THE ROLE OF METHYLAMPHETAMINE ON PLASMA HEXOSAMINE LEVEL UNDER STRESS

A.K. CHATTERJEE AND A. GHOSE
Jiwaji Research Laboratory, Dett. Defence Research Laboratory, Materials, Gwalior-2, India

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Hexosamine level in plasma (PHL) increases under different experimental and clinical stresses, such as, bone fracture, turpentine injections, sham operations, blood letting and epinephrine injection (1), hypothyroidism, administration of thyrotropic hormone (2), tuberculosis (3), pneumonia (4), rheumatic fever (5, 6), cancer (6-8) etc. PHL, however, decreases in lesser food intake (1) and in insulin administration (9).

In the present investigation the effect of a different type of body stress viz., work under low atmospheric pressure on PHL has been studied both with and without the administration of the antifatigue drug methylamphetamine.

Materials and methods: Male albino rats, weighing 200 to 250 g were divided into six groups of seven or more animals each. Animals were made to exercise on a treadmill moving at a speed of 1.25 miles per hour for a period of 50 minutes inside a chamber where a simulated low pressure equivalent to 10" of Hg vacuum and a flow of fresh air was maintained. Thus the pressure in the chamber was equivalent to that attained at 3,500 metres altitude. Animals were clamped in special type of holder so that only their front legs were made to work.

The grouping of the animals and their respective treatment were as follows:

- **Group 0** —without drug and without exercise under room condition.
- **Group I** —without drug and without exercise and exposed for 50 minutes under the low pressure.
- **Group II** —without drug but with the exercise under the low pressure.
- **Group III** —injected with 1.0 mg/kg body wt. of drug followed by the exercise in the low pressure.
- **Group IV** —injected with 2.0 mg/kg body wt. of drug, rest was the same as that of Group III.
- **Group V** —injected with 3.0 mg/kg body wt. of drug, rest was the same as that of Group III.
- **Group VI** —injected with 5.0 mg/kg body wt. of drug, rest was the same as that of Group III.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>No. of animals studied</th>
<th>Mean value</th>
<th>Stand. dev.</th>
<th>Stand. error</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Room condition</td>
<td>7</td>
<td>87.5</td>
<td>16.5</td>
<td>6.3</td>
</tr>
<tr>
<td>I</td>
<td>L.P.</td>
<td>10</td>
<td>72.4</td>
<td>4.7</td>
<td>1.5</td>
</tr>
<tr>
<td>II</td>
<td>L.P., E.</td>
<td>11</td>
<td>82.8</td>
<td>3.4</td>
<td>1.0</td>
</tr>
<tr>
<td>III</td>
<td>L.P., E and 1.0 mg/kg b.wt. drug</td>
<td>8</td>
<td>59.6</td>
<td>9.5</td>
<td>3.4</td>
</tr>
<tr>
<td>IV</td>
<td>L.P., E and 2.0 mg/kg b.wt. drug</td>
<td>12</td>
<td>67.8</td>
<td>12.4</td>
<td>3.6</td>
</tr>
<tr>
<td>V</td>
<td>L.P., E and 3.0 mg/kg b.wt. drug</td>
<td>11</td>
<td>65.6</td>
<td>13.1</td>
<td>4.0</td>
</tr>
<tr>
<td>VI</td>
<td>L.P., E and 5.0 mg/kg b.wt. drug</td>
<td>10</td>
<td>77.7</td>
<td>4.7</td>
<td>1.5</td>
</tr>
</tbody>
</table>

L.P. = low pressure; E = exercise; drug = methylamphetamine.

Test of significance of values obtained in different groups: 0 and I significant, 0 and II not significant, I and II highly significant, II and III highly significant, III and IV or V not significant, II and VI highly significant, III and VI significant, I and III significant, I and IV or V not significant, I and VI significant.
The drug, methylamphetamine hydrochloride was given intraperitoneally half an hour prior to putting in the low pressure chamber. Immediately on termination of the exercise, animals were taken out of the chamber, anaesthetized with ether and blood was withdrawn by a cardiac puncture and collected in a bottle containing sodium fluoride as anticoagulant. Total duration from termination of exercise to collection of blood was approximately 7 minutes. Boas (10) method was followed for the determination of hexosamine in plasma prepared from the blood samples.

Results and discussion: It may be noted in Table 1 that PHL is lowered under simulated low pressure condition (c.f. Groups 0 and I). Thus the simulated low atmospheric (LAP) condition does not influence the PHL in the same direction as is observed in different types of body stresses (1-8). The rise in PHL under different experimental body stresses (1) is rather slow and attains the peak in approximately two days. The significant lowering of PHL under the present experimental condition is rather quick (50 minutes). It is known that moderate anoxia causes an acceleration of the conversion of protein to carbohydrate (11). In the present exposure to LAP glycoprotein seems to have been affected in the same way as general body proteins.

No significant lowering of PHL was observed when the animals were made to work on treadmill under LAP (c.f. Groups 0 and II). The stresses produced by LAP and exercise seem to have opposing effects on PHL, LAP tending to decrease and exercise tending to increase PHL. None of these effects being predominant, PHL in Group II is higher than that of Group I and equal to that of Group 0.

With administration of 1, 2, 3 and 5 mg/kg body wt. of methylamphetamine PHL level is significantly lowered (compare PHL in groups III, IV, V and VI to that of Group II). The lowering is more in groups III to V (1-3 mg/kg body wt.) as compared to group VI (5 mg/kg body wt.). In group III (1 mg/kg body wt.) glucosamine level is significantly lower than that of the control group (Group I). But group VI (5 mg/kg body wt.) has a slightly but significantly higher PHL than that of the control group (group I). Thus the lowering effect of PHL by methylamphetamine in animals working under LAP shows a reversal tendency with increase in dose. Similar effect of methylamphetamine with increase in dosage has been observed in this laboratory in the lowering of blood lactic acid in albino rats under identical experimental conditions (unpublished work). Such type of reversal tendency of methylamphetamine with increase in dosage has also been reported in literature (12-14).

It is proposed that glycoprotein is utilized under low pressure to feed an increased glycolytic process. Manual work under low pressure like many other body stresses produces an inhibition of hexosamine conversion to glycolytic intermetabolites; which is removed and the process is even augmented under some specific concentration of the drug. Also, as a parallel similarity exists on the lowering of PHL and blood lactic acid under the situation (unpublished work from this laboratory), it is suggested that the lowering of hexosamine level after work in low pressure under the influence of methylamphetamine may be regarded as an indicator of the beneficial effect of the drug on exercise in low pressure.

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REFERENCES
EFFECT OF 3',5'-DIMETHYLPYRAZOLE ON COLONIC TEMPERATURE, PLASMA GLUCOSE, NEFA AND CORTICOSTERONE IN THE NON-ACCLIMATED RATS SUBJECTED TO COLD

YUICHI HASHIMOTO, TERUYUKI NISHIMURA, YOSHIKO KUROBE, YASUYUKI KOHASHI, MIYOKO KAKIE AND JOICHI ANDO
Department of Pharmacology, Osaka Medical College, Takatsuki, Osaka

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The increase in urinary catecholamine was observed in the animals subjected to cold (1, 2). Norepinephrine and epinephrine released from sympathetic nervous system and adrenal glands produced to increase plasma glucose and NEFA as fuels. The blockade of catecholamine action and the depletion of tissue catecholamine led to death during cold-exposure (3). Our previous experiments showed that in the course of prolonged cold-exposure the initial increase in plasma glucose gradually returned to the control level. On the contrary, the increased plasma NEFA was observed to be maintained during cold-exposure. This seemed to indicate that plasma NEFA is a favorable fuel for maintaining the body temperature in prolonged cold-exposure (4).

The present experiment was designed to know the changes in colonic temperature, plasma glucose, NEFA and corticosterone in the cold-stressed rats when the hormone sensitive lipase activity was inhibited by 3', 5'-dimethylpyrazole (DMP) and plasma NEFA decreased.

Male rats of Wistar strain weighing 200–220 g were used. One hour before cold-exposure, animals were intraperitoneally injected with 20 mg/kg of DMP and subjected to cold of −8°C for 1.5 hours in a cold room. After cold-exposure animals were decapitated and their blood collected into polyethylene tubes. The collected blood was centrifuged and the obtained plasma was served for the determinations of glucose by the glucose oxidase method, NEFA by the method of Dole (5) and corticosterone by the method of Guillen et al. (6). Colonic temperature was measured with a clinical thermometer. Statistical analysis of data was done according to the student t-test. Significant differences were given at the level of 5% or less than 5%.

The results were shown in Table 1. DMP gave no effects on colonic temperature, plasma glucose and NEFA in the intact rats except the significant increase in plasma corticosterone. The increase in plasma NEFA by cold-exposure was significantly inhibited in the DMP treated rats compared to the control group. On the contrary, the significant increase in plasma glucose was found in the DMP treated rats with cold-exposure. The increase in plasma corticosterone was small in the DMP treated plus cold-stressed rats and the corticosterone level was about the same in both the intact and DMP treated animals subjected to cold.