Dietary Stress and Energy Metabolism: Evaluation of the Adrenal Cortex

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Dietary Stress and Energy Metabolism: Evaluation of the Adrenal Cortex

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Abstract

The adrenal gland is an essential stress-responsive organ that is part of both the hypothalamic-pituitary-adrenal axis and the sympatho-adrenomedullary. The participation of the adrenal cortex in the control of carbohydrate metabolism is unquestionable, but the major pathways employed during deprived glucose states as in diabetes and starvation is not fully explained. A total of forty-eight healthy adult rats (Rattus Novergicus) of both sexes averaging weight 200g were used. The rats were maintained on standard laboratory chow and water adlibitum. They were divided into four groups (n=12);

- Group 1: Diabetic (D)
- Group 2: Diabetic control (DC)
- Group 3: Starving (S)
- Group 4: Starving control (SC).

Group 1: Diabetic were administered 70mg/kg body weight of aqueous solution of streptozotocin single dose intraperitoneally. After which they were given food and water liberally.

Group 2: Diabetic Control (DC), were administered equal volume of distilled water intraperitoneally and were given food and water liberally.

Group 3: Starving (S), were starved of food during the period of the experiment. The rats were sacrificed and the adrenal gland excised and processed for routine embedding and stained for H & E, while some portions of the gland were homogenized and used to determine LDH activities. The results showed significant increase in the activities of LDH in both the treated groups, hypertrophied cortex with heamorrhagic areas. In conclusion dietary stress induced by diabetes and starvation present with similar metabolic coping mechanisms.

Introduction

The adrenal gland is an essential stress-responsive organ that is part of both the hypothalamic-pituitary-adrenal axis and the sympatho-adrenomedullary system. Chronic stress exposure commonly increases adrenal weight, but it is not known to what extent this growth is due to cellular hyperplasia or hypertrophy and whether it is sub region specific [1]. The existence of a functional relationship between the anterior pituitary, the pancreas and the adrenal cortex with respect to the control of carbohydrate metabolism is well established. The role of adrenal cortical hormones in the regulation of carbohydrate metabolism was pointed out by Britton and Silvette [2]. Long and Lukens [3] demonstrated the improvement in diabetes which results from adrenalectomy and Ingle [4] established the diabetogenic potency of pure cortical hormones. Although not all details of the mechanisms are known, participation of the adrenal cortex in the control of carbohydrate metabolism is unquestionable. [5]. Glucose production by gluconeogenesis is that main source of glucose during fasting and contributes significantly to hyperglycemia in diabetes mellitus [6]. Fasting and Diabetes are characterized by elevated glucocorticords and reduces insulin respectively while stress responsiveness is impaired in diabetes [7]. Streptozotocin induced diabetes has been reported to cause an initial increase in the levels of Nitric Oxide Synthase (NOS) and NADPH-diaphorase in the adrenal gland of the rat [8]. Glucose – 6 – phosphate dehydrogenase levels have been reported to increase due to increased production of pentose sugars and NADPH needed for the synthesis of nucleotides [9 & 10]. While chronic food restriction is reported to result in moderate hyperadrenocorticism, which may play a role in activating cellular mechanisms that retard aging [11]. This study investigated the comparative effects of dietary stress (Diabetes and starvation) on adrenal energy metabolism as it relates to the metabolic pathways employed during these deprived glucose states.

Methods

Healthy adult rats (Rattus novergicus) of both sexes, average weight 200g were used. The rats were maintained on standard laboratory chow and water adlibitum for an initial three weeks period of acclimatization. Thereafter they were divided into four groups (n=12).

- Group 1: Diabetic (D),
- Group 2: Diabetic control (DC),
- Group 3: Starving (S)
Group 4: Starving control (SC).
Group 1: Diabetic (D), was administered 70mg/kg body weight of aqueous solution of streptozotocin in a single dose intraperitoneally after which they were given food and water liberally.
Group 2: Diabetic control (DC), were administered equal volume of distilled water intraperitoneally and given water and food liberally.
Group 3: Starving (S) were starved of food during the period of the experiment, but were given water liberally.
Group 4: Starving control (SC), were given free access to food and water for the duration of the experiment.
The blood glucose level was monitored on days 1, 3, and 14 to establish the glycemic states in both groups, using GOD –POD method. Daily body weights were recorded so was food consumption. Four animals (n=4) from each group were sacrificed on days 3, 7 and 14. Some of the rats were sacrificed by cervical dislocation and the adrenal glands were quickly excised, weighed and appropriate portions made for quantitative estimation of LDH (Biolabo s. a. Fismes. France, code 92111). While others were sacrificed by an overdose of pentobarbital and the tissue processed for routine H & E [12]. The cells were estimated using the eyepiece micrometer procedure [13].

**Results**

**Microanatomy:** The adrenal cortex of the diabetic and starving group showed haemorrhagic spots, which are most marked at the cortico-medullary junction. (Plates 2 & 3). The adrenocortical cells showed significant increase in diameter (hypertrophy) on the experimental day 3 (Table 1), while the increase in the subsequent days was not significant (Table 2). Table 3 presents the adrenal and the relative adrenal weights.

**Biochemical:** The activities of LDH in both treated groups showed steady significant increase from day 3 to 14 (Fig. 1) & (Fig. 2).

**Discussion**

The adrenal cortex of the treated groups showed hypertrophy and heamorrhagic spots (Plates 2 & 3). The heamorrhagic spots are most marked at the cortico-medullary junction. A large or moderate haemorrhage may be masked by other severe diseases especially in the neonates: sepsis with shock, CNS injury, asphyxia, intestinal obstruction and/or atresia, pulmonary hypertension, severe anaemia, or circulatory insufficiency, because their clinical manifestations are not specific only for adrenal injury damage. In severely damaged adrenal glands there is a dramatic onset of hypovolaemic shock, hypotension, abnormal thermoregulation, carbohydrate metabolism and water and mineral imbalance, tachycardia, arrhythmia, and cyanosis. Anorexia and rapid weight loss are present [14]. Hypertrophy was observed in which adrenal cholesterol; ascorbic acid concentrations, acid phosphatase and alkaline phosphatase activities were decreased, suggestive of active involvement of adrenal cortex in stress for homeostasis [15 & 16]. The dietary stress conditions such as starvation and diabetic conditions might cause a stress-like activation of adrenal cortex resulting in increased levels of glucocorticoids which in turn activate the intestinal Na⁺K⁺-ATPase activity [17]. Selye reported that the various internal organs, especially the endocrine glands and the nervous system, adjust to the constant changes which occur in and outside the body. This adjustment is referred to as the General Adaptation Syndrome. Selye concluded that the adrenals were the body’s prime reactors to stress. He stated that the adrenals are the only organs that do not shrink under stress; they thrive and enlarge [18]. The increase in the activities of LDH noticed in the treated groups in this study (Figs 1 & 2) suggests the re-arrangements that the cell’s metabolism undergoes in order to ensure survival. Recent studies suggested the metabolic strategy of stressed cell as a dynamic genetic and biochemical changes makes up a cell’s response to a shortage of Coenzyme A (CoA), a key player in metabolism. [19]. Following the shutdown of CoA production, the cells quickly recycled CoA from other sources, extracting life-supporting energy from nutrients in the mitochondria. Low levels of CoA trigger the activation of genes that block other biochemical pathways that ordinarily use this molecule. Instead, the cell shifts most of the available CoA activity to producing glucose from the liver. Other organs then break down glucose into pyruvate inside mitochondria. In the mitochondria, CoA molecules feed pyruvate into a complex series of chemical reactions that produces molecules of ATP [19]. In conclusion dietary stress induced by diabetes and starvation present with similar metabolic coping mechanisms as demonstrated by the results of this study.

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Illustrations

Illustration 1

Photomicrograph of Adrenal cortex showing radiating columnar cells of the zona fasciculata. Control group H&E x400
Illustration 2

Photomicrograph of Adrenal cortico-medullary junction showing haemorrhagic spots. Diabetic group H&E X400
Illustration 3

Photomicrograph of Adrenal cortico-medullary junction showing haemorrhagic spots. Starved group, H&E x400
Illustration 4

Diameter(um) of Adrenal cortical cells (zona fasciculata) after experimental day three (3)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (n) T test</th>
<th>Std Dev</th>
<th>Std Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diab. Cont.</td>
<td>4.17 0.030</td>
<td>0.65</td>
<td>0.26</td>
</tr>
<tr>
<td>Diabetic</td>
<td>5.10</td>
<td>0.26</td>
<td>0.11</td>
</tr>
<tr>
<td>Starv. Cont.</td>
<td>4.17 0.025</td>
<td>0.65</td>
<td>0.26</td>
</tr>
<tr>
<td>Starvation</td>
<td>5.00</td>
<td>0.23</td>
<td>0.10</td>
</tr>
</tbody>
</table>

P is 0.05; Statistically Significant (SS)
Illustration 5

Diameter (um) of Adrenocortical cells (zona fasciculata) after experimental day seven (7)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (n) T test</th>
<th>Std Dev</th>
<th>Std Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diab. Cont.</td>
<td>4.17 0.61</td>
<td>0.65</td>
<td>0.26</td>
</tr>
<tr>
<td>Diabetic</td>
<td>4.38</td>
<td>0.68</td>
<td>0.28</td>
</tr>
<tr>
<td>Starv. Cont.</td>
<td>4.25 0.37</td>
<td>0.66</td>
<td>0.27</td>
</tr>
<tr>
<td>Starvation</td>
<td>4.50</td>
<td>0.68</td>
<td>0.31</td>
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</tbody>
</table>

P is 0.05; not significant
Illustration 6

Effect of dietary stress on the relative Adrenal weight

<table>
<thead>
<tr>
<th>Groups</th>
<th>Duration of treatment(days)</th>
<th>Body wt(g)</th>
<th>Adrenal wts(mg/pair)</th>
<th>Relative adrenal weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diab</td>
<td>3</td>
<td>175.00</td>
<td>0.027</td>
<td>0.31</td>
</tr>
<tr>
<td>Diab cont</td>
<td>3</td>
<td>115.00</td>
<td>0.070</td>
<td>0.61</td>
</tr>
<tr>
<td>Starvation</td>
<td>3</td>
<td>135.33</td>
<td>0.020</td>
<td>0.30</td>
</tr>
<tr>
<td>Starv cont</td>
<td>3</td>
<td>125.00</td>
<td>0.020</td>
<td>0.32</td>
</tr>
<tr>
<td>Diab</td>
<td>7</td>
<td>200.50</td>
<td>0.044</td>
<td>0.44</td>
</tr>
<tr>
<td>Diab cont</td>
<td>7</td>
<td>150.00</td>
<td>0.025</td>
<td>0.29</td>
</tr>
<tr>
<td>Starvation</td>
<td>7</td>
<td>185.33</td>
<td>0.070</td>
<td>0.38</td>
</tr>
<tr>
<td>Starv cont</td>
<td>7</td>
<td>120.00</td>
<td>0.032</td>
<td>0.27</td>
</tr>
<tr>
<td>Diab</td>
<td>14</td>
<td>20050</td>
<td>0.050</td>
<td>0.25</td>
</tr>
<tr>
<td>Diab cont</td>
<td>14</td>
<td>175.00</td>
<td>0.074</td>
<td>0.43</td>
</tr>
<tr>
<td>Starvation</td>
<td>14</td>
<td>115.75</td>
<td>0.080</td>
<td>0.69</td>
</tr>
<tr>
<td>Starv cont</td>
<td>14</td>
<td>185.00</td>
<td>0.070</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Diab=Diabetic; Diab cont=Diabetic control; Starv cont=Starvation control; wt=weight
Illustration 7

Activities of LDH in the Adrenal cortex of Starved group

![The activities of LDH in the adrenal cortex of starved rats](image)
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