
Tuesday, June 10

56-52

072 240

Session TA1
Room 1
8:30 - 11:30 a.m.

**Mechanisms of Cardiopulmonary
Adaptation to Microgravity - 1**

INDICES OF BARORECEPTOR REFLEX SENSITIVITY: THE USE IN REHABILITATION MEDICINE AND SPACE CARDIOLOGY

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INTRODUCTION

Several tests of baroreceptor reflex sensitivity (BRS) were developed and described in the literature . Normal values of BRS decrease with age, are higher for rising pressures and range between 5 to 50 ms/mmHg or even higher. The goal of our first studies was to evaluate different spectral and statistical indices of BRS in normal volunteers of different age and to improve our own method for routine use in rehabilitation medicine and space cardiology.

METHODS

47 normal volunteers (f=25,m=22) were studied while they were lying supine and after prerest in a quiet room for 7min. and for 150 s during deep breathing with 6 breath per min. ECG signal and the finger arterial blood pressure (Finapres) were digitized at 200 Hz. The R-peaks of ECG and the systolic and diastolic pressure values were detected on a beat-to-beat basis. Power spectral analysis was performed by means of an FFT algorithm. BRS indices were calculated at supine rest as the quotient of the mean amplitudes in the HF band (0.5-0.15 Hz) of heart period duration and systolic blood pressure. During deep breathing the amplitudes in the MF bands (0.05-0.15 Hz) were used. In addition the scattergram between the heart period changes and systolic blood pressure changes was used. The BRS index was calculated as the slope of the linear regression line (BRSCC). The mean group values were then calculated for two different age groups (I:age 19-39 years,n=28 and II:age 40-64 years, n=19).

RESULTS

The spectral indices were higher than indices defined from crosscorrelation functions and showed more interindividual variability. We did not find significant differences between male and female subjects. Group differences were tested with an ANOVA Scheffe F-test ($P < 0.05$; #). The BRSCC defined during deep breathing showed the most stable and comparable to the literature results. The expected decrease with aging was shown for all indices.

Baroreceptor reflex sensitivity (BRS) in ms/mmHg ($M \pm SD$)

BRS (ms/mmHg)	I	II
deep breathing using fft	23 ± 16	11 ± 6 #
deep breathing using crosscorr.	15 ± 9	7 ± 4 #
supine using fft	28 ± 17	13 ± 6 #
supine using crosscorr.	14 ± 10	4 ± 2 #

CONCLUSION

BRS indices can be defined during deep breathing and at supine rest using the described methods and might be useful to followup patients during rehabilitation and cosmonauts in space flights.

+Gz AND +Gx TOLERANCE AT HEALTHY PERSONS OF NON-FLYING TRADES AT PRIMARY SELECTION ON THE CENTRIFUGE

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INTRODUCTION

Continued process of perfection of the existing and the development of new types of the space vehicles and orbital stations presents an opportunity for participation in the missions to persons of non-flying trades - competent experts of various areas of knowledge, who have senior age. The researches, carrying out on a human centrifuge in the system of selection of cosmonauts, permit not only to define their initial tolerance to acceleration, but also to reveal latent cardiovascular disorders, which did not expose by the other tests. The publications about the influence of age to G tolerance are non numerous and inconsistent. One authors marked the decreasing of the tolerance to +Gz stress at healthy persons after 40 years [Suvorov P.M., 1968], other - its increase [Hull D.H. et all, 1978] or an absence of sharp dependence [Shuljenko E.B. et all, 1981]. Also it is important to note, that almost all of these data were received at testing on a centrifuge of the pilots of high performance aircrafts.

METHODS

The object of research was experimental materials, accumulated during performing on the centrifuge of SRC of RF - IBMP of the expert tests of candidates to cosmonauts. All surveys, executed during 26 years, were conducted under the uniform circuit with presentation of identical modes of accelerations (+Gx stress - in a kind of "platforms" by levels of 4 and 6 g during 60 s and 8 g - 40 s with the speed of increase and reduction of acceleration 0.2 g/s and angle of seat's back to a vector of acceleration - 78°; +Gz stress - also in a kind of "platforms" by levels of 3, 4 and 5 g during 30 s each with the speed of increase and reduction of acceleration 0.2 g/s). During the whole period of investigation of G tolerance of candidates to cosmonauts an identical set of physiological parameters was measured, that permit to conduct the analysis and comparison of data.

The present work is partly supported by the Contract NAS15-10110.

RESULTS

Generously health persons of non-flying trades at primary testing on the centrifuge had good +Gz and +Gx tolerance in 80-100 % of cases.

An existence of age changes of +Gz tolerance up to 5 g was detected. The highest +Gz tolerance was at the persons in the age from 31 to 45 years, least - in groups of 21-25 and 46-50 years. Lowered +Gz-tolerance at the persons of young age was stipulated mainly by sharp fall of systolic pressure and amplitude of pulse oscillations in the vessels of ear lobe, occurrence of visual disturbances and loss of consciousness, i.e. by the symptoms, connected with insufficient blood circulation in the brain. At the persons of the senior age an extrasystolic arrhythmia became the main limiting factor. With an increase of age from 21-25 to 46-50 years less expressed sinus tachycardia at an effect of +Gz was observed. This difference was the most significant ($P < 0,05$) during +5Gz stress, when at the persons of young age (21-25 years) heart rate reached, on the average, 172 ± 4 beats/mines, and at the persons of the senior age group (45-50 years) - 148 ± 7 beats/mines.

No sharp dependence of changes of +Gz tolerance up to 8 g was found out.

CONCLUSION

1. The variability of age dynamics of +Gz tolerance up to 5 g during primary testing on the centrifuge at practically healthy persons of non-flying trades was established. The highest +Gz tolerance was found at the persons in the age of 31-45 years, the least one - in groups of 21-25 and 46-50 years.

2. Age features of physiological reactions of organism on +Gz acceleration were determined. For the young persons (21-25 years) - asthenic type of reaction of systolic blood pressure in the vessels of ear lobe, development of functional visual disturbances and loss of consciousness were characteristic, for the persons senior than 45 years - disturbances of heart rhythm and limitation of maximal level of heart rate, which indicate about a decrease of functional reserves of their cardio-vascular system.

3. Generously healthy persons of non-flying trades at primary selection on the centrifuge did not show age-depending changes of +Gx tolerance up to 8g.

4. During +Gx accelerations to the persons of the senior age groups, in comparison with young subjects, it was characteristic an increase of frequency of occurrence extrasystolic arrhythmia and less expressed sinus tachycardia.

EFFECT OF DRY IMMERSION ON CALF BLOOD SUPPLY DURING SUSTAINED CONTRACTION AND UPRIGHT EXERCISE IN MAN

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INTRODUCTION

One of the important consequences of gravitational unloading concerns muscular activity and its blood supply, especially during upright exercise. The mechanisms of muscle blood supply during sustained contractions or exercise (natural locomotion) differ considerably. During local contractions muscle blood flow is regulated mainly by local changes inducing hyperemia. During locomotion blood supply of a certain muscle group is a result of a conflict between this muscle group demand and resources of central haemodynamics providing all the contracting muscles with blood without dramatic drop of blood pressure. The situation becomes even more complicated because of the orthostatic effect. Adaptation to simulated microgravity and its cessation is accompanied by pronounced changes of local muscular, central haemodynamic and regulating factors influencing blood supply of active muscles. The aim of the present investigation is to clarify the effect of simulated gravitational unloading (dry immersion) on blood flow during activity of various types - supine sustained contractions provoking "pure" functional hyperemia and natural locomotion in man.

METHODS

12 healthy males aged 21-36 gave their written consent to participate in the experiment. 6 subjects participated in a 5-day immersion study. They performed 3 min sustained contraction of ankle extensors at a tension of 10, 20, and 30% of preimmersion maximal voluntary contraction (MVC) in supine position. Calf blood flow was determined at rest and during the whole recovery period after contraction by venous occlusion plethysmography. Blood pressure was determined every min of postcontraction hyperemia with a sphygmomanometer. To evaluate maximal calf blood flow the subjects performed repeated ankle extensions during the last min of 10 min arterial occlusion. 6 other subjects participated in a 7-day immersion study. They performed graded treadmill exercise before and after 7-day dry immersion. The arterial inflow to calf was investigated during abrupt cessation of treadmill walking / running in the phase of transferring the investigated leg by plethysmographic technique based on the haemodynamic effect of a muscle pump.

RESULTS

Postimmersion calf blood flow after 3 min sustained contraction was higher than preimmersion index, the degree of the effect being more pronounced with the load increasing from 10 to 30% MVC. Peak post- and preimmersion blood flow after 30% MVC contraction was 38.1 ± 1.5 vs. 32.3 ± 2.8 ml \cdot min⁻¹ \cdot 100 ml⁻¹ and integrated hyperemia was 84.8 ± 18.0 vs. 53.2 ± 9.9 ml \cdot 100 ml⁻¹. An increase of postcontraction hyperemia seems to be unrelated to changes of central haemodynamic parameters: postimmersion blood pressure at the end of sustained contraction was not higher than preimmersion. During control upright graded exercise transition from walking to jogging induced substantial increase of calf blood flow and it stayed constant with further increase of running speed. During postimmersion upright graded exercise the calf blood flow was lower than in control exercise. When the maximal running speed and heart rate of more than 185 b \cdot min⁻¹ were reached, postimmersion blood flow was significantly lower than preimmersion index. Maximal calf blood flow after immersion did not differ from control values in both series.

CONCLUSIONS

The dry immersion induces reverse changes in calf blood supply during various types of muscle activity: an increase of postcontraction hyperemia and a decrease of blood flow during upright graded exercise. The latter might be caused by central vasoconstrictive influences directed at maintaining "circulation homeostasis".

CARDIOVASCULAR AND VALSALVA RESPONSES DURING PARABOLIC FLIGHT

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INTRODUCTION

We investigated passive and Valsalva-related mean arterial pressure (MAP), heart rate, and stroke volume responses to acute microgravity and hypergravity in sixteen seated human test subjects. Gravitational changes were induced by flight aboard NASA's KC-135 aircraft, which produces 25-30 sec periods of microgravity (0.01G) alternating with 50-55 sec periods of hypergravity (up to 1.8G).

METHODS

Seated MAP, heart rate and stroke volume responses were measured continuously via finger photoplethysmography (heart-referenced Portapres), electrocardiography, and impedance cardiography, respectively, while aircraft acceleration was recorded simultaneously via accelerometer. Controlled Valsalva maneuvers (30 mm Hg strain for 15 sec) were performed during alternating microgravity and hypergravity periods, every fourth parabola, punctuating periods of passive parabolic flight.

RESULTS

During passive flight, MAP and heart rate declined from high initial levels in acute microgravity and rose from low initial levels in acute hypergravity. Directional changes in heart rate, however, were tempered toward the middle of each gravitational condition, suggesting activation of compensatory baroreflexes. In microgravity, rises in stroke volume occurred that were variably delayed in comparison to falls in MAP and heart rate. In hypergravity, falls in stroke volume occurred simultaneous with rises in MAP and heart rate. Seated MAP rises occurring during late phase II of the Valsalva maneuver were significantly attenuated in microgravity compared to seated late-phase II MAP rises in either hypergravity ($p < 0.01$) or normogravity ($p < 0.01$). Seated MAP rises occurring during phase IV in microgravity were likewise attenuated [versus phase IV MAP rises in hypergravity ($p < 0.05$), but not versus phase IV MAP rises in normogravity]. Seated *early* phase II Valsalva MAP falls (or troughs) were not significantly changed across any of the gravitational conditions, in contrast to the lower early-phase II falls/troughs seen after transitions from the supine to the seated position in normogravity ($p < 0.05$). Valsalva results, however (particularly changes in MAP responses in late phase II, phase III, and phase IV), were dependent to a large extent on the method of Valsalva analysis employed, stressing the differences that can be obtained when using diverse interpretive methodologies.

CONCLUSION

Overall results suggest that gravity-sensitive receptors such as the otolith organs potentially supplement arterial and cardiopulmonary baroreceptors in providing important autonomic feedback information to brainstem cardiovascular regulatory areas.

AN ANALYSIS OF THE CARDIOVASCULAR RESPONSES UNDER HYPER- AND HYPO-GRAVITY ENVIRONMENTS USING A MATHEMATICAL MODEL

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INTRODUCTION

Gravity affects cardiac filling pressure and intravascular fluid distribution significantly. Internal control mechanism responsible for such cardiovascular changes under hypo- and hyper-gravity have not yet been fully understood, although many biological and physiological measurements as to cardiovascular system have been conducted since the man's first exploration to space. One reason for this arises from the difficulty in continuous and simultaneous measurements of hemodynamics of many parts of the body. To overcome the difficulty, a mathematical model was constructed based on the animal and human physiological evidences in our previous study^[1]. In this study, the model is used for explaining hemodynamics during hyper- and hypo-gravity environments obtained by parabolic flight.

METHOD

Parabolic flight was conducted by a small rear-jet MU300. One university male student volunteered as a subject. Nine to eleven parabolic flights per day were performed for 6 days. The subject sat on a chair either in an upright position or a 45 degree reclining position.

Electrocardiogram and finger blood pressure were measured continuously during the flights. Variable parameters of the model were adjusted so that heart rate and blood pressure of the model fit to those of the experiment.

RESULTS AND CONCLUSION

It was shown that the model can reproduce and predict quantitatively experimental heart rate and blood pressure as well as during a parabolic flight. Analysis of internal property of the model revealed hemodynamics of human cardiovascular system during a parabolic flight which explain the mechanism of cardiovascular responses under hyper- and hypo-gravitational environments.

REFERENCES

[1] Nakatomi, T., Hirata, Y., Usui, S. and Nagaoka, S. : " Electric Circuit Model of Cardiovascular System with Gravity Term and Analysis of Cardiovascular Responses during Hyper- and Hypo-gravity Environments(Japanese)", *IEICE*, in press.

EFFECT OF VERY GRADUAL ONSET RATE +Gz EXPOSURES ON THE CARDIOVASCULAR SYSTEM

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INTRODUCTION

The usage of short-arm centrifuge (SAC) could be one of the best means to prevent physiological deconditioning due to microgravity exposure in space or during the weightlessness simulations. However it is difficult to establish how high level, how long and how often we should apply artificial gravity. We reported several studies earlier using our 1.8 meter radius SAC that could fit inside the International Space Station. We designed this study because there are only few reports about the effect of very gradual onset rate of +Gz exposure on the cardiovascular system.

METHODS

Ten healthy male volunteers 20-26 years of age participated. We increased our SAC speed linearly from +1Gz up to +2.7Gz for each subject with four different onset times; 30 min, 15 min, 7.5 min, and 3.75 min. Their onset rates were varied but all were below 0.5g/min. During the +1Gz control condition in the cabin of SAC immediately prior to an exposure, and also during the +Gz exposure, ECG, heart rate (HR) and respiratory rate were monitored continuously, and systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured every one minute using an arm cuff. Also, RR interval was continuously measured with a real-time RR analyzer. Standard deviation (SD), low frequency band [0.04-0.15 Hz] power spectrum (LFP) and high frequency band [0.15-0.40 Hz] power spectrum (HFP) were calculated by fast Fourier transform (FFT) for control data. For the data with +Gz exposures, dynamic FFT was done, shifting beat series every half second.

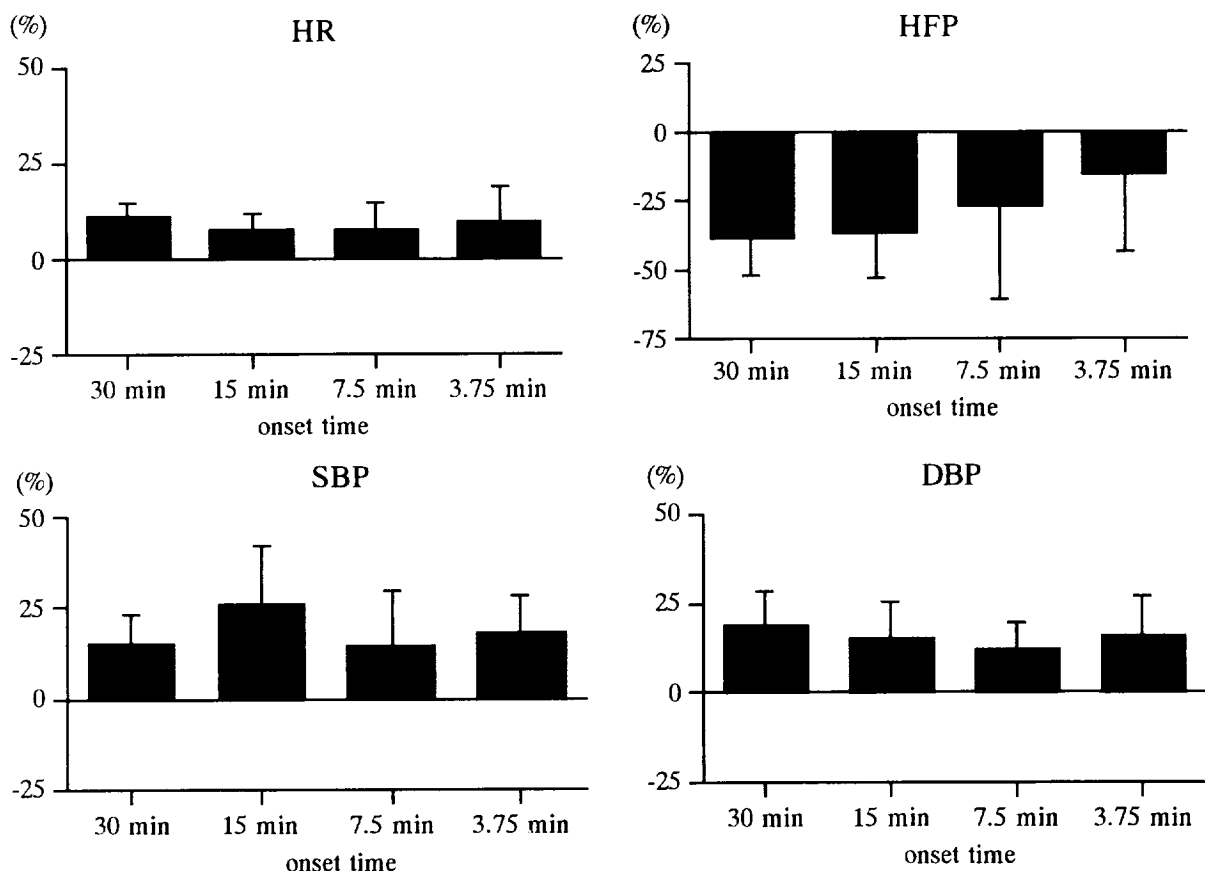


Fig.1. Mean % changes (\pm SD) at the +2.7Gz exposure.

RESULTS

All the subjects completed +Gz exposures without any complaints. No significant differences existed in the controls with various each onset times. Data at the +2.7Gz were normalized by the control. Mean % changes of HR, HFP, SBP, and DBP at the +2.7Gz exposure were significantly different from the controls (Fig.1). However, no significant differences were found with the +2.7Gz exposure between the different onset times (Fig.1). Dynamic FFT analysis of RR interval variability showed gradual changes of calculated parameters. SD and HFP of onset times of 15 min, 7.5 min, and 3.75 min. showed almost similar pattern of decline along the increase of +Gz (Fig.2). It seemed that the declines of vagal activities by +Gz stresses in this study were similar.

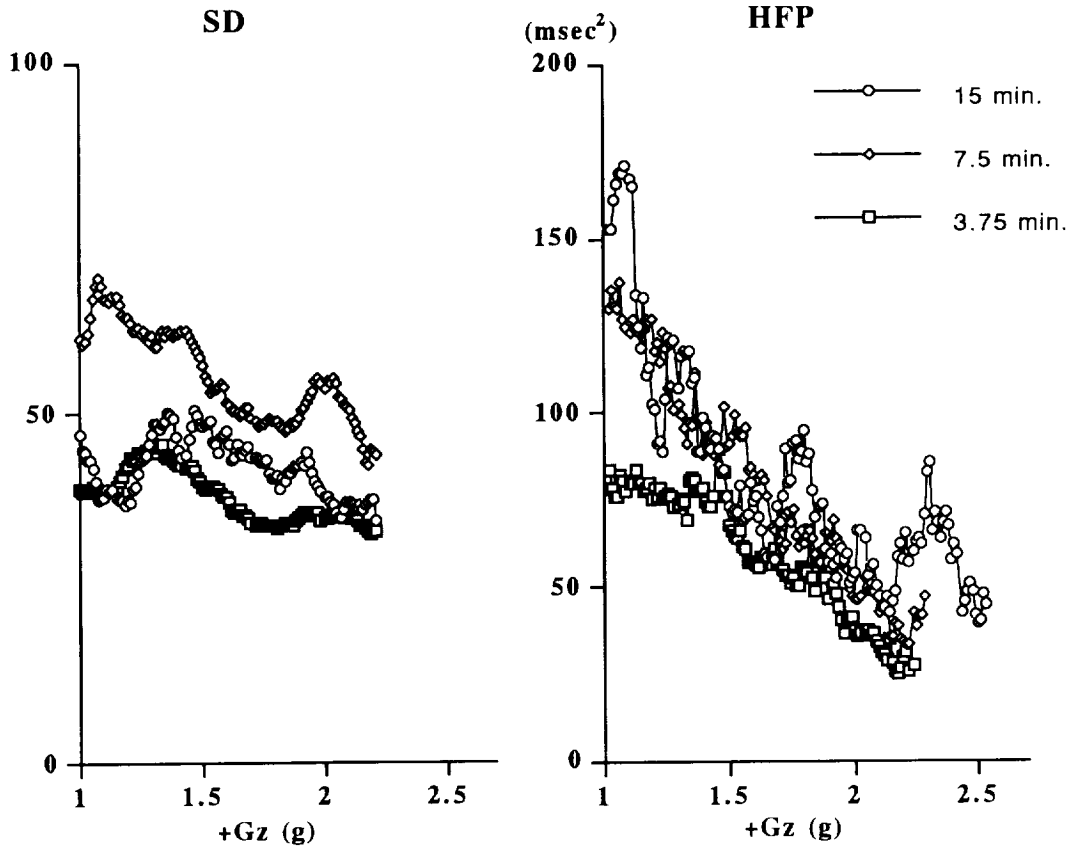


Fig.2. Changes of mean parameters along the +Gz changes. Datum at the point of every Gz was obtained by the spectral analysis of RR interval variability, from the time of the Gz level change for additional 64 seconds.

CONCLUSION

There were no significant differences among the effects of different onset rates, below 0.5g/min, on the cardiovascular system. Accordingly, we have chosen the onset rate of 0.4g/min to search optimal G-load profile avoiding the cardiovascular deconditioning during the weightlessness simulations.

Table I

Series	acceleration		G level	Exposure time	Capsule	head mounted devices	n	completed	%	
	protocol	period								
A	I	1° /sec ²	133s	1.4	60m	fixed	head mounted CCD	9	5	56
	II		159s	1.7				6	2	33
	III		176s	2				2	1	50
B	I	1° /sec ²	133s	1.4	60m	fixed	nothing	4	4	100
	II		159s	1.7				5	4	80
	III		176s	2				6	4	67
C	I	1° /sec ²	133s	1.4	30m	fixed	ventilation-mask	3	3	100
	II		159s	1.7				3	3	100
D	I	0.1° /sec ²	32m	2.2	20m	fixed	nothing	10	3	30
E	I	0.373G/min	3.75m	2.4	0m	freely movable	nothing	10	10	100
	II	0.187G/min	7.5m	2.4				10	10	100
	III	0.093G/min	15m	2.4				10	10	100
	IV	0.047G/min	30m	2.4				10	10	100
F	I	0.4G/min	2.5m	2	60m	freely movable	nothing	63	41	65

Table II

Series	n	incompleted	%	cardiovascular			vestibular	
				hypotension and tachycardia	hypotension and bradycardia	arrhythmia	nausea or vertigo	
A	I	9	4	44	1	0	0	3
	II	6	4	67	1	1	0	2
	III	2	1	50	0	0	0	1
	total	17	9	53	2	1	0	6
B	I	4	0	0	0	0	0	0
	II	5	1	20	0	1	0	0
	III	6	2	33	1	0	0	1
	total	15	3	20	1	1	0	1
D	I	10	7	70	2	1	2	2
F	I	63	22	35	3	4	1	14

NASA SPECIALIZED CENTER OF RESEARCH AND TRAINING (NSCORT) IN INTEGRATED PHYSIOLOGY: MECHANISMS OF PHYSIOLOGICAL ADAPTATIONS TO MICROGRAVITY.

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NASA's Life Sciences Division has developed a major program that supports a series of centers for research and training in areas relevant to the agency's mission. A center for integrated physiology, specifically for the study of the mechanisms of physiological adaptation to microgravity, was opened at University of Texas Southwestern Medical School in June, 1993.

The principal research areas of interest are (a) cellular and molecular mechanisms mediating responses to microgravity, (b) mineral metabolism, (c) skeletal muscle structure and function, and, (d) cardiovascular regulation. Members of the cardiovascular section are also active participants in a separately funded series of space flight experiments (Spacelab and Mir) on human adaptation to microgravity.

Dr. George N. DeMartino and his co-workers are studying the cellular mechanisms of intracellular protein degradation and have documented an important role of the proteasome and its specific regulatory proteins in skeletal muscle. Dr. Randall W. Moreadith and his group postulated that the proto-oncogens *Ski* and *Sno* are involved in the control of muscle development but the results were inconsistent with this hypothesis. Present objectives includes a study of the regulation and function of VIaH, a muscle-specific subunit of cytochrome oxidase. Dr. Nina B. Radford is the current unit director. The unit on mineral metabolism is directed by Dr. Charles Y. Pak. The work of this group has been focussed on the mechanisms that mediate immobilization-induced hypercalcuria and bone loss, and on countermeasures, including the use of biphosphonates that have been shown to be effective during bed rest of relatively short duration. The NSCORT section on skeletal muscle and function includes three projects. Dr. Ronald G. Haller and his colleagues use inborn human oxidative defects as models to provide new insights into mechanisms of deconditioning and adaptation. Dr. Loren A. Bertocci and his co-investigators have applied magnetic resonance spectroscopy to provide new data on substrate regulation in skeletal muscle during exercise and the long-term effects of training and disuse. Dr. James L. Fleckenstein is using magnetic resonance imaging to examine fiber type distribution and water shifts in skeletal muscle. The cardiovascular unit, including Drs. Benjamin D. Levine, James A. Pawelczyk, Craig G. Crandall, and Peter B. Raven have conducted extensive studies on human regulatory mechanisms. The team has convincingly shown that prolonged bed rest causes decreased compliance of both the heart and the peripheral vasculature and also has multiple effects on regulation, including impaired cerebral autoregulation.

Training and educational activities have covered a wide range and included summer research programs for high school and undergraduate students. The NSCORT has provided strong support for the development of a new graduate school Ph.D. program in integrative biology within the Division of Cell and Molecular Biology in Southwestern Graduate School of Biomedical Sciences. Members of the NSCORT also had a major role in organizing and conducting in 1995 an International Workshop on Cardiovascular Research in Space, sponsored by NASA and the International Space Life Sciences Strategic Planning Working Group.