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Effects of simulated increased gravity on the rate of aging of rats: implications for the rate of living theory of aging *

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Summary

Ever since Pearl proposed the rate of living theory of aging numerous studies have demonstrated its validity in poikilotherms. In mammals, however, satisfactory experimental demonstration is still lacking because an externally imposed increase of basal metabolic rate of these animals (e.g. by placement in the cold) is usually accompanied by general homeostatic disturbance and stress. The present study was based on the finding that rats exposed to slightly increased gravity are able to adapt with little chronic stress but at a higher level of basal metabolic expenditure (increased 'rate of living'). The rate of aging of 17-mth-old rats that had been exposed to 3.14 times normal gravity in an animal centrifuge for 8 mth was larger than of controls as shown by apparently elevated lipofuscin content in heart and kidney, reduced numbers and increased size of mitochrondria of heart tissue, and inferior liver mitochondria respiration (reduced 'efficiency': 20% larger ADP: 0 ratio, $P < 0.01$; reduced 'speed': 8% lower respiratory control ratio, $P < 0.05$). On the other hand, steady-state food intake per day per kg body weight, which is presumably proportional to 'rate of living' or specific basal metabolic expenditure, was about 18% higher than in controls ($P < 0.01$) after an initial 2-mth adaptation period. Finally, though half of the centrifuged animals lived only a little shorter than controls (average about 343 vs. 364 days on the centrifuge, difference statistically nonsignificant), the remaining half (longest survivors) lived on the centrifuge an average of 520 days (range 483–572) compared to an average of 574 days (range 502–615) for controls, computed from onset of centrifugation, or 11% shorter ($P < 0.01$). Therefore, these results show that a moderate increase of the level of basal metabolism of young adult rats adapted to hypergravity compared to controls in normal gravity is accompanied by a roughly similar increase in the rate of organ aging and reduction of survival, in agreement with Pearl's rate of living theory of aging, previously experimentally demonstrated only in poikilotherms.

rate of living theory of aging; rate of aging; maximum life span potential; mammals (rats); hypergravity; liver mitochondria respiration

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Introduction

The purpose of the present investigation was to test the hypothesis that the rate of aging of young-adult rats exposed to increased gravity in an animal centrifuge may be greater than that of controls. This hypothesis was based on: (a) the finding of an increased oxygen consumption rate in centrifuged rats (Oyama and Chan, 1973; Daligon and Oyama, 1975); and (b) the 'rate of living' hypothesis which states that a chronically increased level of metabolism of an organism results in an increased rate of aging and reduced life span (Pearl, 1928).

The rate of living hypothesis has been repeatedly confirmed in poikilotherms such as insects (e.g. Miquel et al., 1976) which possess only nondividing somatic cells and lack the functional organ plasticity and sophisticated control systems at the organ level found in mammals. The validity of the hypothesis has not as yet been established directly in mammals (Economos, 1981). An attempt to test the hypothesis in rats (Johnson et al., 1963) by continuous exposure to moderate cold (in order to increase metabolic energy expenditure) has been criticized because of the many homeostatic disturbances caused by such exposure (Shock, 1974).

It is probably not possible to achieve a 'speeding up of the metabolic clock' in mammals without simultaneously triggering a complex of homeostatic responses usually associated with exposure to stressful environments. Nevertheless, the intensity of such responses upon exposure of small quadrupedic animals to slightly increased gravity appears to be relatively low (for instance hormone levels are normal after 1 wk at 4.1 *g*, Oyama, 1978) and the animals are able to adapt despite a significant increase of metabolic rate, thus making the animal centrifuge a rather unique tool for testing the rate of living theory of aging (Economos et al., 1978).

In this study, the rate of aging of rats exposed to 3.14 times normal gravity in an animal centrifuge was compared with that of rats maintained in the centrifuge room at normal gravity. The rate of aging was estimated by quantitative investigation of changes at various levels of biological organization, i.e. alterations in morphology, cellular fine structure and mitochondrial respiration in vitro in selected organs. In addition survival in the centrifuge was monitored to determine the effect of hypergravity (and accompanying increased metabolic rate) on life span.

Materials and methods

The experimental animals were 60 Sprague–Dawley male rats purchased from Simonsen Laboratories (Gilroy, CA) at 2 mth of age, kept until the start of centrifugation in the Ames animal colony under control conditions of temperature (approx. 23°C) and a 12 h light/12 h dark schedule. Water and standard pelleted food were supplied ad libitum. At age 9 mth, 36 apparently healthy rats were selected from the group of 60 animals in the range of body weights 500–620 g and divided at random into a control group and a centrifuged group such that both groups contained rats of uniformly distributed body weights (see Economos and Miquel, 1980, for a rationale). The 18 rats of each group were placed in large cages,

3 rats per cage. (The relatively small size of the two groups was dictated by space limitations in the centrifuge.) The rats were weighed twice every week for 3 wk, once a week for the subsequent 8 wk, every 6–7 wk for the following 8 mth and at about 3-mth intervals thereafter. The food intake of the rats, per cage, was monitored at the same time as the body weights, by measuring the amount of food consumed over the preceding 1/2 or 1 wk.

After 8 mth of centrifugation (for description of housing and technique see e.g. Oyama and Platt, 1965) 16 of the centrifuged rats and all 18 controls were still alive; (two centrifuged rats died – not from accidental causes – after 11 and 171 days of centrifugation, respectively). Of these animals (which were now 17 mth old), 4 controls and 4 centrifuged (the original smallest ones of each group for reasons of size uniformity and convenience in perfusion) were used for an electron microscope investigation of mitochondrial alterations in heart tissue resulting from chronic centrifugation and normal aging. These rats were killed by perfusion with a solution consisting of 1% paraformaldehyde and 1.5% glutaraldehyde in 0.1 M sodium phosphate buffer (pH 7.1–7.3). Tissue blocks from the left ventriculum were removed, rinsed briefly in buffer and placed in vials containing 1.5% osmium tetroxide in the same buffer. (Details of the tissue processing technique for electron microscopic observation have been described elsewhere, Johnson and Miquel, 1974.)

The respiratory control of ADP/O ratios of centrifuged and control rat liver mitochondria were determined with a YSI model 53 oxygen monitor (Yellow Springs Instrument Co. Inc.), according to the method of Estabrook (1967) in four additional control and four experimental animals (the original largest ones of each group). The rats were killed individually by decapitation at the same time on consecutive days. The livers were removed immediately, weighed, and placed in chilled isolation medium containing 0.25 M sucrose, 5.0 mM Tris base and 1.0 mM EDTA adjusted to a pH of 7.4 with HCl. Mitochondrial isolation was accomplished by the method of Johnson and Lardy (1967). The livers were minced with scissors, washed repeatedly, and homogenized with a small amount of isolation medium in a chilled Potter Elvehjeim homogenizer tube. The homogenate volume was adjusted to approximately 50 ml, divided among 4 lusteriod centrifuge tubes, and centrifuged at $600 \times g$ for 10 min at 0–4°C in a refrigerated centrifuge. The supernatant was decanted into clean centrifuge tubes, the pellet resuspended in fresh isolation medium and centrifuged again at $600 \times g$ for 10 min. The second supernatant fraction was added to the first and the pellet discarded. The combined supernatants were recentrifuged at $1200 \times g$ for 5 min; the resulting supernatant was discarded, the pellet was resuspended in 2 ml chilled isolation medium and stored on ice.

To prepare for the assay, the temperature of the water in the circulating bath of the oxygen probe assembly was raised to 30°C. In the reaction vial, 2.3 ml of reaction medium containing 10 mM KH_2PO_4, 100 mM KCl, 1 mM EDTA, 20 mM Tris base and 100 mM sucrose (pH 7.4) was added to 0.5 ml of 30 mM succinate (disodium salt), seated in the circulating water bath and allowed to equilibrate with atmospheric oxygen for 20 min while being agitated with a magnetic stir bar. The probe was then inserted, a steady base line established with a Varian model A-25 strip chart recorder, and 0.1 ml of the mitochondrial suspension was injected to

initiate the assay. When a constant slope was observed on the chart, 400 nM ADP (0.05 ml) was added to the reaction vial and the oxygen consumption was monitored continuously until the supply was exhausted. Assays were also performed adding ADP to the reaction prior to the addition of the mitochondria; each variation of the assay was repeated twice. For every rat, the same time schedule was followed from mitochondrial isolation to the final oxygen consumption experiment.

The protein concentration of the mitochondrial suspension was determined colorimetrically using biuret reagent and a Bausch and Lomb Spec 70 spectrophotometer set at a wavelength of 540 μm to register differences in optical density (Packer, 1967). The optical density of the mitochondrial suspension was compared to that of known concentrations of bovine serum albumin, prepared and measured at the same time.

The sucrose, KH_2PO_4, and KCl used in this procedure were AR grade purchased from Mallinckrodt. ADP was A grade supplied by Calbiochem; Tris base was practical grade from Matheson, Coleman and Bell; the disodium salt of succinate was 95% pure, obtained from the Eastman Kodak Company. Glassware used in these experiments was acid washed and rinsed 5 times with 3D deionized water. ADP was freshly prepared daily.

The heart, testes, kidneys and adrenals of the four experimental and four control animals used in the investigation of liver mitochondria were removed quickly and frozen for a later spectrofluorimetric measurement of lipofuscin content. Chemicals used were Chloroform and methanol of spectral quality (Matheson, Coleman and

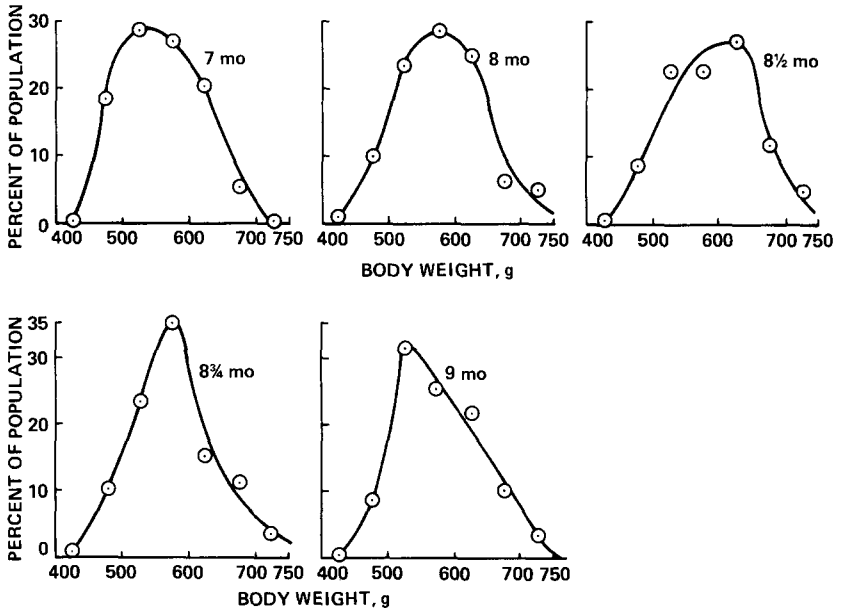

Fig. 1. Frequency distribution of body weights of a group of 60 rats from which the experimental and control groups were formed.

Bell, Norwood, Ohio) and quinine sulfate (Sigma Chemical Co., St. Louis, MO). The extraction procedure and determination of fluorescence were as follows. The organs were sectioned into approximately 0.2 g samples, except for the adrenals which were used in their entirety and weighed to the nearest milligram (wet weight). Chloroform : methanol, 2 : 1 (v : v) was added to the 0.2 g samples in a ratio of 20 : 1 (v : w). Tissues were homogenized for 2 min in a Brinkman Polytron tissue homogenizer Model PT 20 at 8000 rpm. Five ml of distilled water were then added to each sample and vortexed for several minutes. The samples were transferred to 15 ml conical centrifuge tubes and centrifuged at $2000 \times g$. The samples were rewashed with 5 ml of distilled water and centrifuged at $2000 \times g$. The water layer was removed and fluorescence determined in the chloroform : methanol layer in an Aminco Bowman Spectrophotofluorometer. Excitation and emission maxima were found to be 375 nm and 480 nm, respectively, for these extracts. Quinine sulfate in a concentration of 0.1 μg/ml in 0.1 N H_2SO_4 was used as a standard. Fluorescence units were determined by multiplying the meter multiplier setting by % fluorescence per gram tissue per ml chloroform methanol.

The remaining eight experimental and ten control animals were maintained as during the first months of centrifugation for determination of life span. They were inspected periodically for presence of lesions and dates of death were recorded.

Results and Discussion

Physiological data

Figure 1 shows the frequency distribution of body weights of the original group of 60 rats at various ages, 7–9 mth. From this group, 36 rats with stable, slowly increasing weights were selected at 9 mth of age and divided equally into experimental and control groups, such that both groups contained individuals of uniformly distributed body weights; thus each of the two groups had 6 animals with weights in the ranges 501–540, 541–580 and 581–620 g.

Body weight and food intake were monitored periodically. The data are summarized in Table I and represented diagrammatically in Figs. 2–4 (for the first 7 mth of centrifugation). In agreement with previous studies (Oyama and Platt, 1965, 1966), there was a sharp decline of body weight during the first week of centrifugation (Fig. 2), apparently from a similar reduction in food intake (Fig. 3). Thereafter, the roughly linear slow increase of body weight of the control rats was paralleled by a similar pattern in the body weight curve of the centrifuged animals. The food intake of the centrifuged animals (expressed per day per rat) increased steadily (Fig. 3) to reach the level of the control animals at about 4 mth of centrifugation. However, the daily food intake of centrifuged rats per kg body weight (BW) exceeded that of controls (Fig. 4) beginning $2\frac{1}{2}$ mth after centrifugation. The average value for centrifuged animals from $2\frac{1}{2}$ to 7 mth of centrifugation was 48.5 compared to 41.1 for controls, an 18% difference ($P < 0.01$, four measurements each group, Student's t-test).

TABLE I

Body weight (BW) and food intake of the control and centrifuged rats at various times after onset of centrifugation at age 9 mth.

Time (wk)	Controls			Centrifuged		
	Body weight (g)	Grams food per rat per day	Grams food per day per kg BW	Body weight (g)	Grams food per rat per day	Grams food per day per kg BW
0	568 ± 9.1 [a]	26.5 ± 2.9 [b]	46.9	559 ± 8.5	26.6 ± 2.5	47.4
1	562 ± 9.1	25.6 ± 1.6	47.5	482 ± 7.9	11.4 ± 2.6	23.7
2	574 ± 12.5	27.0 ± 2.3	47.0	474 ± 8.1	15.4 ± 3.5	32.5
3	581 ± 7.7	27.6 ± 1.8	47.5	470 ± 7.9	16.2 ± 3.3	34.5
6	588 ± 9.9	25.7 ± 2.5	43.7	483 ± 6.4	20.8 ± 1.7	43.1
9	588 ± 10.0	26.6 ± 1.0	45.2	488 ± 6.3	22.9 ± 1.7	46.9
18	606 ± 9.6	24.0 ± 1.9	39.6	496 ± 6.0	23.4 ± 1.7	47.2
29	642 ± 12.9	26.0 ± 2.7	40.5	511 ± 7.9	24.2 ± 1.1	47.4
41	629 ± 20.9	21.1 ± 2.5	33.5	507 ± 6.7	21.9 ± 0.5	43.2
48	623 ± 19.0	21.6 ± 1.4	34.7	494 ± 6.7	21.9 ± 1.0	44.3
54	623 ± 20.7	20.1 ± 0.8	32.3	474 ± 9.9	23.4 ± 1.3	49.4

[a] Mean ± SEM, 18 rats.
[b] Mean ± SD, food intake of 6 groups, 3 rats/group.

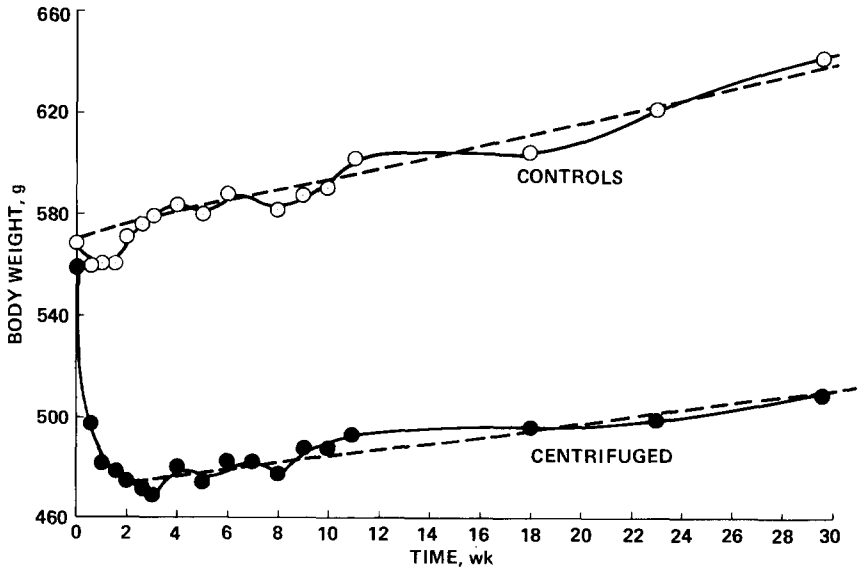

Fig. 2. Time course of body weight of centrifuged animals after onset of centrifugation compared to that of controls.

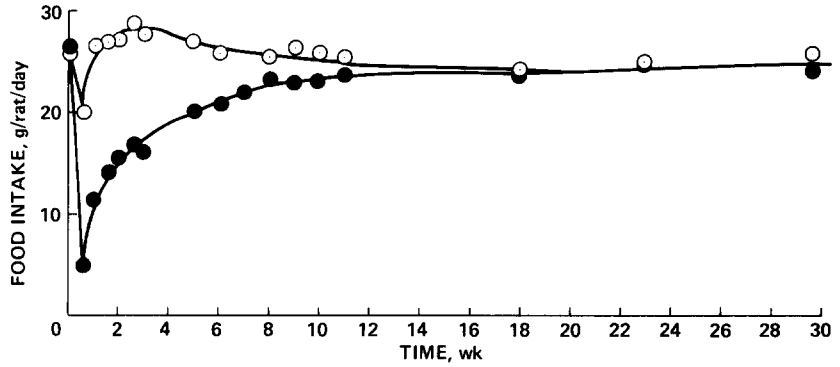

Fig. 3. Transient and steady-state time course of food intake per rat in response to centrifugation (closed circles) and in controls (open circles).

These data are roughly in agreement with previous studies by Oyama and coworkers (Oyama and Chan, 1973; Daligon and Oyama, 1975) who have found a 10–15% increase of metabolic rate or rate of tissue glucose utilization per increase of gravitational force equivalent to one normal gravity.

Morphological data

Table II summarizes body weight and the weights of certain organs of the 4 control and 4 experimental animals used in the investigation of liver mitochondrial

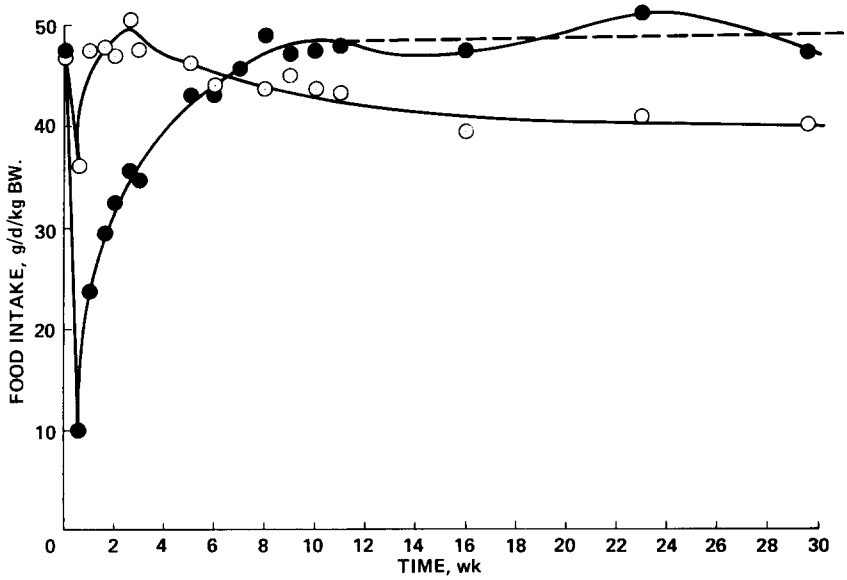

Fig. 4. Same as in Fig. 3, now food intake has been expressed in g per day per kg BW.

TABLE II

Morphological data.

	Controls		Centrifuged		Centrifuged/control	
	Mean ± SD	Organ/body weight [b]	Mean ± SD	Organ/ body weight	Mean organ weights	Organ/ body weight
Body weight [a]	741 ±27		553 ±24		0.75	
Heart	1.47 ± 0.11	0.198 ±0.013	1.34 ± 0.08	0.242 ±0.012	0.91	1.22 [c]
Liver	20.15 ± 2.22	2.72 ±0.22	15.41 ± 1.40	2.74 ±0.21	0.76	1.02
Kidneys	4.17 ± 0.15	0.57 ±0.017	4.10 ± 0.64	0.738 ±0.10	0.98	1.30 [d]
Adrenals	0.039 ± 0.006	0.0053 ± 0.0007	0.049 ± 0.007	0.0088 ± 0.001	1.26	1.66 [d]
Testes	3.08 ± 0.43	0.42 ±0.05	3.42 ± 0.39	0.62 ±0.06	1.11	1.48 [d]

[a] Body and organ weights in grams.

[b] Percentage of body weight, mean ± SD of individual values.

[c] $P < 0.05$.

[d] $P < 0.01$.

function; the animals were killed at 17 mth of age, 8 mth after onset of centrifugation. Because the centrifuged animals weighed 25% less than the controls, a meaningful comparison is that of the organ to BW ratios. From Table II it is evident that while the ratio for liver was not affected by centrifugation, all the other measured organ/BW ratios were higher for centrifuged rats than for controls.

Electron microscopic investigation of myocardiac mitochondria

Considerable amount of experimental work has been done on biological oxidations in tissues from aging animals (e.g. Hansford, 1980; Miquel et al., 1980). The justification for this gerontological interest in mitochrondrial function is that oxidative phosphorylation supplies most of the energy required by animal tissues and that this energy flow deteriorates with aging. The heart is particularly dependent on oxidative metabolism and because of its central role in the physiology of the animal it was deemed of interest to study the effects of centrifugation on the aging of the heart muscle.

Figure 5 illustrates the ultrastructural alterations caused by centrifugation in heart muscle cells. There is an apparent striking enlargement of the mitochondria and reduction in their numbers in response to chronic centrifugation. A preliminary morphometric analysis suggests that centrifugation results in a decrease of up to 20% in the number of mitochondria present in the same cellular volume, in comparison with the values found for control rats. Since previous research has demonstrated that normal aging results in a decrease in the total number of mitochondria present in the myocardium and liver of laboratory rodents (Miquel et al., 1980; Economos et al., 1981), these data suggest that chronic exposure to the hypergravity of centrifugation induced an increase of the aging rate of the myocardium.

Respiratory capacity of isolated liver mitochondria

Studies from a number of laboratories, including our own (see Miquel et al., 1980; Economos et al., 1981), have demonstrated changes in cellular fine structure of hepatocytes in very old animals, particularly at the mitochondrial level. Since rat hepatocytes divide only about once per year, we hypothesized that both fine structural and accompanying functional changes might occur in the cytoplasmic organelles of rats centrifuged for 8 mth which would be more pronounced than those occurring in the controls as the consequence of normal aging.

Normal mitochondrial structure and function are associated with in vitro preservation of the ADP:O ratio and of respiratory control. As reviewed elsewhere (Miquel et al., 1980), both parameters seem to be altered in the mitochondria isolated from the tissues of old rats. Thus, if the liver mitochondria from centrifuged rats were aging faster than those of the control animals, this might result in a higher ADP:O ratio (reduced 'efficiency') and a lower degree of respiratory control (reduced 'speed').

The range of values of respiratory control and ADP:O ratios as well as group averages and their ratios are shown in Table III. It appears that the ADP:O ratio

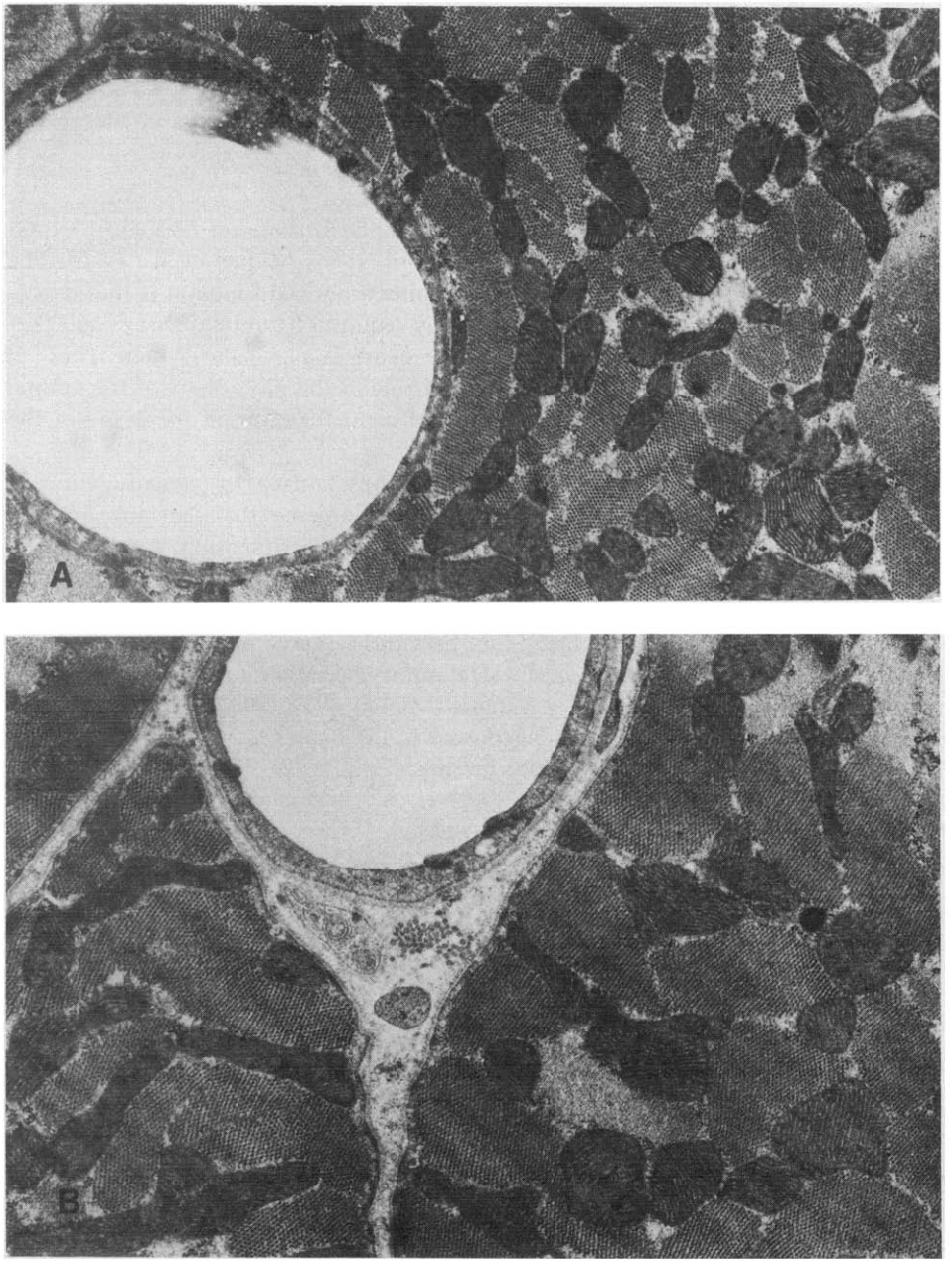

Fig. 5. Rat cardiac muscle. ×26,500. (A) Control rat 17 mth of age, showing abundant mitochondria of normal size and configuration. (B) Seventeen-month-old rat which was maintained for 8 mth in a centrifuge, at 3.14 times normal gravity. There is a reduction of the number of mitochondria, which are often elongated and enlarged.

TABLE III

Liver mitochondria respiratory parameters.

	Centrifuged	Controls	Centrifuged/controls	$P <$
ADP:O [a]	1.87± 0.28 (1.53− 2.01)	1.51± 0.21 (1.32− 1.73	1.24	0.01
Respiratory control	1.71± 0.15 (1.60− 1.79)	1.85± 0.13 (1.80− 1.99)	0.92	0.05
Rate of state 3 respiration [b]	129.6 ± 48.8 (66.2 −208.3)	90.9 ± 29.6 (39.2 ±139.7)	1.42	0.05

[a] μM ADP/μg atoms O_2.
[b] nM O_2/min.

was 20% higher in the centrifuged rats, while the degree of respiratory control was 9% lower. A statistical analysis (Student's *t*-test) using the pooled values of respiratory control and ADP:O ratio (16 values per parameter for each group, range 2–6 measurements per animal) showed that the differences were statistically significant ($P < 0.05$ for mean respiratory control and $P < 0.01$ for mean ADP:O ratio). These findings suggest that the liver mitochondria of centrifuged rats aged faster in approximate proportion with the increase of specific metabolic rate of these animals.

Spectrofluorimetric analysis

The data on lipofuscin content of heart, kidneys, adrenals and testes of the animals whose liver mitochondrial respiration was studied (see above), are summarized in Table IV. Because of the large individual variations it is not possible to derive firm conclusions from this small sample. There seems to be a trend for heart and kidneys of centrifuged animals to have more lipofuscin (3 out of 4 centrifuged rats have larger values than controls), but the average values are not different at the $P = 0.05$ level (Student's *t*-test); however, the heart data become significant if the aberrant low value of one centrifuged rat is not considered. No trend and no statistical significance is shown by the data for testes and adrenals. The finding that the adrenals of centrifuged rats did not contain more fluorescent pigment suggest a lack of apparent acceleration of the aging rate of these organs, which would have been expected if exposure to the moderate hypergravity in this study had been a chronic stress for the animals. Other physiological observations, particularly absence of elevation of the blood levels of hormones associated with stress in adapted animals (Oyama, 1978) corroborate this conclusion. Thus, the greater aging changes observed in other organs of the centrifuged animals as compared with the controls are due to the increased specific metabolic rate (rate of living) of the centrifuged animals and not to a non-specific stress response.

Life span

Pearl's rate of living theory states that an increased level of basal metabolism is accompanied by an increased rate of aging and a similarly reduced maximum life

TABLE IV

Lipofuscin content.

Rat	Controls				Centrifuged			
	Heart	Kidneys	Adrenals	Testes	Heart	Kidneys	Adrenals	Testes
1	24.0 [a]	74.4	703.1	27.4	26.8	93.9	436.4	42.4
2	48.0	84.3	500.0	10.0	95.2	90.9	547.6	10.6
3	47.2	109.2	372.3	39.8	49.0	89.8	390.1	24.2
4	47.6	74.1	455.6	19.4	87.4	95.4	418.6	32.4
Mean ± SD	41.7 ± 10.2	85.5 ± 14.3	507.8 ± 121.8	24.2 ± 10.9	64.6 ± 27.9	92.5 ± 2.3	448.2 ± 59.7	27.4 ± 11.6

[a] Fluorescence units.

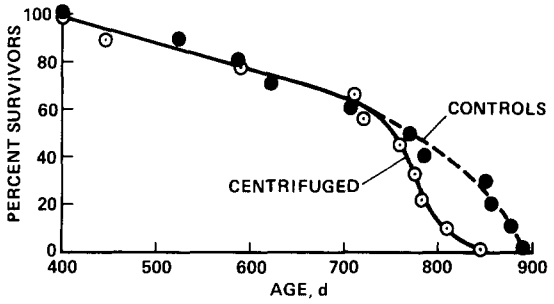

Fig. 6. Survivorship curves of the control and centrifuged groups; survivorship at the onset of centrifugation is taken as equal to 100%.

span potential as well as average life span. Because of technical limitations in the animal centrifuge, it was not possible to study large groups of animals, which is a necessity for statistical comparison of mean life spans due to the large individual variations usually observed in life span of various species. However, it was expected that 10 animals per group would be enough for demonstration of a possible difference of the order of 10–15% in maximal survival between the centrifuged and control animals.

About 2 wk before selection of the 18 experimental and 18 control rats from the initial group of 60 maintained in the NASA Ames Research Center animal facilities from 2 mth of age, the resistance of the animals to a strong 'emotional' stress was tested by redistributing them randomly in the cages to disturb the dominance hierarchy structure established in previous months when the same 3 individuals were kept in each cage. Those rats that showed signs of overt stress and loss of weight 1 wk after redistribution were not used. With this procedure it was attempted to select the healthiest animals that would best adapt to chronic centrifugation. As a result, only one of the 18 centrifuged animals showed obvious signs of severe stress during the first week of centrifugation, lost much more weight than the others, became sick and died 11 days after onset of centrifugation. This rat was therefore not considered in the analysis of life spans. The second death in the centrifuge occurred about 6 mth after onset of centrifugation which is comparable to the time, 8 mth, of the first death in the controls. Figure 6, therefore, shows the survivorship curves for the 9 experimental and 10 control animals which remained after 8 animals from each group were used for determination of the organ aging rate in the studies described above.

Survival times after onset of centrifugation (mean $\pm$ SD) were 440.9 ± 117.5 (range 171–572) days for the experimental animals and 470.3 ± 124.1 (range 249–615) days for the controls; the difference is not statistically significant due to the large variability of life spans and the small group size. However, there was a clear reduction in maximum life span potential (see Fig. 6). To estimate this reduction the four longest centrifuged survivors and the five longest control survivors (one-half of each group) were considered. Mean $\pm$ SD of survival times were respectively 519.6 ± 31.1 (range 483–572) days vs. 574.4 ± 39.0 (range 502–615) days, a difference of about 11% that is significant at the $P = 0.01$ level (Student's t-test).

Conclusion

The present study has validated in a mammal the so-called rate of living theory of aging that had been previously satisfactorily demonstrated to hold in poikilotherms, insects in particular.

Use of the hypergravity simulated in the animal centrifuge as a means for testing the theory was based on two characteristics of this condition that can be generalized from numerous previous studies of the physiology, biochemistry and behavior of rats and other small mammals exposed to chronic centrifugation: (a) hypergravity leads to an increased level of basal metabolism of the animals; and (b) moderate hypergravity ceases to be stressful within 2 wk, i.e. the animals adapt to it without an apparent disturbance of their homeostasis. These observations were corroborated in the present study (the centrifuged rats had increased food intake per kg body weight and they did not have markedly enlarged adrenals – a sign of absence of chronic stress – nor were they apparently stressed after a 2-wk adaptation period when observed periodically outside the centrifuge during 1-h weighing sessions).

Increase of the strength of the gravitational field to 3.14 times of normal gravity (a moderate increase), led to an increase of specific metabolic rate, while the various aspects of organ aging investigated indicated a deterioration or organ function (compared to controls) after 8-mth exposure to centrifugation. Therefore, the observed decrease in survival time on the centrifuge seems to be compatible with Pearl's rate of living theory.

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