800 cal/day and drank ad lib fluids. Caffeine, methyl xanthine-containing beverages, nicotine and alcohol were prohibited.

Lower Body Negative Pressure (LBNP) Protocol

Subjects were placed in a horizontal cylindrical chamber which extended from foot to waist level and was sealed at the waist with a rubber diaphragm. Wall vacuum suction, modulated by a calibrated regulator and continuously monitored, provided graded orthostatic stress. The LBNP protocol shown in Fig 1 was employed, consisting of a 5-min control period, 3 min at -30 mm Hg, 5 min each at -50 to -100 mm Hg in -10 mm Hg increments and a 5 min recovery period following release of suction. LBNP runs were terminated at signs of syncope or presyncope evidenced primarily by bradycardia, hypotension or diminution or reversal of cerebral blood flow which was measured by temporal artery Doppler flow meter. No subject tolerated the full LBNP protocol through -100 mm Hg.

The entire protocol beginning with the control period and ending with recovery will be referred to as a run. Each 5-min period of constant LBNP, including control and recovery periods, will be referred to as a stage.

Drug Interventions

During the three phases of the study (pre-bedrest, bedrest and recovery) the subjects were treated with saline placebo, atropine, phenylephrine and propranolol prior to LBNP as a means of assessing autonomic function during bedrest. Due to insufficient numbers of data points for spectral analysis for the phenylephrine and propranolol runs, only data on placebo and atropine are reported here.

The subjects underwent only one LBNP run per day. Atropine was administered in a therapeutic dose range of .01 to .02 mg/kg. Subjects underwent two orientation LBNP exposures with atropine to select the dosage that would maximize LBNP duration. At a minimum, the dosage of atropine had to produce a 20% increase in basal heart rate. Once the dosage was selected during this familiarization phase, the same dosage was maintained for each subject during pre-bedrest, bedrest and recovery runs.

The LBNP exposures occurred on days 7,8,9 and 10 of the pre-bedrest and bedrest study phases. During the recovery phase, the LBNP drug exposures occurred during the final week.

This protocol was approved by the Ames Human Research Evaluation Review Board and the subjects gave informed consent to all aspects of the study prior to entry.

Instrumentation

ECG tracings were obtained from bipolar sternal electrodes using a Gould analog 9-channel brush recording system. Once per minute, the chart speed was increased to 100 mm/sec. Parallel channels recorded vacuum level, blood pressure, and Doppler temporal artery blood flow. Digital heart rates integrated over 5-sec intervals were obtained with a

Hewlett-Packard Cardiotachometer. Heart rate measurements for each subject represent mean values for the five minute period just prior to each experimental run.

R-R Interval Analysis

R-R intervals were analyzed from portions of the analog data recorded at 100 mm/sec during each stage of the LBNP protocol. For each LBNP run, the number of consecutive R-R intervals/run was computed. To assure an adequate sample size for the Fourier analysis which required 2^n data points, we only accepted runs with a minimum of 128 R-R intervals.

The runs were then paired for intra-subject comparison of the following four conditions: placebo pre-bedrest vs. placebo recovery (ambulatory comparison); placebo pre-bedrest vs. placebo bedrest; atropine pre-bedrest vs. atropine bedrest, and placebo bedrest vs. atropine pre-bedrest. The same subject did not necessarily have equal numbers of R-R intervals during identical stages of paired LBNP runs. Furthermore, each subject did not always achieve the same LBNP stage in each run. These discrepancies were taken into account by selecting matched numbers of consecutive R-R intervals from each achieved stage such that the total number/run was exactly 128. These intervals were selected by an independent observer according to the following protocol. 1) Only data from equivalent stages were compared. For example if a subject reached LBNP stage of -60 mm Hg during one run, but only -50 mm Hg during the paired run, the data from the -60 mm Hg stage was not utilized in this comparison. 2) The number of R-R intervals in each stage with LBNP <0 mm Hg was selected to be equal. 3) The combined number of R-R intervals in the basal and recovery stages (LBNP = 0 mm

Hg) was selected to be approximately twice the number in each stage with LBNP = 0 mm Hg. 4) To minimize step-discontinuities (2) between the first and last R-R intervals of the 128-point data sets, more R-R intervals were acquired from the recovery vs. basal stage, thus allowing the heart rate to equilibrate towards its basal level.

A sufficient number (i.e. 128) of matched R-R intervals was not available in all subjects for certain runs. Therefore, data from only some of the subjects could be utilized for spectral analysis.

Computer Analysis

R-R intervals were digitized by an independent observer using a Talos X-Y digitizer interfaced to a Tektronix 4052A computer. Fast Fourier Transform (FFT) analysis was performed on each 128 R-R interval data set using a standard (Cooley-Tukey) algorithm. The root-mean-square (RMS) value for each data set was computed for the band width encompassing the 2^{nd} through 64^{th} harmonics. The RMS value is a standard measurement most commonly used as an index of the effective voltage of an electrical signal. In the present study, the RMS value is used as an index of the "effective" interbeat interval spectral power and is therefore measured in units of time.

Statistical Analysis

Students' t-test was used for paired-comparisons of RMS values, digital heart rates and LBNP tolerance times. Values are expressed as mean ± one standard deviation. Statistical significance is defined as P value less than 0.05.

RESULTS

Spectral Analyses

The results of the spectral analyses are given in Figs. 2-4. There was no significant difference in spectral RMS values for subjects pre-bedrest vs. bedrest while on placebo (93±33 ms vs. 84±38 ms; n=6 subjects). Similarly, for the comparison of placebo pre-bedrest vs. placebo recovery there was no significant difference in RMS values: 91±31 ms vs 94±36 ms, respectively (n=7). However, when spectral RMS was compared for subjects pre-bedrest vs. bedrest while on atropine (63±24 ms vs. 40±23ms; n=7) a significant ($p<.01$) decrease was noted. Furthermore, spectral RMS on atropine was significantly ($p<.005$) lower than on placebo for subjects at bedrest (44±21 ms vs. 83±31 ms; n=6).

Representative plots of R-R interval time series and their associated spectra in one subject during different interventions are shown in Figs 5-7. Figure 5 compares pre-bedrest and bedrest runs while on placebo. Both R-R interval plots (top panel) show comparable variability and the power spectra (bottom panels) overlap for the entire frequency range. Figure 6, in contrast, compares the atropine pre-bedrest and atropine bedrest runs. The bedrest R-R interval plot shows a visually apparent reduction in variability compared with pre-bedrest (top panel). This is reflected in a reduction in spectral power (bottom panel). Similarly (Figure 7), when the atropine bedrest and placebo bedrest runs are compared, a marked reduction in R-R interval variability with atropine is noted with an associated decrease in spectral power.

Heart Rate Data

Resting heart rate (58.5±8.5 beats/minute) for all ten subjects on placebo at bedrest was higher than pre-bedrest values (54.7±4.4 beats/minute). However this difference was not statistically

significant. Resting heart rate during the recovery period (59.1±8.9 beats/minute) was significantly ($p<.05$) higher than during the pre-bedrest placebo period. The heart rate at bedrest with atropine (83.7±18.9 beats/minute), as significantly ($P<.002$) higher than atropine pre-bedrest values (70.4±12.4 beats/minute), in addition to being significantly ($p<.01$) higher than the placebo bedrest values given above.

Orthostatic Tolerance Times

Orthostatic tolerance time for all ten subjects during the pre-bedrest placebo phase (806±274 sec) was significantly ($p<.05$) higher than during the bedrest placebo phase (589±314 sec), but not different from placebo recovery phase (811±216 sec). Exercise tolerance times for subjects in the atropine pre-bedrest phase (658±352 sec) were higher than during the atropine bedrest phase (505±252 sec). However, this difference was not statisticaly significant.

Discussion

This study demonstrates several findings of potential importance. First, the data support the contention that bedrest impairs cardiovascular reserve, evidenced by a reduction in heart rate variability. Second, the unmasking of this effect by atropine suggests the possible importance of the autonomic nervous system in mediating this deconditioning effect. Furthermore, the study indicates the utility of spectral analysis of cardiac interbeat interval dynamics as a novel tool for assessing subtle perturbations in autonomic function and in monitoring potentially pathologic alterations associated with prolonged recumbency.

Bedrest Deconditioning and Cardiovascular Control

Multiple studies (4,5,17,21,24) have suggested that prolonged bedrest adversely affects cardiovascular performance. One finding which appears to support this hypothesis is an increase in resting heart rate usually observed after enforced recumbency in normal subjects (21,24). In the present study, mean resting heart rate with bedrest was higher than pre-bedrest. However the difference did not reach statistical significance. Resting heart rate during the recovery phase was significantly higher than during the pre-bedrest period, suggesting that certain autonomic perturbations associated with bedrest persisted for at least two weeks following return to sedentary activity in previously well-trained individuals. The mechanism of the relative tachycardia associated with bedrest has not been determined but could be related to a decrease in vagal tone (or decreased sensitivity to vagal stimulation), to an increase in sympathetic tone (or increased sensitivity to sympathetic stimulation), or to some combination of these effects.

While the influence of bedrest on vagal function has not been directly studied, data from both animal (15) and human (5,16) investigations suggested variable alterations in sympathetic function. Krupina et al (15), for example, studied rabbits which had been immobilized for up to six weeks and reported a reduction in catecholamine content in the adrenal gland as well as the hypothalamus. Chobanian et al. (5) compared catecholamine metabolism in six healthy men before and during two to three weeks of bedrest. No changes in pulse rate or blood pressure were noted in response to graded infusion

of norepinephrine following bedrest. While not statistically significant, there was a trend for serum catecholamine levels to decrease in the supine state following bedrest, but to become increased over control levels during tilt testing. This finding suggests an instability in sympathetic control associated with bedrest. In our study, subjects given atropine had significantly higher mean resting heart rates at bedrest vs. pre-bedrest. This observation is consistent with enhanced sympathetic or with decreased parasympathetic effects with bedrest. A reduction in parasympathetic tone with enforced recumbency would complement the well established link between increased vagal tone and resting bradycardia in subjects who undergo exercise conditioning (6,8,19).

In addition to its effort on resting heart rate, bedrest appears to alter two other important indices of cardiovascular reserve: exercise capacity and orthostatic tolerance. While prolonged bedrest appears to reduce exercise capacity (3,4,21), the mechanisms underlying this deleterious effect remain obscure. In particular, it is not certain whether this deconditioning primarily reflects peripheral or central factors, or some combination. Basal cardiac output does not appear to be markedly altered following bedrest (5,20,24). However, Chobanian et al. (5) noted a significant decrease in cardiac output during tilt testing as compared to bedrest levels. This reduction in cardiac output may be related at least in part to a decrease in blood volume, a consistent finding after prolonged bedrest (5,17,20,21). Chobanian et al. (5) also reported that peripheral vascular resistance during passive tilt was higher for subjects at bedrest vs. control state. However,

supine peripheral vascular resistance was not altered by bedrest. The effect of bedrest on inotropic state has not been determined.

Bedrest and Heart Rate Variability

In this study, we investigated another parameter of cardiovascular function, namely heart rate variability. While the normal cardiac rhythm is referred to as "regular" sinus rhythm, interbeat intervals in active healthy subjects show a wide range of variability. These physiologic fluctuations which are important in normal homeostatic regulation are "fine-tuned" by the interaction of the parasympathetic and sympathetic branches of the autonomic nervous system (19). This variability in heart rate includes more than just respiratory (phasic) fluctuations. On the other hand, these fluctuations are not completely random. Spectral analysis of R-R intervals recorded over multiple hours in healthy subjects reveals a broadband frequency spectrum with so-called "1/f scaling" (14). The term 1/f refers to spectra showing an inverse relationship between frequency (f) and power (9,10). Thus in 1/f-like spectra, lower frequencies (harmonics) will show higher power than the higher frequencies. The power spectra shown in figures 4-6 are 1/f-like, with an inverse relationship between harmonics and power.

Loss of physiologic heart rate variability may be seen in a variety of settings including aging (25), placental insufficiency syndromes (13), diabetes mellitus and multiple sclerosis (18). We postulated that prolonged bedrest might cause a similar reduction in heart rate variability associated with autonomic deconditioning. The results of the present study are consistent with this hypothesis. Of particular interest was the observation that the deconditioning effects of bedrest on R-R interval variability were relatively subtle and only apparent

after atropine administration. No significant difference was noted in spectral RMS values pre-bedrest vs. bedrest, although there was a trend for the values to be lower in the bedrest phase. However, with atropine, spectral RMS values at bedrest were significantly diminished compared to pre-bedrest levels. This finding suggests that the normal control mechanisms regulating heart rate variability are reduced with prolonged bedrest and that additional interference with parasympathetic function, in this case with atropine, induces an even more marked reduction in normal R-R interval fluctuations.

The elevated resting heart rate noted after prolonged bedrest (21,24) also suggests reduced parasympathetic tone. Pharmacological doses of atropine in this setting are, therefore, likely to "relegate" control of heart rate variability to the sympathetic system. The decrease in cardiac interbeat interval variability in atropinized subjects at bedrest vs. pre-bedrest suggests that sympathetic function is also impaired with bedrest. The precise mechanisms of this impairment are not known (5,15,16).

Spectral Analysis

The detection of alterations in interbeat interval dynamics with spectral analysis supports the sensitivity of this technique. Up to the present, spectral analysis of heart rate variability has had surprisingly little application in clinical studies. Recently, time series analysis has been used to characterize the pathologic low frequency fluctuations in R-R intervals noted in patients with heart failure, associated with the Cheyne-Stokes breathing (9). Gordon et al. (11) recently reported abnormalities in short term fluctuations in heart rate and respiration in the sudden infant death syndrome. In previous

studies (1,22), frequency analysis was used to define physiological oscillations in interbeat intervals associated with respiration, thermoregulation and baroreceptor control. Akselrod et al. (1) in canine studies demonstrated the utility of power spectrum analysis as a "probe" of cardiovascular control mechanisms. They observed a marked decrease in spectral amplitude after parasympathetic blockade and further reduction after total autonomic blockade. The present study confirms the loss of spectral power associated with atropine administration, as shown in figure 7.

The sensitivity of spectral analysis in this study is further supported by its use in detecting the effect of bedrest on R-R interval variability. The use spectral analysis, therefore, may complement traditional ways of assessing cardiovascular function and monitoring deconditioning effects, such as exercise and orthostatic tolerance testing. In the present study, orthostatic tolerance time pre-bedrest vs. bedrest was not significantly reduced in atropinized subjects at a time when spectral analysis revealed a significant reduction in interbeat interval variability. In contrast, mean orthostatic tolerance time was reduced by 27% ($p<.05$) in subjects on placebo at bedrest compared to pre-bedrest at a time when no significant difference was apparent in spectral power or in the mean resting heart rate. The reason for the apparent differential sensitivity of spectral analysis and orthostatic tolerance testing is not clear. However, the data do support the complementarity of these two indices in assessing cardiovascular reserve.

Spectral analysis is particularly attractive because it provides a quantitative tool for measuring physiological variability. The utility

of this type of analysis is suggested in the following hypothetical examples. Consider two data (e.g.interbeat interval) sets with identical or nearly identical means ($\bar{X}_1 = \bar{X}_2$) but very different variances. In one case the variance is almost nil, while in the other it is very marked. Whereas t-testing would reveal no significant difference ($\bar{X}_1 - \bar{X}_2 = 0$) the spectral power of the sample with greater variability would be higher. Spectral analysis would also provide a way of comparing two time series with identical means and identical variances, since the data sets could comprise very different frequency components depending on the ordering of the data points.

Despite its potential utility, spectral analysis of clinical data is fraught with pitfalls. First, an adequate number of data points must be available. We selected 128 R-R intervals per run to provide a reasonable range of frequencies, i.e. up to the 64^{th} harmonic. A greater number of data points would have provided additional information about higher frequency components, but were not available in this retrospective analysis. In addition, since these 128 point data sets were comprised of samples from serial stages of the LBNP protocol, equal numbers of R-R intervals from matched stages of the LBNP protocol were required for intra-subject comparisons. Another potential pitfall relates to the selection of the first and last sample points, because a marked discrepancy (step-discontinuity) between these points can artifactually alter the frequency spectrum (2). We minimized such step discontinuities by taking a greater number of beats from the final (recovery) vs initial (basal) stage, thus allowing time for the heart rate to equilibrate towards its control level (Figs 5-7).

Future Applications

A more complete characterization of the role of the autonomic nervous system in bedrest deconditioning would have been provided by other interventions, including beta-blocking agents and vagotonic drugs (eg. phenylephrine). Unfortunately, data from these interventions could not be utilized in this retrospective study because there were too few matched runs with adequate numbers of data samples for spectral analysis. Future prospective studies with longer acquisition times per LBNP stage should help in further assessing the role of autonomic perturbations in bedrest deconditioning.

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FIGURE LEGENDS

Figure 1. Lower body negative pressure (LBNP) protocol used in study is depicted graphically. See text for details.

Figure 2. Comparison of spectral root-mean-square (RMS) values for subjects on placebo during pre-bedrest (PRE-BR), bedrest (BR) and recovery (REC) phases of protocol.

Figure 3. Comparison of spectral root-mean-square (RMS) values for subjects pre-bedrest (PRE-BR) and at bedrest (BR) after atropine.

Figure 4. Comparison of spectral root-mean-square (RMS) values for subjects at bedrest while on placebo and atropine.

Figure 5. Representative interbeat interval plots (top panel) and associated power spectra (bottom panel) from subject during placebo pre-bedrest and placebo bedrest phases of protocol. dB = decibels. RMS = root-mean-square value in milliseconds.

Figure 6. Representative interbeat interval plots (top panel) and associate power spectra (bottom panel) from subject during atropine pre-bedrest and atropine bedrest phases of protocol. Abbreviations as in Fig. 5.

Figure 7. Representative interbeat interval plots (top panel) and associated power spectrum (bottom panel) from subject during placebo

bedrest and atropine bedrest phases of protocol. Abbreviations as in Fig. 5.

Figure 1

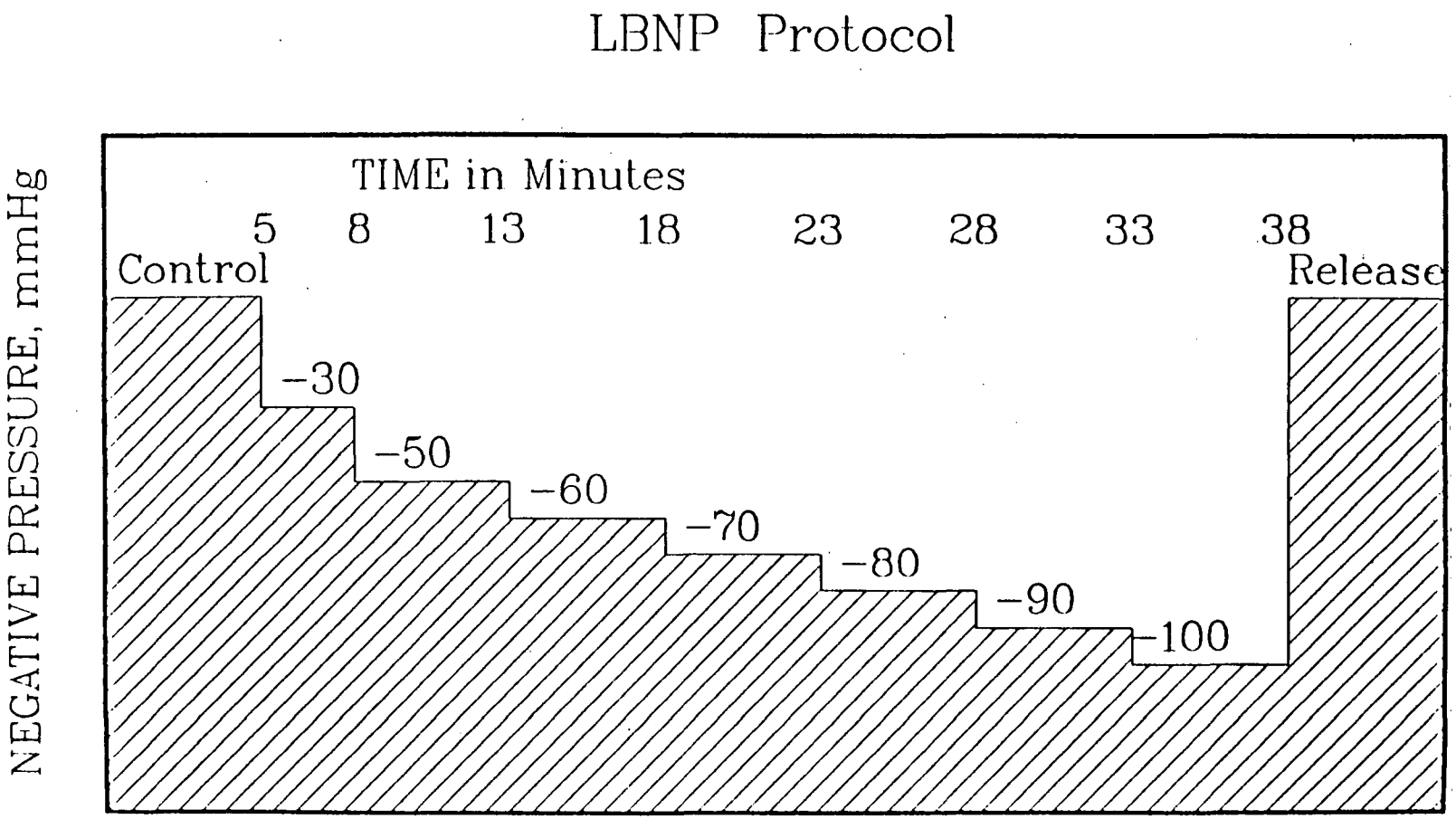
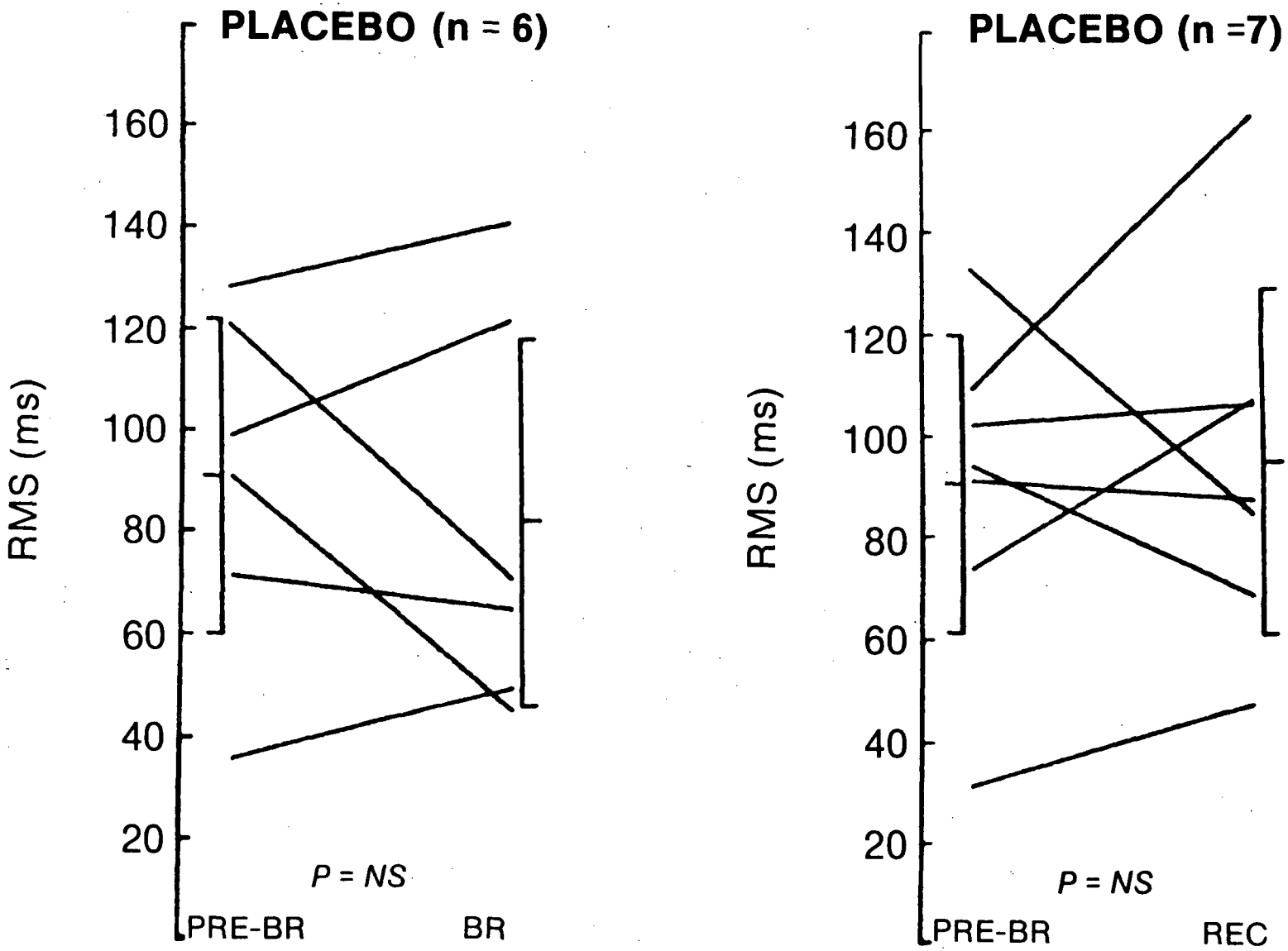

LBNP Protocol
TIME in Minutes
5
8
13
18
23
28
33
38
Control
Release
-30
-50
-60
-70
-80
-90
-100
NEGATIVE PRESSURE, mmHg

Figure 2


PLACEBO (n = 6)
RMS (ms)
160
140
120
100
80
60
40
20
P = NS
PRE-BR
BR
PLACEBO (n =7)
RMS (ms)
160
140
120
100
80
60
40
20
P = NS
PRE-BR
REC

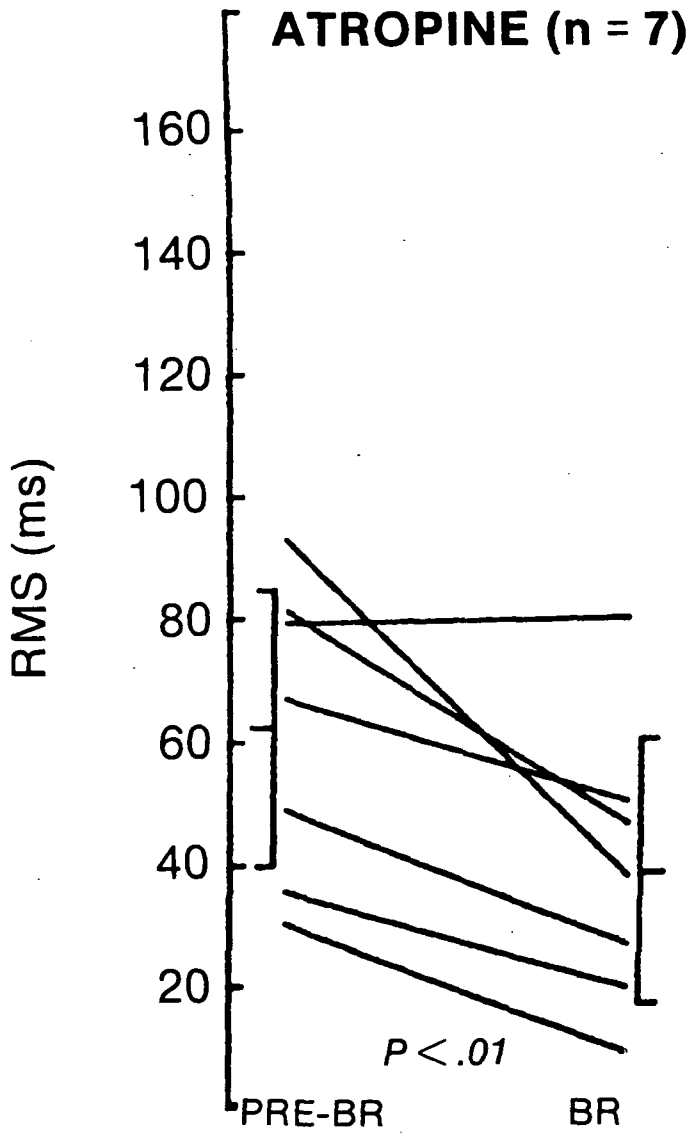


Figure 3

Figure 4

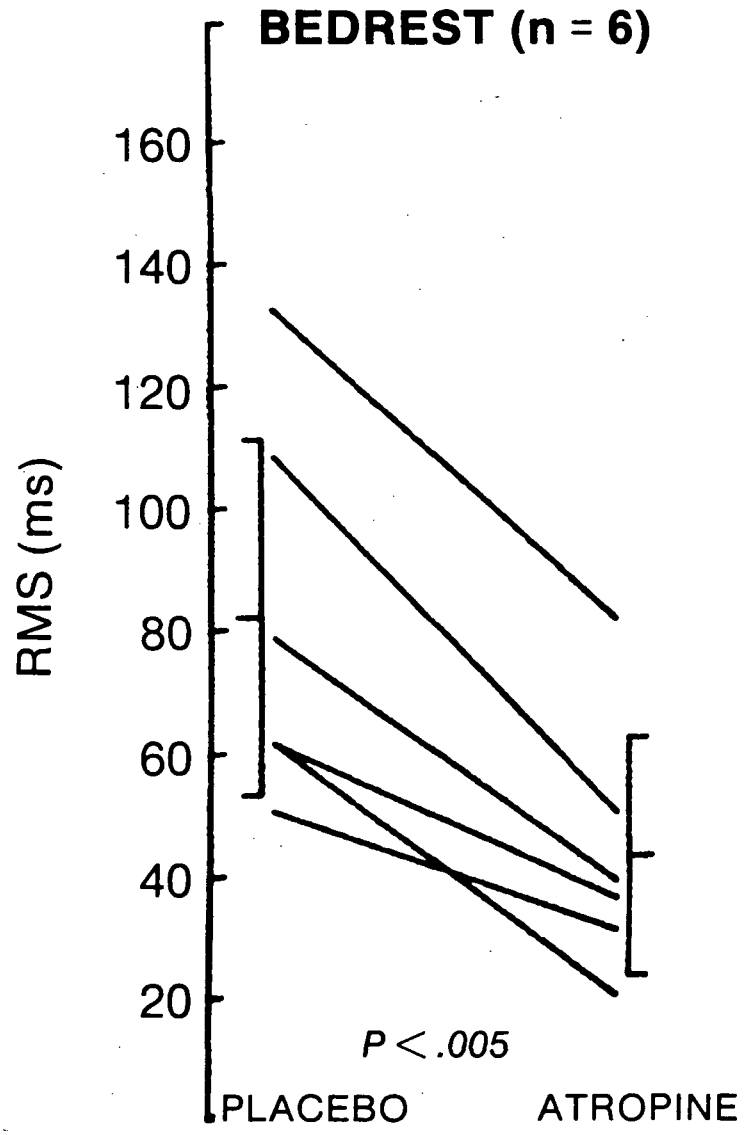

BEDREST (n = 6)
RMS (ms)
160
140
120
100
80
60
40
20
P < .005
PLACEBO
ATROPINE

Figure 5

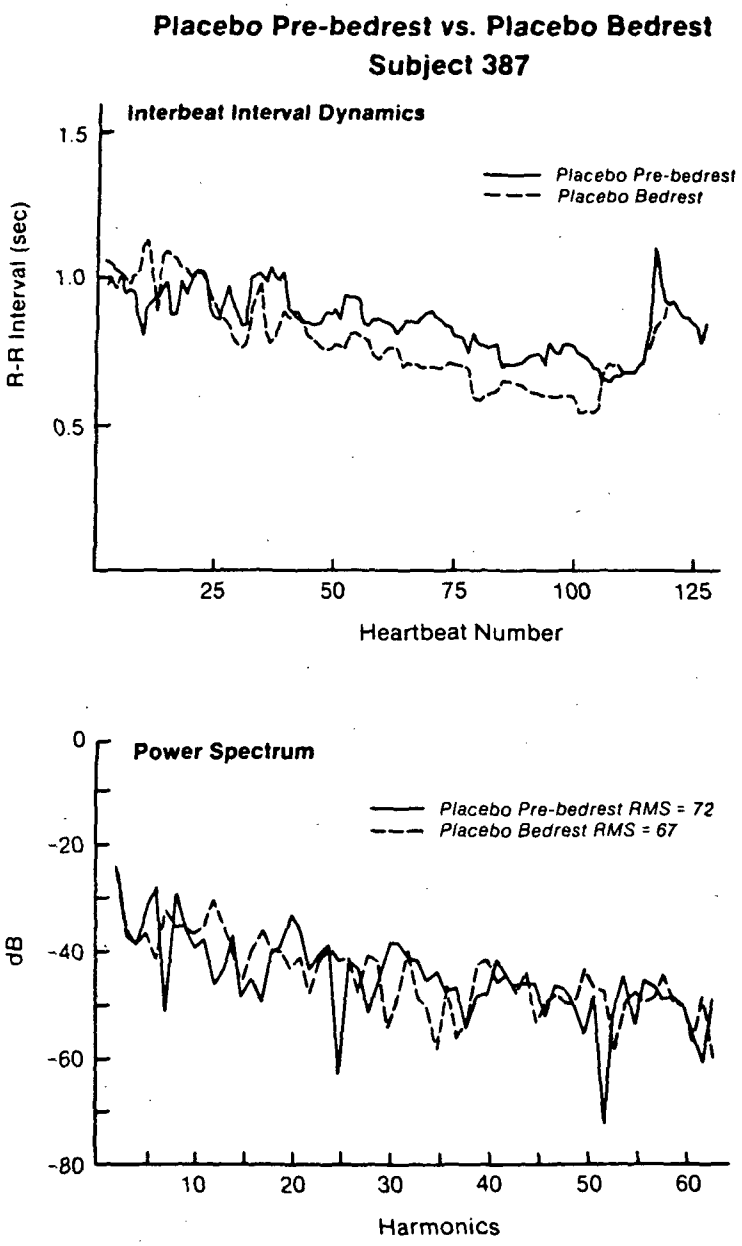

Placebo Pre-bedrest vs. Placebo Bedrest
Subject 387
Interbeat Interval Dynamics
Placebo Pre-bedrest
Placebo Bedrest
R-R Interval (sec)
1.5
1.0
0.5
25
50
75
100
125
Heartbeat Number
Power Spectrum
Placebo Pre-bedrest RMS = 72
Placebo Bedrest RMS = 67
dB
0
-20
-40
-60
-80
10
20
30
40
50
60
Harmonics

Figure 6

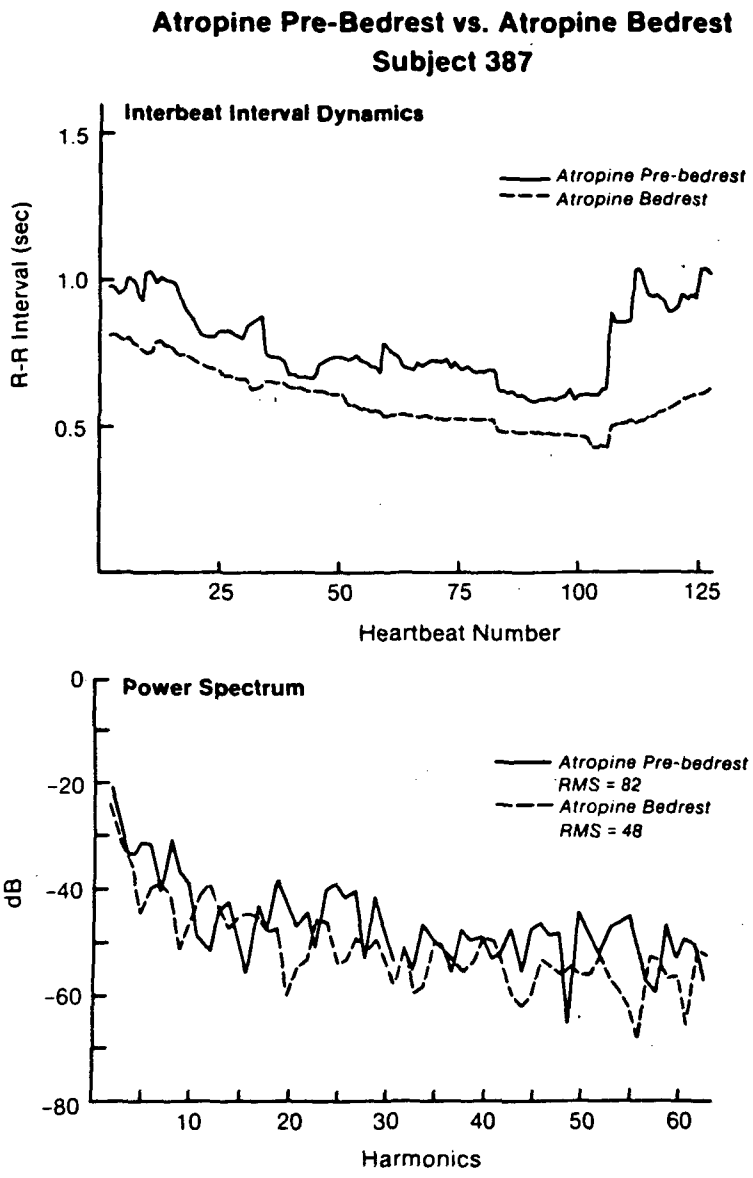
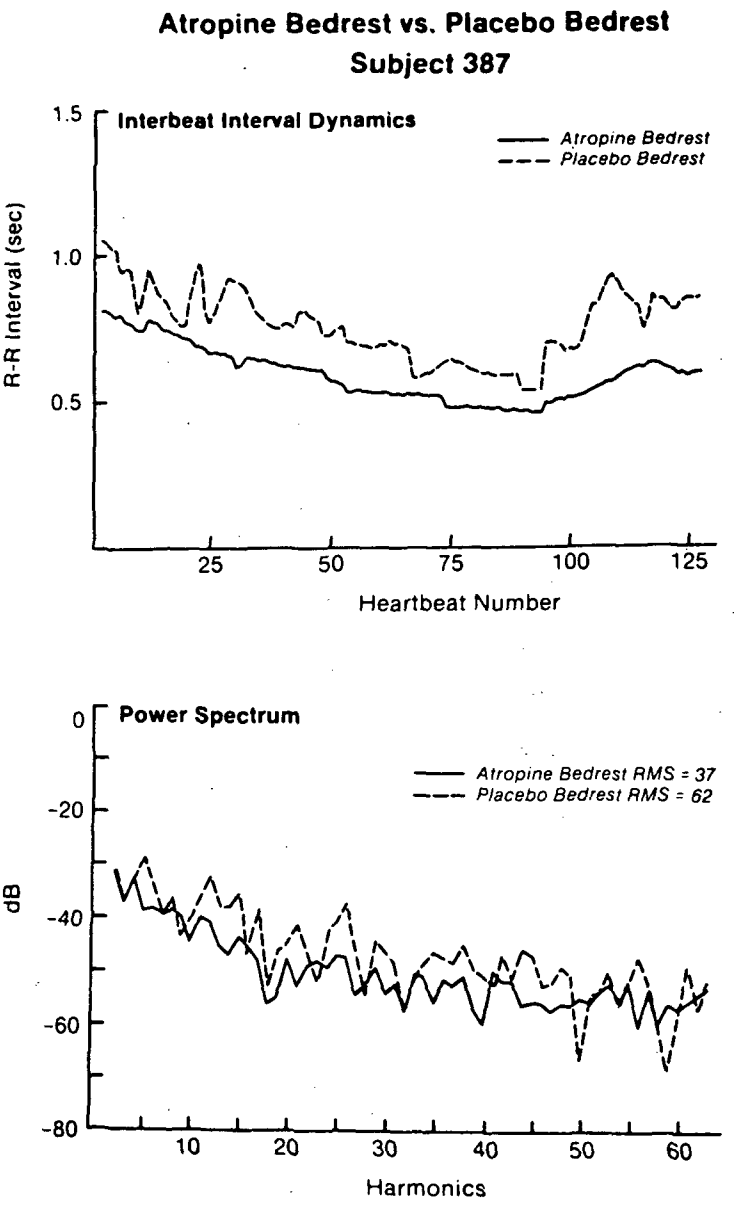

Atropine Pre-Bedrest vs. Atropine Bedrest
Subject 387
Interbeat Interval Dynamics
Atropine Pre-bedrest
Atropine Bedrest
R-R Interval (sec)
1.5
1.0
0.5
25
50
75
100
125
Heartbeat Number
Power Spectrum
Atropine Pre-bedrest
RMS = 82
Atropine Bedrest
RMS = 48
dB
0
-20
-40
-60
-80
10
20
30
40
50
60
Harmonics

Figure 7


Atropine Bedrest vs. Placebo Bedrest
Subject 387
Interbeat Interval Dynamics
Atropine Bedrest
Placebo Bedrest
R-R Interval (sec)
1.5
1.0
0.5
25
50
75
100
125
Heartbeat Number
Power Spectrum
Atropine Bedrest RMS = 37
Placebo Bedrest RMS = 62
dB
0
-20
-40
-60
-80
10
20
30
40
50
60
Harmonics