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BIOCHEMICAL CHANGES OCCURRING WITH ADAPTATION TO
ACCELERATIVE FORCES DURING ROTATION*

James K. Colehour and Ashton Graybiel

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U. S. NAVAL AEROSPACE MEDICAL INSTITUTE
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SUMMARY PAGE

THE PROBLEM

To observe biochemical and associated changes attributable to living in a rotating environment at varying rates of rotation.

FINDINGS

Acute exposure to a rotational velocity of 6.4 RPM in a room 15 feet in diameter resulted in mild stress effects presumably due to Coriolis acceleration produced by head movements out of the plane of rotation. However, adaptation was rapid, and no further stress effects were observed when the rotational velocity was increased to 10.0 RPM and later decreased to 3.2 RPM. It was further observed that rotational-environment recumbency results in mild degrees of hypercalciuria, hypercapnia, and reduced excretion rates of norepinephrine.

ACKNOWLEDGMENT

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INTRODUCTION

There is general agreement that biochemical measurements have contributed to our understanding of the extremely complex mechanisms underlying the manifestations of motion sickness. Limited measurements under field conditions have demonstrated changes due to complex stress factors (2), but more comprehensive and systematic analytic studies are needed before a meaningful synthesis can be attempted. The fact that motion sickness can be readily produced in the Slow Rotation Room (SRR) under "laboratory conditions" (6) seemed to offer the opportunity to extend previous investigations dealing principally with the stress hormones. What follows describes the biochemical measures made as part of an habituation experiment in which four subjects were exposed to rotation over a period of six days, the details of which are reported elsewhere (1).

PROCEDURE

SUBJECTS

Four naval officer aviation trainees served as subjects. They had completed ground school but had not entered actual flight training. All had passed the flight physical examination and were in excellent general physical condition; their otolith organs and semicircular canals were "normal" as indicated by counterrolling and caloric tests.

FORCE ENVIRONMENT

The Pensacola Slow Rotation Room furnished the rotating environment for the experiment. It consists of an eight-sided, light-tight room, 15 feet in diameter, and is driven by an internal combustion engine through a transmission system that permits variable rotational speed. The room, described in detail elsewhere (5), contains all provisions for prolonged living in a confined environment.

EXPERIMENTAL PLAN

The experiment lasted for a period of eight days; during the first two the room was stationary (prerotation period) and during the remaining six days (perrotation period) it rotated at successive, daily speeds, as follows: 6.4, 6.4, 8.4, 10.0, 6.4, and 3.2 RPM.

It is important to point out that rotation of the head out of the plane of the Room's rotation was essential to generate the Coriolis forces contributing to bizarre stimulation of the semicircular canals. Large physical forces were not generated, and the effective vestibular stress had its genesis mainly in the canals. It is also noteworthy that the subject could prevent the stressful stimuli simply by not moving the head or by limiting the motion to swiveling in the horizontal plane. The device was stopped briefly in the morning and

evening of each day to take food aboard and for sample collection during which time the subjects were instructed to remain motionless so that readaptation to the static condition would not occur.

Diet was reasonably constant throughout the experiment. On the first day of rotation, however, the subjects experienced variable degrees of nausea so that normal amounts of food were not consumed. This occurred over a relatively short time period and in all likelihood had only a small effect on the findings of the experiment.

Total urine was collected for three eight-hour periods each day, as follows: day sample, 0800-1600; evening sample, 1600-2400; night sample, 2400-0800. Each sample was immediately stabilized with 6NHCl and refrigerated after collection, and the following determinations were made: the 17, 21 dihydroxypregnane-20-ones according to the method of Kornel(7), and epinephrine and norepinephrine by the method of Crout (4). The cations, sodium, potassium, and calcium, were determined in the same samples by conventional flame photometry.

Blood samples were drawn each morning for CBC determinations; in addition, direct eosinophile counts were made on the same samples.

Alveolar air samples were taken from each subject each morning for the determination of carbon dioxide tensions. Each subject had been instructed in the technique of providing alveolar samples until he achieved reproducibility in the consecutive samples.

RESULTS

GENERAL SYMPTOMATOLOGY

Three of the four subjects vomited early the first perrotational day and restricted their activity somewhat but consumed some food during the day and a normal evening meal. Two of the three had mild symptoms the second day, and in one, these symptoms persisted until the morning of the fourth day. The subject who did not vomit experienced only mild symptoms the first morning, did not restrict his activity, and ate normally. Even after there were no further complaints of motion sickness, very mild symptoms might be inferred from remarks in their logs, such as "got 10 hours of sleep last night so I shouldn't get so tired today," and, "I now feel that I am very well adapted," et cetera. Two of the subjects became bored and restless on the last two days.

LABORATORY DETERMINATIONS

17,21 Dihydroxypregnane-20-one Excretion

The daytime corticoid excretion was highest on the first day perrotation and was roughly twice that of the day before rotation started (Figure 1). Night and evening rates were also relatively high. However, by the second day perrotation the rates had declined and by the third day they were at prerotation levels. When the maximum speed of rotation (10 RPM) was experienced, the corticoid excretion rates were still at prerotational levels as they were on succeeding days of decreasing speeds. Circadian rhythm patterns were normal at this time.

Catechol Amine Excretion

The patterns of excretion of epinephrine and norepinephrine are shown in Figure 2. Significantly elevated levels of the former were recorded in samples taken during days 1, 2, and 5 of the perrotation period, and during the night of day 1 of the same period. Norepinephrine excretion rates decreased from normal, prerotation levels to subnormal levels after the start of rotation. Norepinephrine excretion remained low throughout the period of rotation. Table I shows the mean excretion rates in millimicrograms per minute of all subjects pre- and perrotation and are compared to Sundin's subjects who were in full recumbency (9). Our values perrotation approached but did not reach the ones he found during recumbency.

Table I
Mean Norepinephrine Excretion Rates
($\mu\text{g}/\text{min.}$)

Prerotation	Perrotation	Recumbency
20.4 ± 5.8	12.5 ± 4.1	$9.8 \pm 1.4^*$

*From Sundin, T., reference 9.

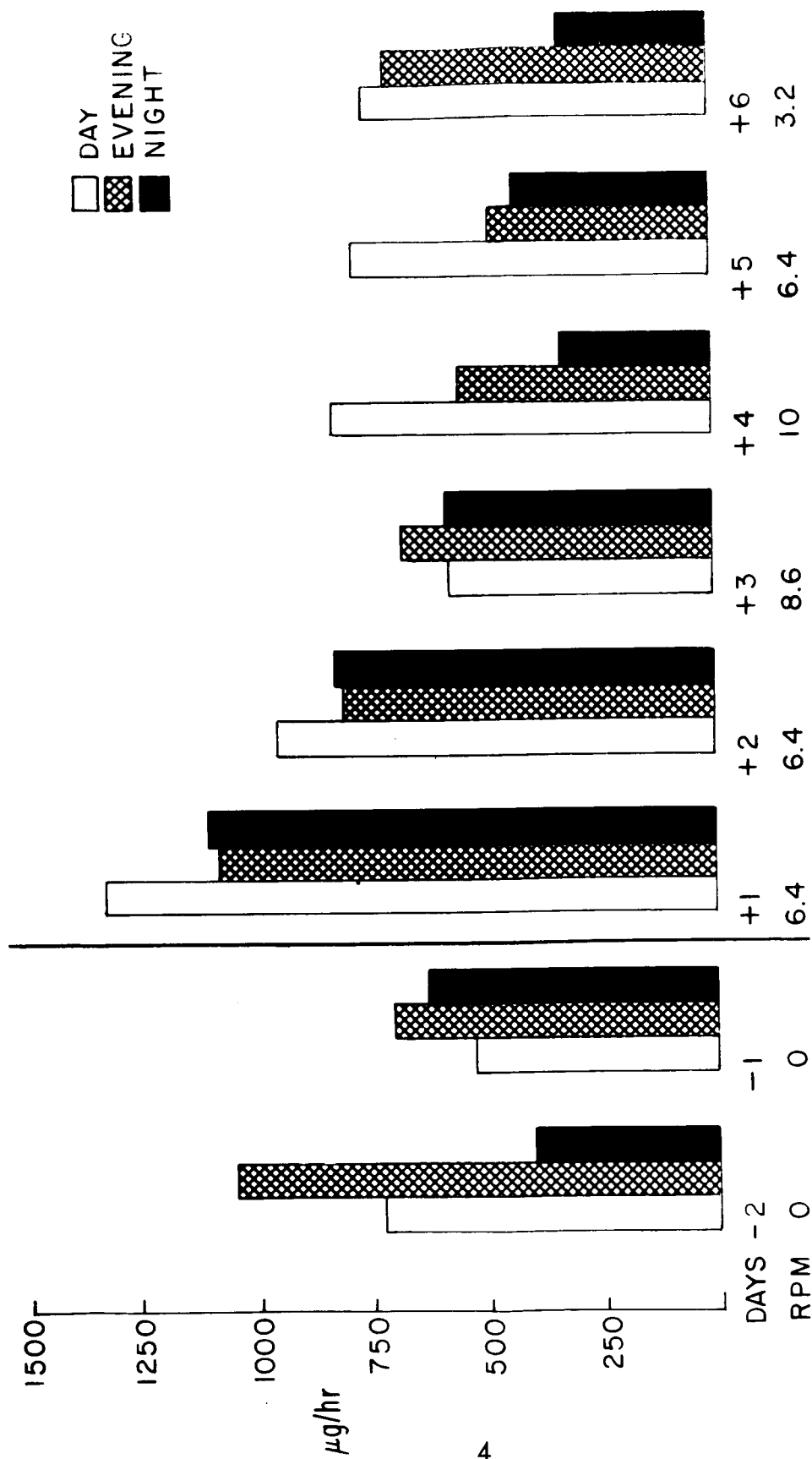


Figure 1

Changes in 17, 21 Dihydroxypregnane-20-one Excretion Rate During Adaptation to Rotation

Note: In this and subsequent figures the minus sign indicates the prerotation days, the plus sign the perrotation ones.

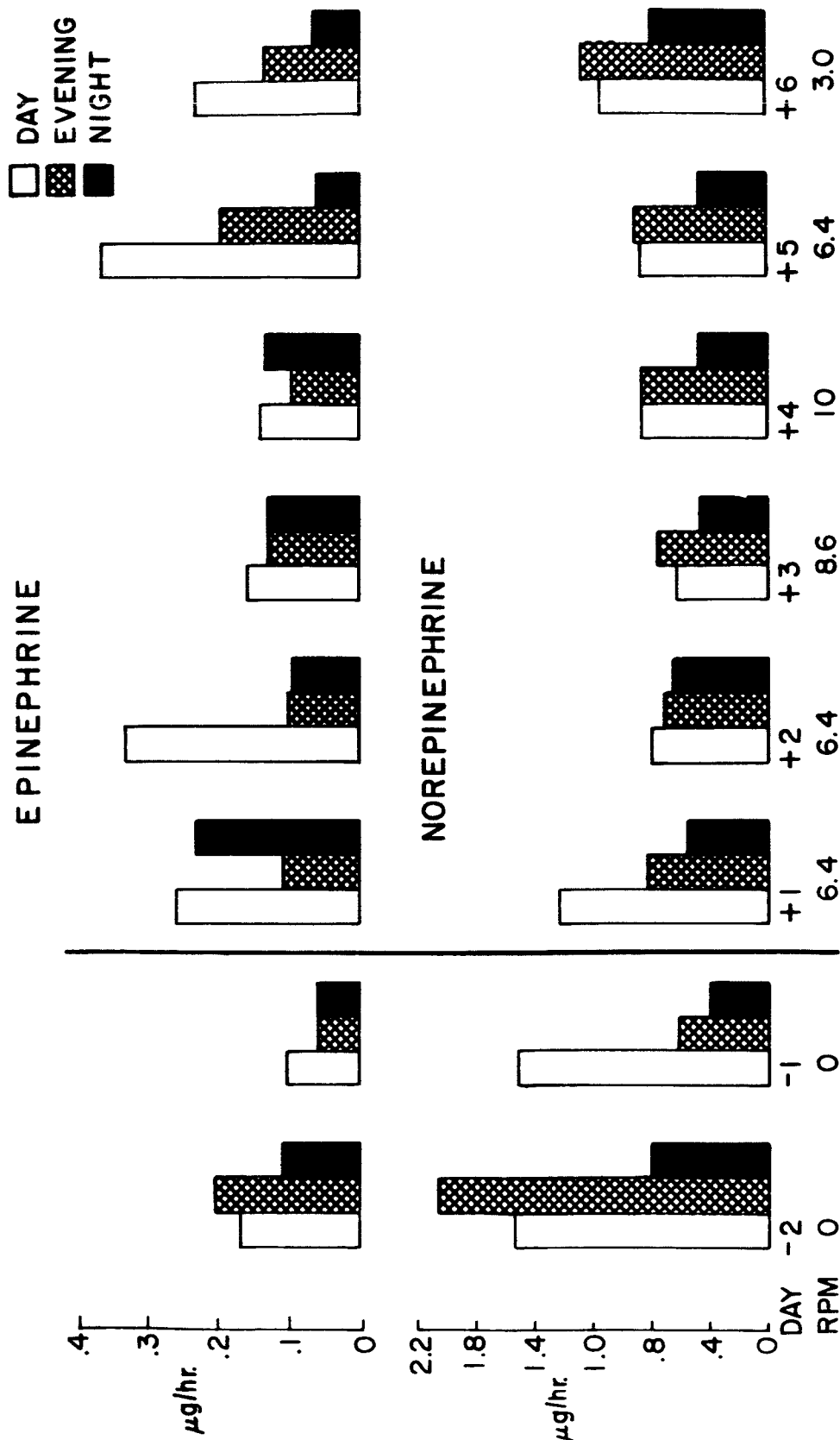


Figure 2
Catecholamine Excretion Rates with Adaptation to Rotation

Changes in Stress-Related Factors

Figure 3 shows the variations in total leukocyte count, eosinophiles, and carbon dioxide tension during the course of the experiment. On the first perrotational day the mean total white cell count was maximal and the direct eosinophile count was minimal. Normal $p\text{CO}_2$ values were found on the two prerotation days but at the start of the second day perrotation there was a minimum of 36 mm. However, on the subsequent day a reversal in trend was observed, and on three out of four of the remaining perrotational days, mean levels of 45 mm were reached.

Cation Excretion

Figure 4 shows the excretion rates of calcium, sodium, and potassium. Both sodium and potassium output increased slightly during rotation, but the increases were not significant. The increases in calcium excretion, however, were highly significant. The greatest excretion of this cation occurred at the highest rotational speed and then diminished somewhat as the speed decreased toward the end of the experiment.

DISCUSSION

The fact that the bizarre stimulation of the semicircular canals, to which the subjects adapted, caused only mild symptoms had two advantages. It avoided complications due to severe nausea and vomiting and did not mask the effects of other relatively mild influences, such as physical inactivity and psychological factors. On the other hand, the individual variance to the mild stimulus tended to minimize changes expressed as mean values for the group.

The excretion rate of norepinephrine, initial fall to low values and slight terminal rise, correlates well with the changes in physical activity of the subjects and does not reflect either the changing patterns of centripetal force or the time-course of the general symptomatology. The low level of physical activity best accounts for the tendency of urinary calcium excretion to rise. Similarly, the increased carbon dioxide tensions after the second perrotational day approach the slightly elevated values found during sleep (8).

The increase in urinary corticoid excretion beginning early in the perrotation period undoubtedly has its origin in the labyrinth (3), probably via the hypothalamic-pituitary-adrenal axis. The lowered $p\text{CO}_2$'s on the second rather than on the first day perrotation is explained by assuming that adaptation with regard to neural respiratory mechanisms has a different time-course than in the case of nausea. The restriction of head movements because of nausea on the first day of rotation was lifted on the second, resulting in greater stimulation to the canals. Adaptation with regard to symptoms requiring longer exposure to the stimulus than in the case of nausea would explain a greater response on the second day. This phenomenon was observed in an earlier experiment (6).

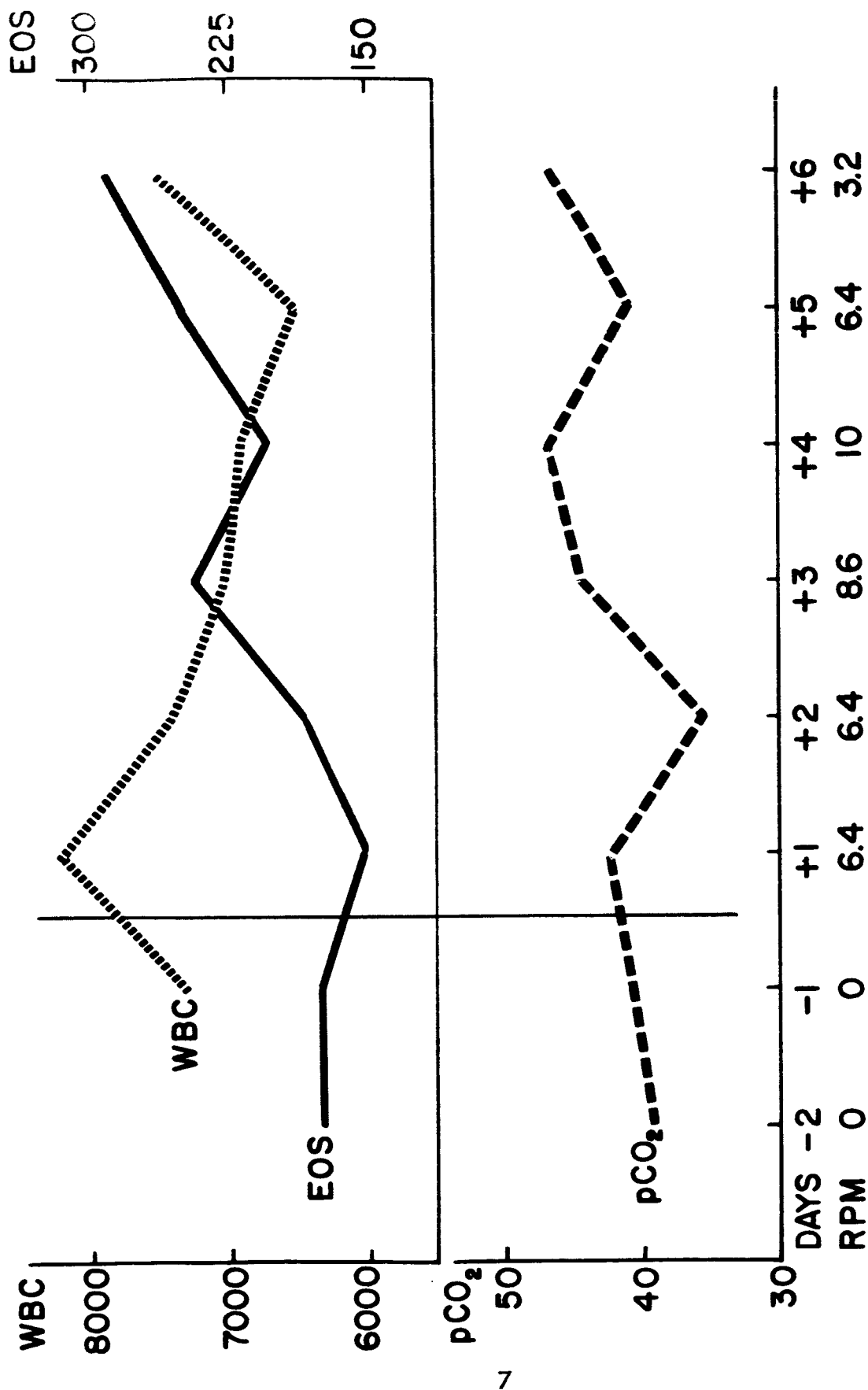


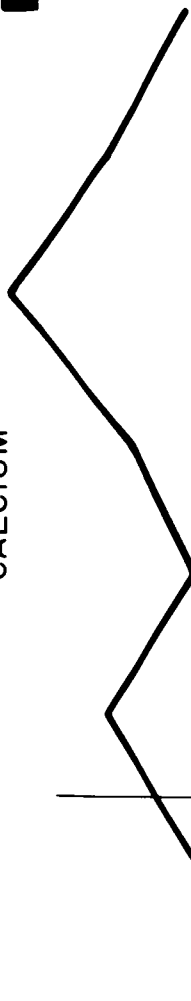
Figure 3
Changes in Stress-Related Factors During Adaptation to Rotation

 CONTROL
 ROTATION

CALCIUM

mg/day

420
380
340
300
260
220



 CONTROL
 ROTATION
 p.005

SODIUM

g/day

3.7
3.3
2.9
2.5



 CONTROL
 ROTATION
 p > .1

POTASSIUM

g/day

3.2
2.8
2.4
2.0



 CONTROL
 ROTATION
 p > .1

DAY	-2	-1	+1	+2	+3	+4	+5	+6
RPM	0	0	6.4	6.4	8.6	10	6.4	3.2

Figure 4

Mean Daily Excretion of Cations with Adaptation to Rotation

The slight increase in release of epinephrine early in the perrotation period might be explained on the basis of lack of familiarity with what to expect. The increase toward the end of rotation is not well explained except by the desire for or anticipation of the termination of the experiment. Variations in total leukocytes and the eosinophile counts at the start of rotation are also best explained on a psychological basis .

The clearly different patterns of change in the release of norepinephrine, epinephrine, and the corticoids are especially noteworthy. This is the first time that we have observed a fall in the excretion of norepinephrine concomitantly with a rise in corticoids. Stated differently, the stimulus to the vestibular organs was more than offset by physical inactivity. Yet, earlier observations had demonstrated an increased release of norepinephrine in normal subjects during acrobatic flight but not in persons with bilateral labyrinthine defects, indicating that directly or indirectly the vestibular organs were involved. Moreover, when subjects were severely stressed in the SRR on another occasion, only minor fluctuations in blood norepinephrine levels were observed (6).

Unless priority is given to biochemical measures, investigations of this nature are difficult to carry out. The biochemist must be given the opportunity to 1) properly adjust the level of stress to fit the subjects' susceptibility, 2) control the many variables which must be taken into account, and 3) have full cooperation of the participants.

REFERENCES

1. Bergstedt, M., Stepwise adaptation to a velocity of 10 RPM in the Pensacola Slow Rotation Room. In: The Role of the Vestibular Organs in the Exploration of Space. NASA SP-77. Washington, D.C.: National Aeronautics and Space Administration, 1965, pp. 339-345.
2. Colehour, J. K., Stress measurements in normal and labyrinthine defective subjects in unusual force environments. In: The Role of the Vestibular Organs in the Exploration of Space. NASA SP-77. Washington, D.C.: National Aeronautics and Space Administration, 1965, pp. 357-364.
3. Colehour, J.K., and Graybiel, A., Excretion of 17-hydroxycorticosteroids, catechol amines, and uropepsin in the urine of normal persons and deaf subjects with bilateral vestibular defects following acrobatic flight stress. Aerospace Med., 35:370-373, 1964.
4. Crout, J.R., Catechol amines in urine. In: Seligson, D.(Ed.), Standard Methods of Clinical Chemistry. Vol. 3. New York: Academic Press, 1961, pp. 62-80.
5. Graybiel, A., Clark, B., and Zarriello, J. J., Observations on human subjects living in a "slow rotation room" for periods of two days. Arch. Neurol., 3: 55-73, 1960.
6. Graybiel, A., Kennedy, R. S., Knoblock, E. C., Guedry, F. E. Jr., Mertz, W., McLeod, M. E., Colehour, J. K., Miller, E. F., II, and Fregly, A. R., The effects of exposure to a rotating environment (10 RPM) on four aviators for a period of 12 days. Aerospace Med., 36:733-754, 1965.
7. Kornell, L., An improved, rapid method for free and conjugated 17-hydroxycorticosteroids in urine. Metabolism, 8:432-440, 1959.
8. Robin, E. D., Whaley, R. D., Crump, C. H., and Travis, D. M., Alveolar gas tensions, pulmonary ventilation and blood pH during physiologic sleep in normal subjects. J. clin. Invest., 37:981-989, 1958.
9. Sundin, T., The effect of body posture on the urinary excretion of adrenaline and noradrenaline. Acta Med. Scand., 161: Suppl. 336, 5-59, 1958.

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13. ABSTRACT Four young men lived in a continually rotating room, 15 feet in diameter, for a period of six days. Rotational velocities on succeeding days were: 6.4, 6.4, 8.6, 10.0, 6.4, and 3.2 RPM. Stress effects measured as increased excretion rates of 17, 21 dihydroxypregnane-20-ones, eosinopenia, hyperventilation, and nausea were observed on the first day of rotation. However, adaptation was rapid, and no further stress effects were observed even with increased rotational velocity. Mild degrees of hypercalciuria, hypercapnia, and decreased norepinephrine excretion rates were observed during the last four days of the experiment as a result of the increased time spent in recumbency.		

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Rotational stress effects						
Recumbency effects						
Corticosteroids						
Catechol amines						
Hypercalciuria						
Hypercapnia						

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