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Influence of Atropine on Atrophy of Denervated Skeletal Muscle of the Rat.

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According to Levine *et al.*,[1] atropine decreases considerably the rate of atrophy of a denervated skeletal muscle of the rat. Since these authors used only the weight loss of the muscle as an index for the degree of atrophy, it was desirable to find out also if atropine diminishes the rate of the loss in contractile power per weight unit of the muscle and of the diminution in its birefringence.[2]

Methods. In 3- to 5-months-old rats (from our own colony of a mixed strain), the sciatic nerve of one side was resected for 1 cm under aseptic conditions. Litter mates were arranged in pairs, one rat serving as control, the other being treated immediately with atropine. The doses employed for the main series were the same as by Levine *et al.*, namely 15 mg/100 g rat daily, divided into 3 equal doses given subcutaneously as a 1% solution in the morning, afternoon and evening until the end of the experimental period.[3] After 2 weeks, the contractile power of both gastrocnemius-solei was determined, the animals killed, the muscle weight and birefringence determined with methods employed in previous investigations.[2]

Results. Although the weight loss determined as the percentage difference between denervated and normal muscle was distinctly less for the atropine treated rats than for the controls, no significant differences were found between contractile power or birefringence of the denervated muscles of the treated rats in comparison with the denervated muscles of the control. For both the treated rats and the controls, the difference in contractile power or birefringence between denervated muscle and normal muscle were of the same magnitude as reported previously for denervation atrophy of 2 weeks' duration in normal rats.[2] However, the weight of the normal muscle of the treated rats was always considerably less than that of the control litter mates (Table I). This difference in the weight of the normal muscles of control and treated rats, is probably due to the fact that from the beginning of the atropine treatment, the treated rats develop distinct anorexia and, in consequence, develop a severe cachectic inanition. In Table I, the initial and the final weights of the treated and the control rats are tabulated with the weights of their normal and denervated gastrocnemii at the end of the experimental period. In calculating the percentage differences between treated and control rats and between their normal muscles, the small initial difference in rat weights has been adjusted. As in all types of weight loss, also in this inanition, the percentage difference between normal muscle of treated and control rats is somewhat larger than the percentage difference between the total weights of the rats. Since the normal muscles of treated rats show such a distinct inanition weight loss, a calculation of the weight loss due solely to denervation by comparing denervated with normal muscle of the same treated rat would be only permissible if in simultaneous denervation and inanition atrophy the two rates of weight loss add algebraically. For various biological reasons this is not probable, and Hines and Knowlton[4] have demonstrated that fasting after denervation produces less weight loss than

[1] Levine, R., Goodfriend, J., and Soskin, S., *Am. J. Physiol.*, 1942, **135**, 747.

[2] Fischer, E., *Am. J. Physiol.*, 1939, **127**, 605; 1940, **131**, 156; PROC. SOC. EXP. BIOL. AND MED., 1941, **47**, 277.

[3] Soskin, S., personal communication.

[4] Hines, H. M., and Knowlton, G. C., *Am. J. Physiol.*, 1935, **110**, 8.

TABLE I.

Rats treated daily with atropine. Doses in mg/100 g rat. Odd experimental numbers controls; even numbers treated rats (figures given only for one litter); m, the means for 8 rats each. Duration of denervation and treatment, 2 weeks. The figures for loss or gain designate the percentage difference between treated and control rats corrected for the small difference in initial weight.

Exp. No. and dose of atropine	Animal wt Initial, g	Final, g	Loss, %	Gastrocnemius Normal, g	Loss, %	Denervated, g	Atrophy, %	Loss, %	Atrophy inanition correct., %	Gain, %	Theoretical atrophy inanition + denervation, %
15 mg											
A 1	245	269		1.376		.800	41.9		41.9		
A 2	234	166	28.1	1.052	19.8	.696	34.8	16.9	51.6	23.2	61.7
A 3	238	245		1.572		.847	46.1		46.1		
A 4	235	184	24.9	.941	39.3	.706	25.0	45.6	54.4	18.0	85.4
m (control)	251	267		1.486		.787	47.1		47.1		
m (atrop.)	250	197	26.0	1.017	31.3	.700	31.2	33.7	52.7	11.9	78.4
10 mg											
m (control)	300	302		1.806		.938	48.1		48.1		
m (atrop.)	306	266	13.6	1.443	21.6	.822	43.1	10.4	52.2	14.7	69.7
5 mg											
m (control)	269	278		1.620		.882	45.5		45.5		
m (atrop.)	267	262	5.8	1.484	7.8	.809	45.4	0.2	49.7	9.2	53.3

the sum of the weight losses due to fasting alone and denervation alone.

From a practical standpoint, a denervation atrophy delaying drug is only of value if the weight difference between denervated muscle of the treated rat and normal muscle of the control is less than the difference between denervated and normal muscle of the control. In the next to the last vertical column of Table I this method of calculation was used after adjusting the weight of the normal muscle of the control in proportion to the initial difference in rat weights. It is obvious from these figures that atropine does not decrease, but actually increases the rate in weight loss after denervation. However, this increase is less than the algebraic sum of atropine and denervation weight loss (last column Table I). To make sure that the simulated beneficial effect of atropine is only due to the atropine inanition, in 2 further experimental series only ⅔ or ½ respectively, of the original dose of atropine was administered. The mean values for these series are found also in Table I. It is obvious that as soon as the inanition effect of atropine becomes small the simulated atrophy retarding effect of atropine disappears. This explains also why Levine *et al.* found that only extremely large doses of atropine were effective in their experiments.

Summary. Atropine does not retard the diminution in contractile power per weight unit nor the diminution in birefringence in denervation atrophy of rat muscle. The apparent retardation of weight loss of the denervated muscle in atropine-treated rats found by comparing the percentage weight difference between normal and denervated muscle of treated rats with the difference found in controls, does not indicate a true atrophy retardating effect of atropine. Continuous administration of atropine in such large doses produces cachectic inanition of the rats, in consequence of which the weight difference between denervated and so-called normal muscle is diminished, since the latter weighs considerably less than a truly normal muscle.