Failure of Cortisone and ACTH to Regulate Cardiac Hypertrophy

Numerous investigators – reviewed by VAN LIERE et al[1] – have shown that vigorous exercise produces cardiac hypertrophy. The latter is presumably caused by enlargement of the myocardial fiber and hence might reasonably be expected to involve accelerated protein synthesis. BEZNAK has shown[2,3] the process of cardiac hypertrophy to be dependent upon hormones which have been implicated in the regulation of protein metabolism. The present experiments extend this field by a study of the effect of cortisone and ACTH, since such hormones have been shown to exert effect upon protein metabolism, depending on the dosage used[4,5].

Materials and methods. Male Sprague–Dawley rats were maintained on Purina laboratory chow and water ad libitum. Exercise was imposed by a treadmill with an electric grid at the rear, driven at 1 mph. Exercise periods were 1 h twice daily, 6 times weekly, with a 4 h rest period between daily runs. Cortisone acetate or ACTH in saline was injected i.p. just before the first exercise period of the day. Animals were randomized into the following groups: saline, not exercised (control-controls); saline, exercised (control-runners); cortisone or ACTH, not exercised (cortisone or ACTH-controls); and cortisone or ACTH exercised (cortisone or ACTH-runners). Each hormone was given in two doses (Tables I and II).

All groups which were given cortisone or 1 USP unit/dose of ACTH, and their control groups, were exercised for a total of 65 h. Hormones were administered for a total of 34 days. The rats given 3U ACTH/dose, and their control runners, were exercised for a total of 39 h. A total of 154 rats was used; individual groups ranged from 7–20 rats.

On the day after the exercise was concluded, the rats were weighed, killed by stunning and decapitation, and the hearts removed, trimmed, washed with tap water, blotted and weighed. The heart-weight/body-weight ratio (HW/BW) was expressed as g/kg. Statistical analysis was by the *t* test.

Results. Table I contains the data relating to cortisone. Statistical analysis of these data showed that exercise caused hypertrophy, but that the degree of the latter was not changed by either dose of cortisone. The cortisone-controls showed a mean HW/BW which approached ($p = 0.08$) significant reduction from the controls.

Similarly, in the study of ACTH (Table II) exercise resulted in cardiac hypertrophy, but the degree of hypertrophy was not changed by either doses of ACTH.

Discussion. The results clearly show that if rats are forced to exercise vigorously, a significant cardiac hypertrophy is produced. Although it has been shown that cardiac muscle fibers increase in size following exercise, the exact mechanism of hypertrophy is not understood, although there is an increase in the oxidative metabolism of the myocardium resulting in an increase in protein disposition[6]. Furthermore, although some endocrine secretions have been shown to regulate the degree of hypertrophy, the full control system has probably not been observed. In view of the known influences of adrenal steriods upon growth and protein metabolism it seemed reasonable to expect that such hormones might enter into the system.

SPRAGUE et al.[7] have reported a significant gain in body weight as a result of cortisone and ACTH therapy, which they attribute to a high food consumption. Although our animals were fed ad libitum, no such excess gain occurred. In view of this, and since the hormone treatments were without effect on HW/BW the efficacy of the treatments under our conditions was checked. Significant hypertrophy of the adrenal gland was observed in response to ACTH and a significant atrophy, to cortisone.

In conclusion, the data clearly indicate cardiac hypertrophy in response to exercise; but neither cortisone nor ACTH, in otherwise effective doses, regulated the degree of hypertrophy under the conditions of the experiment. Since ACTH was not effective, the failure of cortisone to regulate can not be attributed to its not being the physiological corticoid in the rat[8].

Table I. Effect of injection of cortisone

	No. of animals	HW/BW ratios
Control-controls	11	3.28
Control-runners	7	3.78
Cortisone-controls (3 mg)	11	3.14
Cortisone-runners (3 mg)	7	3.65
Control-controls	10	3.13
Cortisone-runners (6 mg)	11	3.56

HW/BW = heart-weight/body-weight

Table II. Effect of injection of ACTH

	No. of animals	HW/BW ratios
Control-controls	34	3.37
Control-runners	19	3.78
ACTH-controls (1 U)	18	3.41
ACTH-runners (1 U)	17	3.59
Control-controls	15	3.01
Control-runners	8	3.23
ACTH-controls (3 U)	10	3.13
ACTH-runners (3 U)	10	3.28

Résumé. L'hypertrophie cardiaque provoquée chez des rats mâles par un exercice forcé n'a été régularisée ni par la cortisone ni par l'ACTH utilisées chacune à 2 doses différentes.

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