

Metabolic Responses of Adrenalectomized Rats to Exercise (36805)

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Although it has long been known that the imposition of forced exercise on man and other animals results in an increased release of the adrenal hormones (1-4), the effects of these hormones on the metabolic responses to exercise have not been fully explored. Gray and Beetham (1) reported an increase in the level of plasma catecholamines in young men after either acute or chronic exercise bouts. Others have found that the intensity of the exercise markedly influenced the concentrations of the individual hormones (2) and that the intensity of the work performed could be related to the presence or absence of cortisone or hydrocortisone (3).

Previous studies have shown that exercise lowers serum insulin, liver fat, serum and liver cholesterol, body weight gain, and in some instances food intake (5-8). While some of the reduction in body weight gain could be attributed to a decreased food intake and an increased metabolic rate during the brief exercise period, not all of the differences in caloric balance could be explained on this basis. Earlier (8) we suggested that the effects of exercise on the above parameters might be mediated through the adrenal hormones, since these hormones have been shown to inhibit insulin release and enhance lipid mobilization. To test this hypothesis it was first necessary to determine if the diet would provide enough salt, protein, and lipid such that adrenalectomy *per se* would not inhibit food intake or body weight gain. Once this was established we then sought to determine the effect of exercise on serum insulin, liver fat, liver and serum cholesterol and carcass composition of adrenalectomized and sham-operated rats. The present paper reports the results of these studies.

Methods and Materials. Thirty-two 70-day-

old, specific pathogen-free male Wistar¹ rats, weighing 280-300 g, were divided into two groups. One group was bilaterally adrenalectomized² via a dorsal incision while the remaining animals were subjected to a sham operation. After recovery, half of each group was forced to run 1/4 mile/30 min/day on a treadmill. The sedentary control animals were placed in an identical apparatus but without a moving floor.

Animals were housed individually in wire mesh cages in a temperature-humidity controlled room with equal periods of light and dark. A 48% protein, 28% fat, 15.5% carbohydrate diet³ was fed *ad libitum*; water likewise, was available at all times. The diet was identical to that used previously (7, 8) except for the addition of 0.9% NaCl needed to compensate for the excess Na loss by the adrenalectomized animals.

At the end of the 8 wk experimental period, the animals were deprived of food for 12 hr and anesthetized with sodium amytal (60 mg/kg, ip). The thoracic cavity was opened, blood was withdrawn by heart puncture and an aliquot was used for the determination of glucose (9). The serum from the remaining blood was collected after centrifugation (3000g, 15 min) in a refrigerated centrifuge and used for the determination of immunoreactive insulin (10), cholesterol (11) and

¹ Manor Research Farms, Ralston Purina Co.

² The carcasses were examined at the end of the experiment and no adrenal tissue was found.

³ Composition of diet: 48% lactalbumin, 15.5% carbohydrate mixture, which approximated the carbohydrate consumption of an average U.S. "market basket" diet, 6.7% safflower oil, 21.4% beef tallow, 5.4% mineral mix, 2.4% cellulose, 0.5% vitamin mix and 0.9% NaCl. A full description of this diet without the added NaCl may be found in Ref. (6).

TABLE I. Effect of Adrenalectomy and Exercise on the Food Intake, Body Weight Gain, and Final Carcass Composition of Rats.

Treatment	Exercise	Body wt gain (g)	Food intake (g/day)	Carcass		Protein: fat ratio
				Fat (%)	Protein (%)	
Adrenalectomy	+	156 ± 12 ^c	15 ± 1	10 ± 1	25 ± 1	2.52 ± 0.20
Sham	+	132 ± 7 ^a	14 ± 1	10 ± 1 ^a	24 ± 1	2.41 ± 0.12 ^a
Adrenalectomy	—	187 ± 12	15 ± 1	12 ± 1 ^b	22 ± 1	1.96 ± 0.28
Sham	—	186 ± 5	15 ± 1	18 ± 1	22 ± 1	1.28 ± 0.08
Analysis of variance						
Adrenalectomy		ns	ns	<i>p</i> < .01	ns	<i>p</i> < .05
Exercise		<i>p</i> < .01	ns	<i>p</i> < .01	<i>p</i> < .01	<i>p</i> < .01
Adrenalectomy × exercise interaction		ns	ns	<i>p</i> < .01	ns	ns

^a The mean of the exercise group is significantly different from that of the sedentary group of the same adrenal status (*p* < .05).

^b The mean of the adrenalectomized rats is significantly different from that of the sham-operated animals on the same exercise treatment (*p* < .05).

^c Standard error of mean of 8 rats.

triglycerides (12). The liver was excised, blotted, weighed, and used for the determination of total lipid (13) and cholesterol (11).

The ingesta-free, liver-free carcass was autoclaved (15 lb/in², 15 min) and homogenized with crushed ice (carcass:ice, 1:2). Aliquots of this homogenate were used for the determination of total lipid (13) and protein (14). Differences between the means of each group for each determination were tested by student's *t* test. Data were also analyzed statistically by means of the analysis of variance.

Results. The experimental design implies that the crucial difference in the response to exercise between the adrenalectomized and sham-operated rats was the presence or absence of the adrenal glands. In the present study, perhaps due to the high protein and electrolyte content of the diet, no differences due to adrenalectomy were observed in the body weight gains, food intakes, or the body composition of the exercised rats (Table I). However, adrenalectomy did affect the body composition of the sedentary animals. Exercise served to lower the body weight gain and the carcass fat content and increased the carcass protein to fat ratio in the sham operated animals but not the adrenalectomized animals. An analysis of variance of these data revealed a significant effect of exercise on

body weight gain, percentage carcass fat, percentage carcass protein and the protein:fat ratio, a significant effect of adrenalectomy on percentage carcass fat and the carcass protein:fat ratio, and a significant adrenalectomy/exercise interaction effect on percentage carcass fat.

Serum cholesterol and whole blood glucose levels were unaffected by exercise or adrenalectomy (Table II). Liver cholesterol levels were lower in sedentary adrenalectomized animals than in the sham-operated animals. Liver lipid was unaffected by adrenalectomy but was lower in the exercised animals than in the sedentary animals. A trend towards lower serum triglycerides with adrenalectomy was observed but these differences were not statistically significant. The imposition of daily forced exercise resulted in less liver cholesterol and serum insulin in the adrenalectomized rats and less liver cholesterol in the sham-operated rats. An analysis of variance of these data showed a significant exercise effect on liver lipid, liver cholesterol and serum insulin.

Discussion. The performance of the adrenalectomized rats indicates that the ability to withstand a moderate level of forced exercise was unimpaired by the removal of the adrenals. The lack of effect of adrenalectomy on the metabolic responses to exercise does not

TABLE II. Effect of Adrenalectomy and Exercise on Liver and Blood Composition.

Treatment	Exercise	Serum		Whole blood		Liver		Serum	
		cholesterol (mg/100 ml)	glucose (mg/100 ml)	lipid (%)	cholesterol (mg/g)	triglycerides (mg/100 ml)	insulin (μ U/ml)		
Adrenalectomy	+	95 \pm 5 ^c	81 \pm 4	5.4 \pm 0.1	4.72 \pm 0.12 ^a	90 \pm 6	58 \pm 4 ^a		
Sham	+	96 \pm 3	83 \pm 5	5.2 \pm 0.1	4.66 \pm 0.13 ^a	98 \pm 2	62 \pm 5		
Adrenalectomy	-	106 \pm 10	80 \pm 5	6.1 \pm 0.6	5.39 \pm 0.17 ^b	76 \pm 6	77 \pm 4		
Sham	-	107 \pm 7	76 \pm 3	6.1 \pm 0.3	6.32 \pm 0.13	92 \pm 5	75 \pm 5		
Analysis of variance									
Adrenalectomy		ns	ns	ns	ns	ns	ns		
Exercise		ns	ns	$p < .01$	$p < .01$	ns	$p < .01$		
Adrenalectomy \times exercise interaction		ns	ns	ns	ns	ns	ns		

^a The mean of the exercised group is significantly different from that of the sedentary group of the same adrenal status ($p < .05$).

^b The mean of the adrenalectomized rats is significantly different from that of the sham-operated animals on the same exercise treatment ($p < .05$).

^c Standard error of mean for 8 rats.

appear to support the suggestions of others (1-5, 8, 15) that the adrenal hormones (both corticoids and catecholamines) play important roles in the adaptation of rats to forced exercise. The results do not rule out, however, a contributory role of these hormones in influencing carcass fat in exercised rats, since a significant effect of the exercise/adrenalectomy interaction on this parameter was observed.

In the present study, as in other studies (5-8), moderate forced exercise appeared to increase the mobilization of the carcass fat with both exercised groups having less carcass fat and more carcass protein than the sedentary groups. The differences in carcass fat content between the exercised and sedentary animals and between the adrenalectomized and sham operated sedentary animals suggests that two different control mechanisms exist for the utilization and storage of fat. One of these mechanisms is quite adaptable and independent of the adrenal hormones; the other is dependent on the action of the catecholamines and adrenal corticoids. The former mechanism apparently is activated by exercise or by the absence of adrenal stimulation and appears to result in an increased mobilization of carcass fat.

The lower levels of serum insulin with exercise observed in this and other studies (7, 8) do not appear to be related to adrenal activity. It is more likely that the insulin level reflects both a decreased need due to the activation of a noninsulin-dependent glucose transport by exercise (16, 17) and an inhibition of release by the products of the exercise induced increased fat mobilization.

Summary. Metabolic responses to exercise were determined in adrenalectomized and sham-operated rats. Exercised animals were forced to run 1/4 mile in 30 min each day for 8 wk. All animals were fed *ad libitum* at 48% protein, 28% fat, 15.5% carbohydrate diet. Extra (0.9%) NaCl was added to the diet given to the adrenalectomized rats. Under these experimental conditions, exercise reduced body weights gains to a similar degree in both the adrenalectomized and sham-operated animals and similarly lowered liver fat, liver cholesterol and serum insulin. No

differences in food intake, body weight gain, blood glucose, serum insulin, carcass protein, or serum triglycerides were observed with the removal of the adrenals. Adrenalectomy did, however, affect the percentage carcass fat and the level of cholesterol in the livers of the sedentary animals. From this data it was suggested that two separate mechanisms exist for the mobilization of carcass fat: one activated by exercise and the other by the adrenal hormones.

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