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SKELETAL MUSCLE METABOLISM IN HYPOKINETIC RATS

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Intact control (weight bearing) and suspended rats gained weight at a similar rate during the 6 day period following tail-casting (26 ± 2 grams and 21 ± 3 grams, respectively). Adrenalectomized weight bearing rats gained less weight during this period (18 ± 1 grams) while adrenalectomized suspended rats showed no significant weight gain (3 ± 2 grams). Cortisol treatment of both of these groups of animals caused a loss of body weight (16 ± 1 and 17 ± 1 grams, respectively).

The slower growth rate of adrenalectomized weight bearing rats was reflected in little growth of the extensor digitorum longus muscle and no significant growth of the soleus muscle. In the adrenalectomized suspended rats, the extensor digitorum longus failed to grow and the soleus atrophied to a greater extent. Both muscle showed a loss of mass in the cortisol treated rats in accord with the overall loss of body weight. These results show that adrenalectomy caused stress in both weight bearing and suspended rats but had greater effect in the suspended group. This effect was enhanced by administration of a physiologic dose of cortisol acetate.

Comparison of protein metabolism, in soleus muscles of weight bearing and suspended rats had shown previously that the atrophy was due to both slower protein synthesis and faster protein degradation. This difference in protein synthesis was abolished in adrenalectomized animals and not restored by administration of cortisol, which decreased this process in both groups of adrenalectomized animals. The difference in protein degradation was only partially lowered by adrenalectomy. Administration of cortisol increased this difference. In the extensor digitorum longus muscle, cortisol slowed protein synthesis to the same extent in both groups. Cortisol lowered protein degradation in this muscle of control

animals but had no effect in the suspended ones. These results support previous findings in fed adrenalectomized rats that this cortisol dose slows protein synthesis and either has no effect or diminishes protein degradation. Furthermore, these findings suggest that the slower protein synthesis and, in part, the faster protein degradation of the unloaded soleus muscle may be due to higher levels of circulating glucocorticoids in the suspended animals. However, part of the response of protein degradation must be unrelated to steroid levels.

Amino acid metabolism was also studied in these animals. Previous work showed a slower synthesis of glutamine by soleus muscle of suspended animals despite greater activity of glutamine synthetase. This slower synthesis was reflected in lower ratios of muscle glutamine to glutamate in the unloaded (1.42) than in the weight bearing (2.68) soleus. Adrenalectomy had no significant effect on this ratio in the soleus. In contrast, adrenalectomy lowered this ratio by 36-40% in the extensor digitorum longus muscle and cortisol treatment increased the ratio in the weight bearing, but not in the unloaded soleus. The lack of response in the unloaded muscle probably is due to limiting amounts of tissue ammonia.

Since muscle glutamine synthetase activity is very sensitive to alterations of steroid levels, it was measured in these muscles. Adrenalectomy resulted in lower activity in weight bearing and unloaded soleus (75% and 94%, respectively) and extensor digitorum longus (86-90%) muscles. In the weight bearing muscles, cortisol restored these activities to 81-83% of normal. After cortisol treatment, the activity in the unloaded extensor digitorum longus was similar to the control muscle but much lower (-54%) than in this muscle of intact suspended rats. This finding suggested that

the higher activity of glutamine synthetase in extensor digitorum longus muscles of control and suspended rats was probably due to higher circulating glucocorticoids. In the soleus muscle, despite administration of the same cortisol dose to adrenalectomized weight bearing and suspended rats, the enzyme activity was 59% greater in the unloaded muscle. This finding suggested a greater sensitivity of this muscle to glucocorticoids, as suggested by an earlier observation of increased numbers of receptors after unloading (Steffen and Mussachia, The Physiologist 25 (suppl.) S151-S152, 1982).

In muscle, branched-chain amino acids serve as the primary donor of a-amino groups for glutamate, and hence for production of alanine and glutamine. In soleus or extensor digitorum longus muscles, unloading lead to faster degradation of leucine, isoleucine and valine. Although adrenalectomy abolished this difference in the extensor digitorum longus muscles, it had no effect in the soleus. Cortisol administration increased degradation of leucine to the same extent in extensor digitorum longus muscles of weight bearing and suspended animals. Therefore, higher circulating glucocorticoids in suspended rats may account for this difference in branched-chain amino acid degradation in this muscle. In contrast, the soleus muscle of adrenalectomized suspended rats was more responsive to cortisol administration (as noted for glutamine synthetase). While greater numbers of receptors may be important in the unloaded soleus muscle, the data for untreated adrenalectomized rats suggest that some other factor may be important, as well, for the increased leucine degradation following unloading of the soleus muscle.

In summary, these results showed several important findings. 1) Metabolic changes in the extensor digitorum longus muscle of suspended rats are due primarily to increased circulating glucocorticoids. 2) Metabolic changes in the soleus muscle due to higher steroid levels are probably potentiated by greater numbers of steroid receptors. 3) Not all metabolic responses of the soleus muscle to unloading are due to the elevated levels of glucocorticoids or the increased sensitivity of this muscle to these hormones.

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