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THE RELATION OF CONTRACTURE TO THE INCREMENT IN THE RESTING HEAT PRODUCTION OF MUSCLE UNDER THE INFLUENCE OF POTASSIUM

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It has been shown that the heat production of the sartorius muscle of the frog is increased by potassium chloride in concentrations of four to ten times that found in normal Ringer's solution [Solandt, 1936]. This increment was considered to be independent of any shortening process and was described as an increase in the resting metabolism. In higher concentrations there was no liberation of heat in excess of normal unless a contraction occurred. Hegnauer *et al.* [1934], on the other hand, state that the rate at which oxygen is taken up by the muscle under the influence of potassium is only increased by concentrations which give rise to shortening. In view of these findings it appeared advisable to extend the study of the changes in heat production due to potassium in order to determine the possible relationship between increased metabolism and mechanical changes induced in the muscle.

Method

The rate at which heat was liberated by the muscle was determined in the manner described by Solandt [1936]. The double sartorius preparation from frog (*Rana pipiens*—Canadian) was used throughout. This was mounted on a Downing-Hill muscle thermopile which was then enclosed in a brass chamber. It was set up so that the muscle supported a light lever by a thread which passed through a tube fixed in the upper part of the instrument. The latter was immersed in a water bath at 29·4° C., and arrangements were made for running solutions in and out of the chamber from glass containers kept in the same bath. As the solutions were thus always at bath temperature they did not upset the thermal equilibrium of the thermopile system to any marked extent.

The flow of current set up in the thermopile circuit due to the heat liberated by the muscle was recorded by a d'Arsonval moving-coil galvanometer. The millimetre scale on which the deflexion of the reflected beam was recorded was calibrated in absolute units of heat. This was done by passing condenser discharges through filter paper (soaked in Ringer's solution) which was substituted for the muscle.

In performing an experiment the apparatus was set up as described, Ringer's solution was run into the chamber and kept aerated with oxygen. At the end of 1 hr. the solution was removed, and after 2 min. a reading of the resting heat was taken. The Ringer's solution containing an increased amount of potassium was now added, left for 3 min. and then removed. A reading was again taken 2 min. after removal. The procedure was repeated at regular intervals during the period of the experiment.

The Ringer solution used as normal contained 0·625 g. NaCl, 0·015 g. KCl, 0·020 g. $CaCl_2$ made to 100 c.c. with distilled water. The amount of potassium was increased as desired by adding a calculated amount of isotonic aqueous KCl solution.

The mechanical changes induced in the muscle by the concentrations of K studied (1–60 times that of normal Ringer's solution) were determined in an independent series of experiments. The procedure here was to set up a double sartorius preparation horizontally in Ringer's solution with just sufficient tension applied to keep it extended. Using a dissecting microscope a suitable blood vessel in the muscle was sharply focused and marked by a cross-hair in the eyepiece. In this way when a solution of increased potassium concentration was added the slightest amount of shortening could be observed directly, and twitching of single fibres could be detected.

Results

Fig. 1 shows the changes in the rate at which heat is liberated by muscle during the time it is exposed to solutions having potassium concentrations of 7, 8, 9, 10, 12 and 22 times that of normal Ringer. The observed galvanometer deflexions at intervals of 6 min. are plotted for a K concentration of 7 times normal, as an example of the regular rise and fall obtained in these experiments. Although each curve shown was the result of one experiment, essentially the same results were obtained on at least three occasions for each K concentration represented. The plotted results show that the resting heat production was increased by potassium. This was true for all K concentrations from 4 to 60 times that of normal Ringer. There was a subsequent depression in heat production which was marked in the case of the solutions rich in K. For the solutions with K concentrations less than 12 times normal the resting heat production did not return to a normal value during the experiment (5 hr.) although there was a steady retreat from the maximum in all cases.

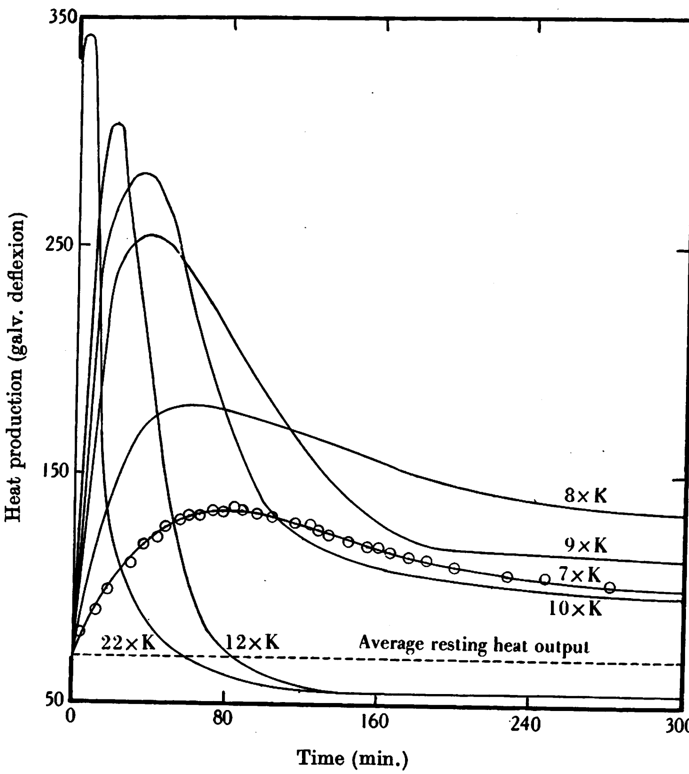

Fig. 1.

For concentrations of K from 4 to 6 times that of Ringer the effects were variable. There might be a slow steady rise during the 5 hr. of the experiment or a maximum might be attained before that time. Occasionally no rise took place for a variable initial period, after which an abrupt rise to a maximum would occur. For concentrations over 6 times normal, the responses were more consistent as represented in Fig. 1. From these curves it is evident that the increase in heat production proceeds more and more rapidly as the concentration is raised, and that at the same time the subsequent fall is hastened. Fig. 2 shows how the time to reach a maximum decreases as the concentration is raised.

The value of the maximum rate of heat production is shown in Figs. 1 and 2 as increasing rapidly with increasing strengths of K up to 9 times normal and at a slower rate thereafter up to 22 times the K concentration

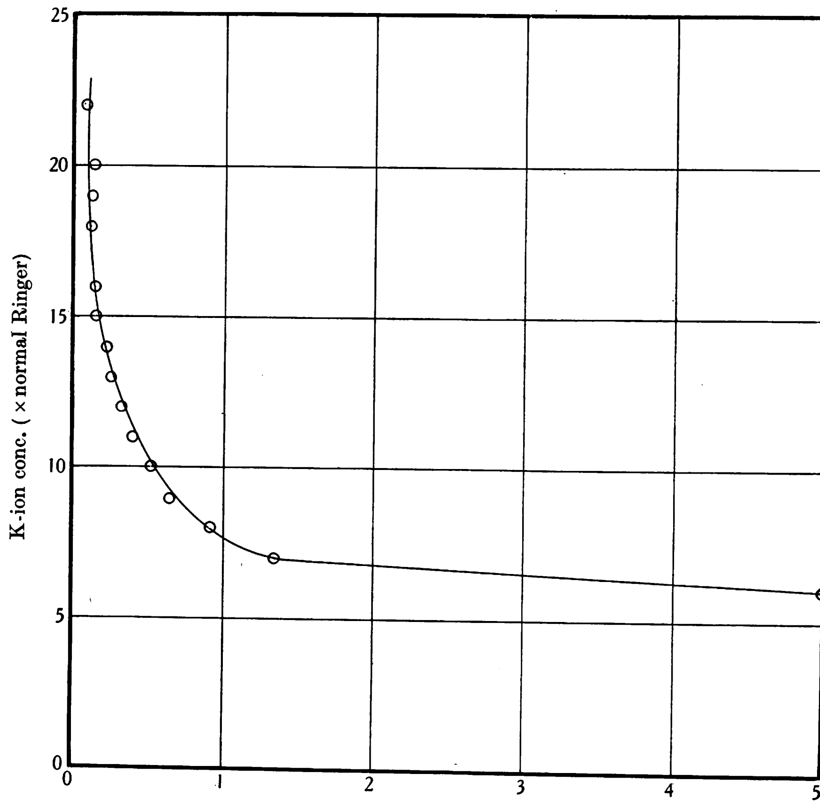

Fig. 2.

of normal Ringer's solution. In concentrations of over 22 times normal, the maximum had already been attained before a reading could be made.

Although there is this general correlation between the maximum level of heat production and the strength of K used, the individual results vary so much that it is evident that some other factor, uncontrolled in these experiments, must be operating. In preparing the curves of Fig. 1, the observed values were adjusted to a common initial average rate of resting heat production.

It is of interest that the time course of the rise and fall of metabolism was not subject to the variation shown by the initial levels of resting heat production.

In addition to the liberation of heat shown in Fig. 1, it was found that there was a brief explosive outburst of heat occurring immediately the K solution was added. This was first recognized at the higher concentrations when it was noticed that during the 2 min. before taking the first reading the galvanometer beam first fell from a high value and then rose to reach the value plotted in the curves of Fig. 1. On investigating further it was discovered that though decreasing in size with decreasing concentration, this initial liberation of heat could still be recognized at 8 times the normal concentration of K. The amount of heat liberated in this early rise increased as the concentration of K was raised up to the point where it could no longer be separated from the secondary delayed increase.

To determine if the secondary rise was the direct result of the early brief increase the KCl solution was replaced after the first 5 min. by the original Ringer which had been kept in a separate container in the bath, and now the metabolism returned directly to the original level within 10 min. Evidently, then, the secondary rise is dependent on the continued action of the high concentration of K.

The average resting value of heat production was 5·91 millicalories per g. per min. at 29·4° C. This varied from 3·75 to 9·20 in a series of 14 determinations.

The mechanical changes in the muscle were observed as described. In Ringer solution the isolated muscle occasionally showed fibrillar twitchings, 1 to 3 per min., throughout the first hour it was observed. With concentrations of K up to 4 times that in Ringer's solution no increase in the amplitude or frequency of the twitches occurred. Where twitching had been present in Ringer's solution it soon ceased under the influence of the increased strength of K. Beginning at a concentration of 5 times normal it was found that a brief series of twitches occurred when the solution was added. When these disappeared no further change was observed during the remainder of the hour. The twitches became more frequent and more numerous as higher concentrations of K were used. In all cases up to concentrations of 60 times normal all twitches ended within 4 min. The original length of the muscle was regained with the lesser concentrations, 15 to 20 times normal, immediately all the twitches ceased, and no shortening occurred in the succeeding hour. With higher concentrations there was a variable amount of residual shortening which passed off in 5 to 40 min.

Discussion

The above results indicate that K in excess of 4 times that of normal Ringer leads to two periods of increased metabolism. These are an immediate increase which in every case attains a maximum and falls rapidly towards zero within the first 4 min., and a delayed increase which has the variable time course shown in Fig. 1. Correlated in time with the initial phase of increased heat production are the twitches induced in the muscle by the stimulating action of the K, and they would appear to account for this increase in metabolism. No mechanical change could be observed in the muscle, however, to account for the delayed rise so that this is apparently a result of a stimulation of resting metabolism. As the latter was shown to depend on the continued action of K-rich Ringer's solution it cannot be simply an evidence of the recovery heat due to the initial twitches.

Hegnauer *et al.* [1934] showed that the oxygen consumption of the frog's muscle was increased by treating it with K, and that during the first hour the maximal increase was produced by a concentration of 100 mg. p.c., i.e. by 7 times the amount in Ringer. If the amount of heat liberated during the first hour is determined by measuring the areas under the curves of Fig. 1, we obtain results which may be considered as comparable, i.e. for the first hour the maximum increase is produced by 10 times the concentration of K in normal Ringer's solution.

The shape of the curves of Fig. 1 explains why Solandt [1936] failed to demonstrate any increment in resting heat production with high K concentrations. The technique used at that time would not detect a change in heat production as ephemeral as is the increment in resting heat production due to these high K concentrations.

Comparing the present work with the curves obtained by Fenn [1931], the changes in heat production may be considered as tending to parallel the changes in oxygen consumption when the muscle is treated with increasing amounts of K. Since Hegnauer *et al* [1934] were able to demonstrate a direct relationship between the oxygen utilized and the changes in phosphocreatine content of the muscle, it is probable that the increased heat production, like the increased oxygen utilization, is related to the breakdown of phosphocreatine and that a decrease in heat production similarly is related to a resynthesis of this compound.

The demonstration of the two phases of increased metabolism induced by K and their tendency to occur simultaneously in higher concentration may explain why chemical stimulation of muscle using isotonic potassium sulphate was found to be associated with a higher oxygen consumption [Fenn, 1931] than electrical stimulation. The oxygen consumption for a given tension induced by K stimulation would be made up of the increase due to the shortening, and the increase in the so-called resting metabolism.

Summary

The increased heat production and the mechanical changes occurring in the frog's sartorius muscle when treated with potassium in concentrations from 1 to 60 times that of normal Ringer were studied. Two phases of increased metabolism were demonstrated, one associated in time with the twitching which occurred during the first 4 min. after immersion, the other appearing after this while the muscle is apparently inactive. The amount of heat liberated in the first 4 min. increases with the increase in the number and strength of the twitches induced as the K concentration is raised above four times the normal. The rate at which the so-called resting metabolism rises to a maximum and subsequently falls becomes progressively more rapid and the level attained is increased as the concentration is raised from 4 to 60 times that of Ringer.

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