Heart Norepinephrine Levels After Exercise Training in the Rat*

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Rats exercise trained by swimming one hour daily five days per week for three months developed cardiac hypertrophy. The NE concentration (0.469 μg/g) and total NE content (0.741 μg) of the hypertrophied hearts were not significantly different from levels in hearts of unexercised control rats.

The mammalian heart is rich in sympathetic nerve terminals which are involved in synthesis, uptake, and release of the neurotransmitter norepinephrine (NE).1,2 Intense sympathetic stimulation during exercise leads to a release of NE from peripheral adrenergic nerve endings, including those of the heart. This is associated with an elevation in circulating levels of NE in both animals and man.3,4 Acute exercise stress in the rat also is reported to increase the rate of synthesis of NE in the heart,5 and either increase,6 decrease,7,8 or produce no change8,9 in heart NE concentration depending on the experimental conditions.

Myocardial adaptive changes during exercise training in man and animals is well recognized to result in a reduction of heart rate at rest and during submaximal exercise10-13 and in the development of cardiac hypertrophy.10,11-16 A reduction in sympathetic tone of heart is believed to contribute to the development of "athletic bradycardia."12 The finding of De Schryver et al.7,17 of a pronounced decrease in cardiac NE content in rats trained by running, lent support to this hypothesis. However, Ostman and Sjöstrand18 were unable to confirm this observation. Because of these conflicting data we determined cardiac NE levels in rats following three months of exercise conditioning and compared them with levels in the hearts of control animals.

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METHODS AND MATERIALS

The experiments were performed on male, albino Charles River CD strain rats housed in pairs in wire cages in air conditioned quarters and fed standard laboratory chow and tap water ad libitum. The body weights of the rats prior to undergoing exercise training ranged from 182 to 216 grams. Rats were randomly divided into two groups, one group serving as unexercised controls while the second underwent 12 weeks of exercise training. Training consisted of 1 hour swim sessions, 5 days per week in a 128 gallon, 107 cm × 77.5 cm × 94 cm high plastic tank at a water temperature of 34°C. Twenty-four hours after their last training sessions, 25 trained rats were killed by decapitation along with the same number of unexercised controls.

The heart was rapidly removed from each dead animal, blotted free of blood, weighed, frozen on dry ice within 15 minutes of removal and then stored at −20°C until analyzed.

Heart NE was separated and assayed by the method of Laverty and Sharman.19 Essentially this procedure consists of homogenization of the tissue, resin column extraction, acetylation, condensation of the acetylated derivatives with ethylenediamine and fluorometric analysis. Heart NE was expressed as μg/g wet tissue weight and as μg per heart.

Analysis of variance was used to compare the heart and body weights and heart NE content of animals from the two groups (A and B on Fig 1). Cardiac hypertrophy in the exercise trained rats was tested by plotting heart weight against body weight for the trained and control rats and comparing the slopes of the regression lines obtained from this relationship by analysis of variance.20,21

RESULTS

Table 1 shows the mean values ±SEM for body weight and heart weight of the exercise trained rats, and the ratio of heart weight to body weight.

Table 1—Effect of Exercise Training on Mean Body Weight, Heart Weight, and Heart to Body Weight Ratio

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Untrained N = 25</th>
<th>Trained N = 25</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>489.4</td>
<td>478.3</td>
<td>NS</td>
</tr>
<tr>
<td>± SEM</td>
<td>9.7</td>
<td>11.5</td>
<td></td>
</tr>
<tr>
<td>Heart weight (mg)</td>
<td>1280.1</td>
<td>1385.3</td>
<td>0.01</td>
</tr>
<tr>
<td>± SEM</td>
<td>22.4</td>
<td>25.2</td>
<td></td>
</tr>
</tbody>
</table>

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group as compared to the control group. Although there was no significant difference in body weight between these two groups, the trained group had a mean heart weight significantly heavier than that of the control group (P < 0.01).

Figure 1 shows the relationship between heart weight and body weight in the individual animals of the exercise trained and control groups with the regression lines derived from this relationship for each group. The correlation coefficients are 0.6459 for the control group and 0.8975 for the exercise trained group. The heart to body weight ratio for the exercise group is \(2.04 \times 10^{-3}\) as compared to \(1.49 \times 10^{-3}\) for the control group. It is apparent from the figure that the regression line of the exercise trained group (A) has a greater slope and lies above that of the control group (B), indicating the presence of cardiac hypertrophy in the exercise trained group. The difference in the slopes of the regression lines is significant at the \(P < 0.001\) level.

Table 2 shows the mean cardiac NE concentration in micrograms per gram of tissue and in micrograms per heart for the exercise trained and control groups. The differences noted between groups are not statistically significant.

**Discussion**

Sympathetic stimulation accompanying swimming has been demonstrated in rats to cause an approximate twofold elevation in plasma NE.\(^3,4\) Rats subjected to acute swimming stress have previously been demonstrated by us\(^5\) and by others\(^6\) to develop a transient reduction in heart NE concentration suggesting that cardiac NE release exceeded synthesis and uptake. De Schryver and colleagues\(^7,17\) also observed a reduced concentration of cardiac NE in rats exercised by running on a treadmill or rotating drum every other day for three months. The training regimen used by these investigators was not intense enough to produce cardiac hypertrophy. In contrast in this study, we failed to find any significant difference from control levels in NE content of rat hearts hypertrophied by chronic swimming exercise five days per week for three months. Our findings are in agreement with those of Ostman and Sjöstrand\(^18\) who produced cardiac hypertrophy in rats by running them on a treadmill daily for 15 weeks.

It would appear then that with chronic heavy exercise training sufficient to produce cardiac hypertrophy, the rate of NE synthesis and/or uptake is increased sufficiently both to compensate for the NE released by sympathetic stimulation during exercise, and to keep pace with the increase in heart muscle mass. Thus, adrenergic transmitter concentration remains undiminished. In contrast cardiac hypertrophy induced in animals by experimental aortic or pulmonary artery stenosis is reported to result in a decrease in cardiac NE concentration and total amount per heart, which is most marked in the severely hypertrophied or failing heart.\(^22-25\) It is interesting to compare our results with those of Fischer and associates,\(^25\) who produced cardiac hypertrophy in rats by experimental aortic stenosis. These investigators observed a significant decrease in cardiac NE concentration in rats which developed moderate hypertrophy of about the same magnitude as our trained rats. This apparently was due to an increase in heart tissue without a corresponding increase in amount of adrenergic transmitter. Total amount of NE per heart was depleted only in those animals with severely hypertrophied hearts.

**References**

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