FACTORS OTHER THAN ACTIVE RELAXATION RESPONSIBLE FOR THE LENGTHENING OF UNLOADED UNSTRIATED MUSCLE

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Unloaded unstriated muscle relaxes under certain conditions (Singh and Singh, 1948 *a*, 1949 *a*, 1950 *a*, *b*, 1951 *a*, *b*, *c*, 1952 *a*; Singh, 1951). If adrenaline is added to saline in which are immersed unloaded transverse pieces of the stomach muscle of the frog *Rana tigrina*, or virgin guinea pig's uterus, they lengthen; unloaded dog's stomach muscle relaxes after stimulation with electric current and chemicals. This might be due to two causes: (*a*) active relaxation, (*b*) something pulling it out, such as elasticity of connective tissues or membranes, etc. If the latter explanation is correct, it means the muscle is loaded and relaxation really passive.

There are certain observations which show that relaxation in the above instance is active (Singh and Singh, 1952 *a*):

(1) Unstriated muscle, if loaded, and the load exceeds a certain minimum, lengthens (Winton, 1930). If a force was always tending to pull it out, then the unloaded muscle should gradually lengthen when immersed in saline; but what happens is the opposite, so that any such force does not appear to be operative.

(2) Cyanide abolishes the relaxation, which is again partially restored with glucose (Singh and Singh, 1951 *b*). This shows that during relaxation metabolic processes are involved.

(3) An interesting property of unstriated muscle is that under certain conditions, loaded muscle lengthens, but not the unloaded one (Singh and Singh, 1952 *a*).

In the present research, this last property has been investigated.

Experimental

Two sets of experiments were performed. In the first set, the effect of asphyxia (by hydrogen) or sodium cyanide (1 in 10,000) on the normal tone of loaded and unloaded muscles was studied. In the second set, potassium contraction was first induced, and then the muscle asphyxiated or treated with

cyanide. The length of the unloaded muscle was measured before and during asphyxiation with hydrogen or after treatment with cyanide.

RESULTS

Effect of asphyxia or cyanide on normal tone.—These experiments were performed on dog's stomach muscle at various temperatures from 20 to 37° C., on frog's stomach muscle from 20 to 30° C., on fowl's gut from 20 to 37° C. and on guinea pig's uterus at the same temperatures. The length of the unloaded muscle was measured before asphyxiation by hydrogen or treatment with sodium cyanide (1 in 10,000), and at 5 minutes' intervals after beginning of asphyxiation or treatment with cyanide. This is important because loaded muscle may show contraction after preliminary relaxation on asphyxiation or treatment with cyanide (Singh, 1949), and if the observations are made at long intervals, then this preliminary relaxation might be missed.

The loaded and unloaded muscles differ markedly in their behaviour on asphyxiation or treatment with cyanide at different temperatures; the former relaxes readily at high temperatures, and the latter may do so only at low temperatures (20° C.). At temperature of 25° C. (10 experiments), 30° C. (10 experiments), 37° C. (10 experiments), unloaded dog's stomach muscles did not relax at all; they rather contracted slightly. Loaded muscles relaxed readily and then tended to contract. At 20° C., in 14 out of 34 experiments, unloaded muscles relaxed by about 2 to 20 p.c.; loaded muscles also relaxed at this temperature, but less readily than at higher temperatures. Unloaded frog's stomach muscle did not show any significant relaxation at 20° C. (12 experiments), 25° C. (12 experiments) and at 30° C. (12 experiments); loaded muscle relaxed readily. Unloaded fowl's gut relaxed by 20 p.c. in one out of 12 experiments at 37° C., and did not show any significant relaxation at 30, 25, and 20° C.; loaded muscle relaxed profoundly, especially at 37° C. Unloaded guinea pig's uterus did not show any relaxation at 20, 25, 30 and 37° C. (2 experiments each); loaded muscle relaxed readily.

Effect of iodoacetic acid on normal tone.—Sodium iodoacetate (1 in 10,000), causes relaxation of fowl's gut, frog's stomach, guinea pig's uterus at 37° C. if loaded, but not if unloaded (6 experiments each). Dog's stomach muscle also relaxes if it shows lactic tone.

Effect of temperature.—Gradual lowering of temperature from 37° C. to 25° C. or lower, causes relaxation of dog's stomach muscle, guinea pig's uterus, fowl's gut and human appendix if loaded, but not if unloaded. Frog's stomach muscle behaves similarly if the temperature is lowered from 30° C. to about 10° C.

Sodium azide also caused relaxation of loaded frog's stomach muscle, but not that of unloaded muscle at 25° C. (6 experiments).

Effect of asphyxia on the potassium contraction.—In dog's stomach muscle, tone was increased by replacing 40 p.c. of the sodium of the saline by potassium, and the above experiments were repeated. On asphyxiation or treatment with cyanide, loaded muscles relaxed but the unloaded ones did not do so at 37, 30 and 25° C. (12 experiments each). At 20 to 22° C. a few unloaded muscles also relaxed (Table I); loaded muscles also relaxed, but less readily than at higher temperatures.

TABLE I

Dog's stomach muscle. Effect of asphyxia (by hydrogen) and sodium cyanide (1 in 10,000) on the contraction produced by replacing 40 p.c. of the sodium of the saline with potassium

No. of experiments	Temperature °C.	Length in saline mm.	Length in potassium mm.	Length during asphyxia of duration			Length after aeration	Length in cyanide		
				5 min.	10 min.	15 min.		5 min.	10 min.	15 min.
1	20	59	55	55	55	56	56	55	55	54
2	20	44	40	39	39	39	39	39	39	39
3	20	41	39	39	39	39	39	39	39	39
4	21	56	49	50	48	45	46	46	46	46
5	21	53	50	52	53	53	54	53	53	53
6	21	55	52	..	..	..	..	55	55	..
7	22	49	44	44	45	45	45	45	45	43
8	22	48	42	42	42	42	42	42	42	41
9	22	43	41	..	..	..	..	42	42	42
10	22	56	53	54	54	54	54	53	53	52
11	22	35	32	32	32	32	32	32	32	32
12	22	45	42	..	..	..	..	42	42	42
13	22	40	38	..	..	..	..	39	39	39
14	22	43	40	..	..	..	..	42	42	42
15	22	55	49	49	49	49	50	50	46	47
16	22	33	30	..	..	..	..	30	30	30
17	22	41	39	..	..	..	..	39	39	39
18	22	51	42	..	..	..	..	43	44	44
19	22	41	39	..	..	..	..	39	39	39
20	22	42	39	..	..	..	..	38	38	38

DISCUSSION

These experiments clearly reveal that relaxation in unstriated muscle is of two kinds, one active and the other passive. Active relaxation is

decreased by all agencies that diminish metabolism; passive relaxation is affected oppositely. There must be, therefore, two systems in unstriated muscle, in one the relaxation being active and in the other passive (Singh and Singh, 1950 *b*, 1951 *d*, 1952 *b*; Singh, 1952, 1953). Relaxation of unloaded unstriated muscle at 20° C., must therefore be due to cessation of stimulation (Singh and Singh, 1952 *a*). These experiments therefore show that in unstriated muscle, both contraction as well as relaxation are energised. The metabolic mechanisms for contraction and relaxation are different, and they are differentially suppressed by cyanide. If the metabolic mechanism for contraction is suppressed, then the loaded muscle relaxes actively as well as passively, and the unloaded one only actively. If the metabolic mechanism for relaxation is suppressed also, then only the loaded muscle relaxes passively; active relaxation is absent. It is not possible to say whether cyanide can suppress only the mechanism for active relaxation; under such conditions, the muscle will relax neither actively nor passively on the addition of cyanide.

If both the systems are active at the same time, then the muscle would be contracting and relaxing at the same time. This should be distinguished from accommodation to the stimulus. Previously, we have described the inhibitory action of glucose on the mechanical response of unstriated muscle (Singh and Singh, 1948 *b*, 1949 *b*, 1950 *c*); this has been ascribed to the antagonism of glycolytic and non-glycolytic metabolic mechanisms. It is more likely due to increase of active relaxation during contraction. If this explanation is correct, then the inhibitory action of glucose should be present only in those muscles, which show active relaxation. Agencies that depress active relaxation would therefore enhance the mechanical response; this they may do so, also by diminishing accommodation (Singh and Singh, 1952 *c*).

Substances that diminish accommodation, also decrease the inhibitory action of adrenaline. These substances also antagonise active relaxation (Singh and Singh, 1949 *a*). It is therefore probable, that the inhibitory action of adrenaline in some muscles is due to active relaxation during contraction; this inhibitory action of adrenaline is therefore due to the contractile mechanism. Adrenaline may also inhibit through the excitatory mechanism only, as rabbit's gut, though very sensitive to adrenaline, does not relax actively.

When a muscle is contracting, its mechanical response is affected by three agencies: (1) the excitatory and the contractile processes (which cannot be easily dissociated); (2) active relaxation; (3) accommodation. Substances that stimulate metabolism will increase the mechanical response by increasing

the first process; substances that depress metabolism will do so by decreasing the second and third processes. Similarly, the metabolic stimulants will decrease the response by stimulating the second and third processes.

The two systems in unstriated muscle are probably represented by two different bonds in actomyosin. Bonds responsible for passive relaxation are dissolved by salts, nad those for active relaxation, are dissolved by urea. The former bonds are modified to produce twitch and lactic tone respectively. The latter bonds are modified to produce alactic tone and tone which is decreased by glucose or oxygen. There may still be further subdivisions to account for the various contractions of unstriated muscle.

Summary and Conclusions

(1) Substances that depress metabolism suppress relaxation of unloaded muscle and increase that of loaded muscle.

(2) It is therefore concluded that relaxation in unstriated muscle is of two kinds, one active and the other passive.

(3) Substances that increase metabolism may diminish the mechanical response, by simultaneously increasing active relaxation, while the muscle is contracting.

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