Role of Adrenaline and Noradrenaline in Chemical Regulation of Heat Production

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ABSTRACT

HSIEH, A. C. L. AND L. D. CARLSON. Role of adrenaline and noradrenaline in chemical regulation of heat production. Am. J. Physiol. 190(2): 243-246. 1957. - Cold-adapted spinal rats showed a greater increase in oxygen consumption following adrenaline than did warm-adapted ones. Thyroidectomy reduced the responses of warm- and cold-adapted spinal rats to about the same levels. In curarized rats, exposure to cold resulted in a greater increase in oxygen consumption and lower blood glucose concentration than adrenaline injection did. While noradrenaline had little effect in warm-adapted rats, there was a marked calorigenic response in cold-adapted rats. The results indicate, in addition to the increased calorigenic action of adrenaline in cold-adapted rats, a greatly increased calorigenic response to noradrenaline. The possibility that noradrenaline may be the mediator in chemical regulation of heat production is discussed.

COTTLE and Carlson (1), by exposing curarized rats to cold, have demonstrated that cold-adapted rats have an increased ability to produce heat by chemical regulation. The increased calorigenic effect of adrenaline in cold-adapted rats (2), forms an attractive explanation for this increased potential for chemical regulation. Since the term 'chemical regulation' has been used to imply the production of heat by means other than muscular contraction, the activity which follows the administration of adrenaline to unanesthetized rats (3, 4) complicates application of such results to this question. Therefore, in our experiments, the effects of adrenaline have been tested under conditions of minimal muscular activity after spinal transection or curarization. Changes in oxygen consumption and blood glucose concentration were the indices used.

Although noradrenaline has little calorigen-...
TABLE I. EFFECTS OF ADRENALINE ON OXYGEN CONSUMPTION AND BLOOD GLUCOSE OF SPINAL RATS*

<table>
<thead>
<tr>
<th></th>
<th>Before adrenaline</th>
<th>Maximum response</th>
<th>Increase</th>
<th>% Included</th>
<th>40 Min. after adrenaline</th>
<th>Before adrenaline</th>
<th>40 Min. after adrenaline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold-adapted</td>
<td>950±43</td>
<td>1710±60</td>
<td>760±130</td>
<td>80</td>
<td>1400±100</td>
<td>157±11</td>
<td>287±43</td>
</tr>
<tr>
<td>Warm-adapted</td>
<td>640±44</td>
<td>950±140</td>
<td>310±120</td>
<td>48</td>
<td>800±90</td>
<td>158±8</td>
<td>340±35</td>
</tr>
<tr>
<td>Cold-adapted thyroidectomized</td>
<td>490±40</td>
<td>660±60</td>
<td>170±30</td>
<td>35</td>
<td>610±70</td>
<td>156±12</td>
<td>283±30</td>
</tr>
<tr>
<td>Warm-adapted thyroidectomized</td>
<td>370±32</td>
<td>490±50</td>
<td>120±25</td>
<td>32</td>
<td>490±50</td>
<td>106±46</td>
<td>303±40</td>
</tr>
</tbody>
</table>

± = Standard deviation; n = 5.
* These experiments were conducted at a room temperature of 30°C ± 1°C.

After anesthetization the trachea was cannulated, and the spinal cord was transected at the level of C8. Respiration was maintained artificially, and oxygen consumption was recorded every 10 minutes. After 2 hours, allowed to permit the animal to recover from the operation, adrenaline chloride (Adrenalin, Parke-Davis) 0.2 mg/kg, was injected intramuscularly. The oxygen consumption was followed for 3 hours. Twenty minutes before and forty minutes after the injection of adrenaline, 0.1 cc blood was withdrawn from the tail, and the glucose concentration was determined by a colorimetric method (10).

Eighteen curarized cold-adapted rats were used to compare the metabolic effects of cold exposure and a single injection of adrenaline and noradrenaline. In six experiments the room was cooled to 5°C ± 1°C. In 12 experiments the room was maintained at 30°C ± 1°C. Six of these rats received adrenaline chloride, 0.2 mg/kg; the remaining rats received l-noradrenaline (Levophed, Winthrop-Stearns), 0.2 mg/kg.

RESULTS

After injection of adrenaline the oxygen consumption of all the rats increased (tables 1 and 2). This increase reached a maximum about 15 minutes after the injection, and consumption returned to initial levels about 100 minutes later. The intact, cold-adapted rats showed the greatest increase in oxygen consumption. In the thyroidectomized groups, the increase was about the same regardless of previous cold exposure, and less than that in the intact cold-adapted rats.

The initial glucose levels of the four groups of spinal rats (table 1) were not significantly different. Forty minutes after adrenaline, blood glucose concentration of all the rats increased similarly, and there was no significant difference between groups.

The initial glucose concentrations of the curarized rats (table 2) were considerably higher than those found in the spinal rats. This difference may have resulted from a greater initial release of adrenaline in the curarized rats. On exposure to cold, the curarized rats increased their oxygen consumption, but there was no significant change in blood glucose levels. Adrenaline was followed by a somewhat smaller rise in oxygen consumption and a 50% rise in blood glucose concentration. After injection of l-noradrenaline the increase in oxygen consumption was much greater than that following either adrenaline or cold exposure; the blood glucose levels, however, did not change significantly.

The time course of the response in oxygen consumption following a single injection of l-noradrenaline is given in figure 1. The oxygen consumption of the warm-adapted group increased very little. The possibility that the results were affected by an interaction between l-noradrenaline and the d-tubocurarine used in these experiments was ruled out by the finding that noncurarized, cold-adapted rats increased oxygen consumption from 1040 cc/hr/kg to 1420 cc/hr/kg.

TABLE 2. EFFECTS OF COLD EXPOSURE, l-NORADRENALINE AND ADRENALINE ON BLOOD GLUCOSE AND OXYGEN CONSUMPTION OF CURARIZED COLD-ADAPTED RATS

<table>
<thead>
<tr>
<th></th>
<th>50 Min. Cold Exposure</th>
<th>Max. O2 Consum.</th>
<th>40 Min. After Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose, mg %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold</td>
<td>284±40</td>
<td>307±36</td>
<td>415±45</td>
</tr>
<tr>
<td>Adren.</td>
<td>280±35</td>
<td></td>
<td>269±28</td>
</tr>
<tr>
<td>N-Adren.</td>
<td>268±50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oxygen consump., cc/hr/kg</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold</td>
<td>1250±100</td>
<td>1500±100</td>
<td>1430±110</td>
</tr>
<tr>
<td>Adren.</td>
<td>1200±90</td>
<td>1560±85</td>
<td>1430±110</td>
</tr>
<tr>
<td>N-Adren.</td>
<td>1250±110</td>
<td>2410±180</td>
<td>1470±100</td>
</tr>
</tbody>
</table>

± = Standard deviation; n = 6.
ADRENALINE AND NORADRENALINE IN HEAT PRODUCTION

FIG. 1. Effects of L-noradrenaline, 0.2 mg/kg, on the oxygen consumption and rectal temperature of cold-adapted rats (solid dots) and warm-adapted rats (open circles). Experiments were conducted at 30°C ± 1°C. L-noradrenaline was injected intramuscularly at the point indicated by the arrow. Vertical bars indicate the standard deviation. Each point represents the mean of 4 experiments.

± 50 cc/hr/kg3/4 to a maximum of 2153 ± 200 cc/hr/kg3/4 after L-noradrenaline (Hsieh and Carlson, unpublished data).

DISCUSSION

The oxygen consumptions following injection of adrenaline agree with the findings of Ring (2) for intact rats and indicate that the enhanced calorigenic effect of adrenaline in rats is mainly an increase in heat production by chemical regulation. A mechanism by which the potential for chemical regulation could be increased in cold-adapted rats has been suggested and discussed in a previous paper (9).

The blood glucose measurements following injection of adrenaline (table 1) can be taken to indicate that the glucogenic action of adrenaline in rats is not affected by cold adaptation or by thyroidectomy. The results can also be explained on a basis of coincident alteration of glucose utilization and glucogenesis. Thus, if both the glucogenic action of adrenaline and the ability to utilize glucose are increased in the cold-adapted rat, the blood glucose levels following a given dose of adrenaline would be the same in cold-adapted as in warm-adapted rats. Reduced glucose utilization, coupled with reduced glucogenic action of adrenaline, following thyroidectomy could also give similar results. There is evidence for increased glucose utilization in cold-adapted rats (11). The exact one-to-one relationship between glucogenic action of adrenaline and glucose utilization that would have to exist make it difficult to accept simultaneous increase and decrease of these factors as the explanation for the experimental results.

Adrenaline has been suggested as a possible mediator in chemical regulation (12). If release of adrenaline, either by the adrenal medulla or by the sympathetic nervous system, was the sole cause of the increase in metabolism on exposure to cold, then adrenaline given alone should simulate cold exposure. This is not the case. The two main discrepancies are: a) the persistence of a metabolic response to cold (9) with a reduction in response to adrenaline (table 1) after thyroidectomy, and b) the different effects of cold exposure and adrenaline on blood glucose levels (table 2).

The results with L-noradrenaline (table 2 and fig. 1) indicate that the main change in cold-adapted rats may be an alteration in the response of the tissues to this substance. The close similarity between the metabolic effects of L-noradrenaline and of cold exposure and the small amounts of L-noradrenaline required to produce these effects, strongly suggest that noradrenaline may be the mediator in chemical regulation of heat production.

The metabolic actions of adrenaline in normal animals, such as increased oxygen uptake and hyperglycemia, have been repeatedly observed to be greater than those of noradrenaline (13), pointing to a functional differentiation between the two substances. The surprising observation in this study is that L-noradrenaline exerts a strong calorigenic effect in cold-adapted rats without producing a hyperglycemia and no such effect is produced in nonadapted rats.

REFERENCES