Abstract: Effect of immobilization stress was studied in male albino rats. Experimental rats (E) were restrained in close-fitting wiremesh cylinders. Control rats (C) were not subjected to restraint. Food and water were made available to C for all the 24 hrs while the E were given them for only 6 hrs daily. The initial lower food intake of E was later reversed to near normal levels. There was a steady fall in the body weights of E, while the C displayed a normal growth rate.

Cerebrum, cerebellum, pituitary and adrenals of E weighed significantly more. There was an apparent increase in the weight of thyroid. Gonads displayed no change in weight. The results indicate that chronic restraint causes loss of body weight inspite of a near normal food intake. It also produces an increase in the weight of brain, and certain endocrine organs.

Key words: stress, immobilization, pituitary, adrenal, body weights, food intake, brain, thyroid, gonads

INTRODUCTION

Stress can be productively considered as a "non-specific result of any demand upon the body". The release of adrenal hormones as one of the most important feature of animal responses to stress was well-established since the time of Selye (1). Studies suggest that the glucocorticoids are the adrenal steroids that mediate and/or modulate a range of responses to stress (2). Restraint stress constitutes a high stressor as it induces the release of a greater quantity of corticosteroids than either handling or isolation of animals (3).

A stressful situation induces the organism to mobilize not only the adrenal system but also the Central Nervous System (CNS) and the pituitary (4). Stress is known to decrease testosterone secretion as well (5). The present work therefore was undertaken to study the effects of chronic immobilization stress on food intake, body weight and weights of various endocrine organs in the rat.

METHODS

Adult male albino rats grown in our laboratory were used in this study. They were housed in individual polyvinyl cages. They were randomly assigned to two groups - control or chronic stress group. The latter group was immobilized in snugly-fitting wire-mesh cylinders which could be adjusted to prevent any movement of the body within. They
were immobilized for 18 hrs daily from 4 p.m. to 10 a.m. the next day, for 5 days a week for 4 weeks. The control rats were left undisturbed in their home cages all the 24 hours. They were given food and water ad libitum. The experimental rats were given food and water only for 6 hours from 10 a.m. to 4 p.m. every day.

Daily food intake and body weights were recorded between 10 and 10.30 a.m. At the end of the study period, all the rats were sacrificed and the various organs removed and weighed to the nearest 0.1 mg.

Data were analysed using student's 't' test and P value determined. P value of less than 0.05 considered significant.

Table I shows the mean food intake and mean body weights of control and experimental animals with S.E.M. and the P values. The control rats show a normal growth curve during the 4 weeks of study whereas the experimental rats showed a significant loss of body weight. Initially the stressed rats ate significantly less than controls but improved their food intake to near normal values towards the end of the study period (Fig. 1).

Chronic stress increased the weights of the organs studied (Table II). Both cerebrum and cerebellum increased in weight to a significant level. Pituitary weight was more and adrenal weight much more in stressed animals than in controls. There was an

### Table I: Effect of Immobilization stress on body weight and food intake in gms ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Food intake</th>
<th>Body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Experimental</td>
</tr>
<tr>
<td>Initial</td>
<td>13.75± 0.62</td>
<td>2.56±***</td>
</tr>
<tr>
<td>1st week</td>
<td>16.75± 0.37</td>
<td>6.06±****</td>
</tr>
<tr>
<td>2nd week</td>
<td>15.25± 2.62</td>
<td>8.0±**</td>
</tr>
<tr>
<td>3rd week</td>
<td>12.75± 0.03</td>
<td>10.37±*</td>
</tr>
<tr>
<td>4th week</td>
<td>15.0± 2.5</td>
<td>11.68±</td>
</tr>
</tbody>
</table>

P Value  
* < 0.05  
** < 0.02  
**** < 0.001

compared to control values  
compared to initial values
apparent increase in the weights of thyroid and gonads. Most of the gonads showed a marked decrease, but a few of them showed a well developed testes unilaterally. Therefore the mean gonadal weight showed a marginal increase.

**DISCUSSION**

In this study, the experimental animals subjected to prolonged immobilization stress, initially displayed a highly significant suppression of food intake, probably due to the release of corticotropin-releasing hormone (CRH) from the hypothalamus. Stress is known to stimulate limbic areas and pathways projecting from these areas to the hypothalamus stimulate CRH secretion into the pituitary-adrenal axis (4). CRH thus released may be a mediator of stress-related suppression of food intake (6). Britton et al have reported that CRH causes (i) decrease in the number of approaches to the food pellets and (ii) decrease in the amount of food eaten per approach (7). This and other reported data suggest that CRH may have an appetite-suppressing action (8, 9).

Although chronic stress decreases the body weight gain and food intake (10), certain amount of habituation is also noticed in rats exposed to prolonged stress (1). Whereas the control rats displayed a normal growth curve, the experimental animals showed a persistent decrease in their body weights and this was in spite of improvement in food intake over 4 weeks' period. The increased levels of corticosteroids (CS) during stress may be suppressing CRH release, which may explain the gradual improvement in food intake to near control values in the stressed rats. However, immobilization per se increases protein catabolism (11). Normal rats subjected to food deprivation can maintain growth

**TABLE II** : Effect of Immobilization stress on the weights of various organs in gms or mg/100 gms of body weight ± S.E.M.

<table>
<thead>
<tr>
<th></th>
<th>Cerebrum gms</th>
<th>Cerebellum gms</th>
<th>Pituitary mg</th>
<th>Adrenals mg</th>
<th>Thyroid mg</th>
<th>Gonads gms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.55 ± 0.03</td>
<td>0.177 ± 0.02</td>
<td>2.62 ± 0.32</td>
<td>14.24 ± 1.1</td>
<td>6.58 ± 0.59</td>
<td>1.297 ± 0.054</td>
</tr>
<tr>
<td>n=10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>0.789 ± 0.029</td>
<td>0.244 ± 0.019</td>
<td>3.89 ± 0.21</td>
<td>26.62 ± 1.39</td>
<td>8.6 ± 0.85</td>
<td>1.362 ± 0.12</td>
</tr>
<tr>
<td>n=16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P Value</td>
<td>&lt;0.001</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt; 0.001</td>
<td>NOT SIGNIFICANT</td>
<td></td>
</tr>
</tbody>
</table>
and minimize weight loss by increasing the efficiency of utilization of whatever food was taken during the 24 hours period (12). Stress may hamper this mechanism. Therefore it is not surprising that the rats under study subjected to prolonged immobilization continued loosing weight inspite of near normal food intake.

Stress stimulates the limbic system and various hypothalamic areas. It also increases various neuronal pathways in the brain (4). These may collectively account for the increase in weight of the brain as a whole.

Stress induced activation of pituitary-adrenal system appears to be mediated predominantly by hypothalamic neurons containing not only CRH but also arginine vasopressin (AVP), both of which influence the release of pituitary corticotropin (13, 14, 15). In chronic stress there is increased secretion of CS. This would normally decrease the amount of CRH secreted by a negative feedback effect on the hypothalamus. However, in chronic stress CS may exert a positive feedback effect on the pituitary itself overriding the hypothalamic inhibition (16). There may also be a decreased sensitivity of the axis to feedback inhibition by CRH (17). This would explain, the increase in pituitary weight and secretion, which in turn would continue augmenting the activity of the adrenal gland. Also CRH not only stimulates pituitary to increase its corticotropin secretion, but also increases the sympathetic outflow to the adrenals resulting in increased output of both cortical and medullary hormones (18). This could be the reason for the significant increase in adrenal weight in the present study.

Chronic stress increases the plasma TSH levels in rats (19, 20). This could bring about an increase in the weight of thyroid seen in our study. Immobilization stress of 5 hours duration decreases the circulating testosterone in male rats (5). Stress increases CRH and CRH acting within the brain suppresses the release of LH and GH but not FSH secretion in rats (21). This may explain the decrease in testosterone levels in plasma. Since FSH is not inhibited it did not produce any significant change in the weight of the testes.

To summarize, the present study suggests that a high stressor of the nature of immobilization, has multiple and varied effects on the body as a whole. Whereas, the initial decrease in food intake is reversed over a period of time, the body weight continues to decrease. The significant increase in the brain, pituitary and adrenal weights suggests an increase in their activity as a result of the continued stress.

REFERENCES

2. Giralt MC, Garoia-Marquez, Armario A. Previous chronic ACTH administration does not protect against the effects of acute or chronic stress in male rats. Physiol Behav 1987; 40(2): 165-70.


---

**In Infectious Hepatitis**

**Liv.52® — your first choice scores over other therapies**

**STEROIDS**

"The mean recovery period for Liv.52 treated cases, with or without prednisone was 5 weeks, while cases receiving prednisone alone recovered in a mean period of 10 weeks."


**ANTIBIOTICS**

"...Liv.52 accelerates the rate of recovery in cases of infective hepatitis as compared to cases who were given broad spectrum antibiotics and steroids only."

(Agarawal|Sareen: 1976)

**SUPPORTIVE THERAPY**

"The symptoms improved earlier in the Liv.52 group than in the Vitamin C plus B-complex group."

(Ramalingam et al.: 1971)