14757

Efficiency of Muscle Contraction Following Tetanic Stimulation.

S. A. Guttman and McKeen Cattell.

From the Department of Pharmacology, Cornell University Medical College, New York City.

The enhanced contraction of a muscle to single test shocks after tetanic stimulation of its motor nerve was first reported by Schiff.[1] Waller[2] observed an increase in the action potentials of a nerve subjected to tetanic stimulation. Hofmann[3] studied post-tetanic enhancement in muscle. Since the more recent work of Guttman, Horton, and Wilber[4] many publications have appeared on this subject. The phenomenon has been demonstrated in nerve, muscle, and ganglion. It occurs in muscle which has been either directly or indirectly stimulated, and in denervated and curarized muscle. The present study was initiated with the object of determining whether post-tetanic facilitation in striated muscle is related to an improvement in the efficiency of contraction.

Methods. The apparatus and technic employed was similar to that described by Cattell and Feit.[5] A double sartorius preparation from the frog (*Rana pipiens*) was set up on a thermopile and the response to maximal induced break shocks was photographed by means of an optically recording isometric lever. The thermopile-galvanometer system had a sensitivity such that heat resulting from a single twitch of the muscles produced a deflection of from 150-300 mm on a scale placed three meters from the mirror of a moving coil galvanometer (Zernicke Zc). The maximal deflection was taken to be proportional to the initial heat production. Changes in the efficiency of contraction were determined by changes in the ratio of the tension developed to the initial heat in individual twitches. The moist chamber was immersed in a water bath, the temperature of which was maintained at 22°C.

In all instances the muscles were immersed in Ringer's solution (NaCl 0.675%, $CaCl_2$ 0.020%, KCl 0.015%, phosphates 0.01% to give a pH value of 7.2) for at least one hour before making observations. The Ringer's solution was removed and the muscles were allowed to remain in moist oxygen for about half an hour before starting the experiment. This procedure tends to promote a uniformity of response and a steady galvanometer reading. The experiments were all performed in an atmosphere of moist oxygen. Maximal break shocks and a tetanizing current, applied for various lengths of time, which varied from 90 shocks per second to lower frequencies, were employed. The source of stimulation was either the secondary of an inductorium or a thyratron stimulator.

In all of the 24 experiments performed test shocks were given to determine the tension developed (T) and the initial heat production (H), and from these T/H values were calculated for individual twitches. The muscle was then subjected to a brief tetanus of a few seconds duration following which test shocks were delivered at various intervals. Heat measurements could not be made until about 3 minutes after each period of tetanus because of the rapid heating during tetanus and subsequent cooling. During cooling the galvanometer at first drifted rapidly and then more slowly. True stability of the galvanometer was generally not reached for at least 10 minutes after a tetanus but it was possible to correct for the slower type of decay. The drift during the 4-second period required for

1 Schiff, J. M., *Muskel und Nervenphysiologie Lahr*, 1858, 189.

2 Waller, A. D., *Phil. Trans. Roy. Soc., B*, 1897, **188**, 1.

3 Hofmann, F. B., *Arch. f. d. ges. Physiol.*, 1903, **93**, 186; 1903, **95**, 484; 1904, **103**, 291.

4 Guttman, S. A., Horton, R. G., and Wilber, D. T., Proc. Soc. Exp. Biol. and Med., 1936, **34**, 219; *Am. J. Physiol.*, 1937, **119**, 463; Horton, R. G., Wilber, D. T., and Guttman, S. A., *Am. J. Physiol.*, 1937, **119**, 338.

5 Cattell, McK., and Feit, H., *J. Physiol.*, 1937, **91**, 259.

the galvanometer to reach its maximum deflection resulting from the superimposed heat from the twitch was determined by recording the change during 6 five-second periods before a test shock and exterpolating to obtain the correction for the position at the end of the 4-second period. It is unfortunate that heat values could not be obtained immediately, since this fact prevented the study of the first part of the post-tetanic enhancement curve.

Results. Fig. 1 is a graph of a typical experiment in which the tetanus (about 50 per second for 30 seconds) produced enhancement. The twitch tension directly after the first tetanus was 29% greater than that developed prior to the tetanus. The heat production in the twitch 3 minutes after the tetanus, when the tension had fallen to about 12% above the pre-tetanic values, was 21% greater and the T/H ratio 10% below the pre-tetanic value. In the course of 25 minutes tension values gradually approached those of the pre-tetanic twitches. Heat values dropped rapidly reaching a low of 2.5% below the normal in 19 minutes. Correspondingly, the efficiency (T/H) rose from the initial 10% below normal to a peak of 10% above normal in 6 minutes after the tetanus and then gradually returned to the control value. Following the second period of tetanus an almost identical pattern was observed save that the low T/H values directly after the tetanus were not observed.

The result illustrated above is typical of the findings observed in post-tetanic enhancement in 14 experiments. From 4 to 6 minutes after tetanus the T/H values were depressed in the average 8.5% but then increased, generally within 1 to 3 minutes, to a peak average of 6% above the pre-tetanic level. Return ot T/H ratios to the original value generally occurred in from 20 to 30 minutes.

Fig. 2 is a graph showing the results in an experiment in which the muscle exhibited post-tetanic depression. Three series of tetanizing shocks were administered. The duration of the first was 10 seconds, the next 3 seconds, and the last 10 seconds. Following the first period of tetanus the twitch tension was 48% and the heat 41.6% of the pre-tetanic value, resulting in a T/H ratio 15% above the pre-tetanic level. These indices returned towards their respective pre-tetanic values as indicated in the graph. The changes following the two succeeding periods of tetanus were not as marked but followed the same pattern. The results described for this preparation are typical of 10 experiments in which post-tetanic depression was observed, *i.e.*, the depressed response shows a slightly improved T/H ratio, which gradually returns to the control value over a period of from 5 to 10 minutes. This is in line with the effect of activity on the efficiency of contraction reported by Cattell and Feit.

Discussion. From these data it is apparent

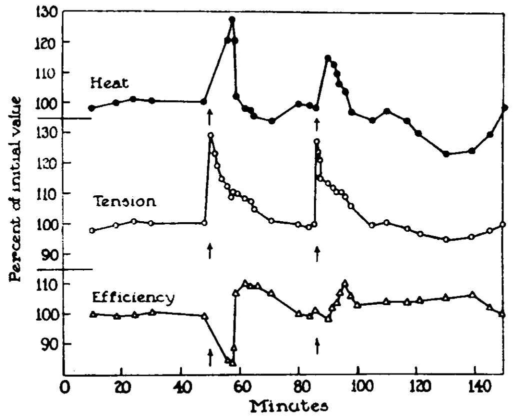

FIG. 1.
The effect of brief periods of tetanus (at arrows) on the twitch tension initial heat and efficiency of contraction in a muscle showing post-tetanic enhancement.

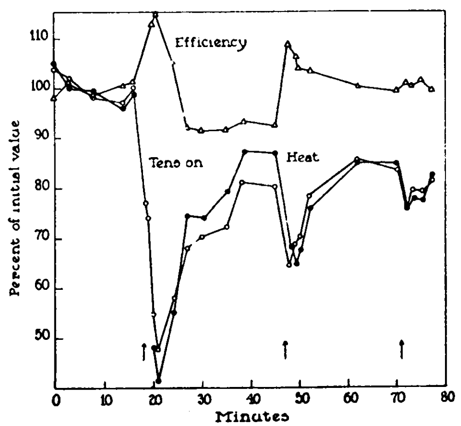

FIG. 2.
The effect of brief periods of tetanus (at arrows) on the twitch tension initial heat and efficiency of contraction in a muscle showing post-tetanic depression.

that enhancement of twitch tension produces a certain pattern of change in efficiency. The twitches directly following a tetanus are greatest and the decay has a linear relationship. While twitch responses occurring shortly after a period of tetanus show characteristic changes in efficiency, they are not large in comparison with the changes in tension. Enhancement, as measured by twitch tension, is at first associated with a small decrease in efficiency and then a small increase in efficiency with a return to pre-tetanic levels. On the other hand, when the post-tetanic twitch is depressed, the efficiency is temporarily increased.

Post-tetanic twitch responses may show enhancement or depression with tensions of 50% greater to 50% less than the pre-tetanic values. The initial heat developed with each twitch varies with the tension so that the efficiency of contraction is not markedly altered, and cannot account for the changes in tension.

Summary. 1. The twitch tension and the initial heat developed was determined in frog double sartorius preparations during the period following tetanic stimulation. 2. When enhancement occurs there is at first a small decrease in efficiency, followed by a rise slightly above the original level, with return to the pre-tetanic level, as the enhancement subsides. 3. When post-tetanic depression occurs there is a small increase in efficiency followed by a gradual return to the pre-tetanic value. 4. The efficiency changes are small in comparison with the changes in twitch tension, and thus cannot account for the changes in the mechanical response.

14758

Estimation of the Anticephalin Activity of Whole Blood.

Leandro M. Tocantins.

From the Division of Hematology, Department of Medicine, Jefferson Medical College, Philadelphia, Pa.

The demonstration of anticephalin* activity in plasma is rendered difficult by a number of interfering factors. The time and manipulations involved in the separation of the plasma, the addition of anticoagulants and the subsequently required recalcification, the inactivating effect of contact with glass or similar surfaces are among some of the factors that interfere with the accurate testing of this activity in plasma.[1,3] Since anticephalin manifests itself chiefly during the initial stages of coagulation (before the conversion of prothrombin), any imperfections in the collection of blood or in its mixture with the anticoagulant will affect the results. It would seem desirable, therefore, that the activity be estimated without the use of anticoagulants, and as soon as the blood is collected.

As shown elsewhere[4] the response of a given plasma to activation by cephalin, the magnitude of the clot-decelerating effect of incubation of the plasma with cephalin, and the difference between the rate of coagulation of plasma on glass and on paraffin or lusteroid

* The term *cephalin* is used to designate the alcohol-insoluble lipid fraction extracted with ether from acetone-dried human brain.[1] Cephalin suspensions so obtained are obviously not pure. Most indications point to a cephalin as the active fraction of the thromboplastic lipoprotein[2] and it may so be considered until convincing evidence to the contrary is available. The term *anticephalin* is intended to designate that activity of plasma directed against the thromboplastic action of cephalin.

1 Tocantins, L. M., Proc. Soc. Exp. Biol. and Med., 1943, **54**, 94.

2 Quick, A. J., *Hemorrhagic Diseases and the Physiology of Hemostasis,* 1942, p. 68.

3 Tocantins, L. M., *Am. J. Physiol.,* 1943, **139**, 265.

4 Tocantins, L. M., *Am. J. Physiol.,* in press.