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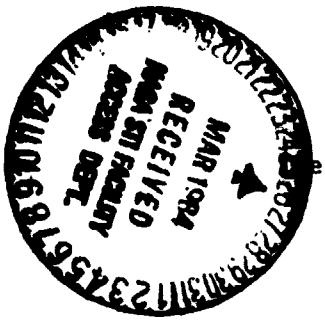
FINAL REPORT

NSG - 2225

A Research Grant From NASA



to

e University of Virginia

for the period

April 1977 to July 1983

titled

Rat body size, composition and growth at hypo- and hypergravity

by

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INTRODUCTION

At the time of the initiation of this grant (1977) the Division of Life Sciences of NASA was deeply concerned with testing the possibility that hypokinesia might be a useful simulation of weightlessness in the rat. Consequently the original title of this grant was "Mammalian body size, composition and growth as influenced by hypokinesia" and approximately the first year was devoted to an evaluation of the influence on body composition of cage restraint as a form of hypokinesia. Some of the results of these early efforts are included in Publication No. 11. We soon realized that hypokinesia was a poor simulator of weightlessness in its effects on rat body composition. With the approval of our NASA monitor and funding officials we returned to the other respect of our proposal, the effects of hypergravity (centrifugation) on body composition.

In 1979 we were given an opportunity to study the effects on rat body composition of weightlessness on a Soviet Cosmos mission. This study was funded primarily by Contract NAS2 - 10195 but much of the processing of data and write-up was supported by the present research grant. The present title of the grant reflects both the hypogravitational and hypergravitational aspects of the total research effort.

ACHIEVEMENTS

Note on cost effectiveness: Many federal programs are evaluated as yield per dollar invested. This principal is not directly applicable to scientific research since while the quantitative yield (number of papers, or journal pages) is readily apparent, the quality of the yield usually becomes apparent

only in retrospect at a later date. However, the present grant is an extreme case. The four years of funding (1977 to 1981 with no-cost extensions to 1983) totaled $101,000 and each year 35% was deducted as overhead. This left $16,412 for each of the four grant years available to the investigator. While this level of funding is appropriate for library research, by careful husbandry and "scrounging" we were able to do laboratory research involving certrifugation at a distant site. Dollar efficiency is rarely an important consideration in scientific research, but certainly in this case NASA received a bargain.

Publications:

1. Pitts, Grover C. Physiological regulation of body energy storage. Metabolism 27:469-478, 1978. This is a "spin-off" paper in basic science, only indirectly related to gravitational physiology. It presents evidence that while the energy storage in adipose tissue appears to be regulated, the regulatory mechanism provides scope for wide variations in the midrange.

2. Pitts, G.C. and J. Oyama. Rat growth during chronic centrifugation. Life Sci. Space Res. 17:225-229, 1979. This study revealed that rats chronically centrifuged at 4.2g starting at the age of weaning followed a lower growth curve and achieved a smaller mature mass than controls at terrestrial gravity. Most body components contributed proportionately to this difference in total mass. All changes in the centrifuged group returned to control levels during 57 days of retirement to terrestrial gravity.

3. Donald, Patillo, Grover C. Pitts and Stephen L. Pohl. Body weight and composition in laboratory rats: effects of diets with high or low protein concentrations. Science 211:185-186, 1981. This is another spin-off paper in basic science only indirectly related to gravitational physiology. Rats on

high levels of dietary protein deposited more body fat than those on lower levels.

4. Pace, Nello, D.F. Rahlmann, A.H. Smith and Grover C. Pitts. Effects of the Cosmos 1129 Soviet paste diet on body composition in the growing rat. Environmental Physiology Laboratory, University of Caifornia, Berkeley. Report EPL 81-1. In a study of the effects on rat growth of the Soviet paste diet Grindeland, Yang, Madsen and Keil of Ames Research Center reported that the diet did not support optimal growth and suggested the desirability of body composition studies. The present authors volunteered to do such studies and make the results available to all of the American investigators planning rat studies on Cosmos 1129. This report is the result of that study. We found that the group on the Soviet diet was 10% lower in total body mass, 13% higher in resting metabolic rate, 50% higher in body fat and 16% lower in fat-free body mass. It was difficult to establish the dietary factors responsible but some possibilities were discussed.

5. Pitts, G.C. and J. Oyama. Response of rat body composition to simultaneous exercise and centrifugation at 3.14g. Pflugers Archiv - European Journal of Physiology 391 Supplement:R66, 1981. This is a separately printed abstract of the paper which follows.

6. Pitts, G.C. and J. Oyama. Response of rat body composition to simultaneous exercise and centrifugation at 3.14g. The Physiologist. 24 Supplement:S95-S96, 1981. Muscles contracting against increased loads may show increases in mass (hypertrophy). Nevertheless, rats subjected to such load increases by centrifugation show a decrease in muscle mass. Since rats may protect themselves against exposure to such increased loads by lying down most of the time, we decided to look for the load effect in animals volitionally running in a runniing wheel while centrifuged. Controls were

severely restrained by small cages during centrifugation. The two groups were statistically identical. If the load effect were present but concealed by opposing factors, our statistical treatment should have revealed it. Probably there is no load factor operating in the centrifuged rat.

7. Pace, Nello, Grover C. Pitts, Arthur H. Smith, D.F. Rahlmann, Arkadyi S. Ushakov and Tamara A. Smirnova. Body composition data from the rat subjects of Cosmos 1129 Experiment K-316. Environmental Physiology Laboratory, University of California, Berkeley. Report EPL 82-1, 1982. In this report full results of the body composition analyses on rats used in Cosmos 1129, Experiment K-316 are presented in complete detail which is not permitted in the physiological press.

8. Pitts, Grover C. Effects of chronic acceleration on body composition. The Physiologist, 25 Supplement:S13-S16, 1982. This is an invited paper for the Symposium on Gravitational Physiology at the Fourth Annual Meeting of the IUPS Commission on Gravitational Physiology. It is a short review of my contributions to the effects on rat body composition of centrifugation and weightlessness.

9. Pitts, G.C., A.S. Ushakov, N. Pace, A.H. Smith, D.F. Rahlmann, and T.A. Smirnova. Effects of weightlessness on body composition in the rat. Am. J. Physiol. 244 (Regulatory Integrative Comp. Physiol. 13):R332-R337, 1983. This is the definitive report for the physiological community of our results on body composition of rats exposed to 18.5 days of weightlessness on Cosmos 1129. The results included 1) a reduced fraction of total body water, 2) a net shift of body water from skin to viscera, 3) a marked diminution in fraction of extracellular water in the fat-free body, 4) a marked reduction in fraction of bone mineral, 5) no change in the quantity of stored fat or adrenal masses, and 6) a net increase in total muscle mass.

10. Pitts, Grover C. Distribution of fluids in the body of the centrifuged rat. The Physiologist. In press. This is to be presented at the Fifth Annual Meeting of the IUPS Commission on Gravitational Physiology, Moscow, USSR. It demonstrates that centrifugation throughout the period of rapid growth causes some changes in the masses of fluids and solids in the rat. However, all such changes are reversible upon retiring from the centrifuge to terrestrial gravity.

11. Pitts, Grover C. Body composition in the rat: interactions of exercise, age and sex. Am. J. Physiol. Submitted for publication. This is a contribution to basic science indirectly related to gravitational physiology. It is demonstrated that an exercise regimen initiated at 7 weeks of age or younger results in a change in the fat-free body mass in either sex. But the fat-free body mass increases in females and decreases in males. Exercise initiated at 11 weeks of age or older has no effect on the fat-free body mass.

12. Pitts, Grover C. Muscle and bone masses as a function of body size in the rat. Manuscript in preparation. With increasing body size muscle mass changes much more rapidly than does skeleton mass.

13. Pitts, Grover C. A theory of the regulation of catch-up growth. Manuscript in preparation. Some rather complex mechanisms for the control of catch-up growth have been proposed. This manuscript will propose a much simpler mechanism based on whether or not the perturbing mechanism causes loss of cells.

Significant contributions:

1. In the rat eating a balanced diet ad libitum it is very difficult to perturb the fat-free body mass. Indeed centrifugation is the only factor we have found which will do so in the adult. However, all of these body composition effects of centrifugation are reversible upon retirement to

terrestrial gravity, even in rats which have been centrifuged for approximately one year starting at weaning (Publ. 2, 8, 10 and earlier publications).

2. Contrary to expectations total mass of skeletal muscle in the rat is reduced as a consequence of chronic acceleration (2, 8 and earlier publications).

3. Contrary to expectations total mass of skeletal muscle in the rat appears to be increased as a result of weightlessness. The evidence is good but this needs to be corroborated. (7, 8 and 9).

4. It is generally acknowledged that overload (as in centrifugation) will cause skeletal muscles to increase in mass (hypertrophy). Contribution number 2 shows that we observed the reverse. Our efforts to show that the hypertrophic response to overload was actually present but concealed by opposing influences were to no avail. Apparently centrifugation does not result in an overload response. (6).

5. While masses of many body components change as a result of centrifugation during growth, the only change associated with centrifugation per se is the gain in mass of fat-free skin (2, 8 and 10).

6. The effects of gravity on mammals are a function of body size and a priori there was reason to believe that rats were too small to respond to the - 1g in weightlessness. We showed that rats did respond to weightlessness. The changes seen included: a reduction in total body water, shifts in fluid compartments, a reduction in bone mineral and an increase in total skeletal musculature (7 and 9).

7. Our analysis of the changes in body fat content in mammals suggests that the regulation of body fat content is such as to protect the body from very low and very high values but allows considerable variation throughout the

midrange (Publication 1).

8. Rats on diets containing high levels of protein deposit more fat than those on isocaloric diets containing low levels of protein. This is contrary to generally accepted nutritional beliefs. (Publication 3).

9. Mass of the fat-free body compartment in the rat may be altered by exercise and diet in animals 7 weeks of age and younger. At 11 weeks of age and older the regulatory mechanism protecting the fat-free body mass against perturbation has apparently matured and fat-free body mass remains constant in the face of such perturbations. (Publication 11).

10. There is a striking sex difference in the response of young rats (7 weeks of age and younger) to a daily exercise regimen. In exercising males the fat-free body compartment grows more slowly than in unexercised controls and in females, more rapidly. In both sexes exercise decreases body fatness. (Publication 11).

APPENDIX

Reprints of publications 1 through 9 attached hereto.