Body fat regulation during pregnancy and lactation: the roles of diet and insulin

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Obesity is a condition characterized by an excess of body fat, hyperphagia, hyperinsulinaemia and moderate hyperglycaemia (Bray & York, 1979). The lactating rat, despite being hyperphagic, is hypoinsulinaemic (Flint et al., 1979), moderately hypoglycaemic (Robinson et al., 1978) and may display an extensive catabolism of body fat (Steingrimsdottir et al., 1980; Rolls et al., 1984). The purpose of the present work was to investigate some of the physiological and metabolic changes which occur in the obese lactating rat.

Previous work has shown that rats with dietary obesity, fed a cafeteria diet during pregnancy and lactation, lost considerably more weight than lean rats during lactation (Rolls & Rowe, 1982). However, it was not clear what were the relative contributions of pre-existing obesity, non-foetal weight gain in pregnancy and the diet available to the change in body weight during lactation. A net deposition of body fat occurs during pregnancy, but it is not clear whether there is an optimal level of body fat required to support lactation.

The first experiment was designed to answer these questions (see Rolls et al., 1984). Adult hooded Lister rats were made obese by offering them a variety of palatable, high-energy foods (cafeteria diet) for approx. 10 weeks. Age-matched lean rats were fed just chow during this time. During pregnancy, obese and lean rats were offered either just chow, or a cafeteria diet in addition to chow. Non-foetal weight gain was greatly increased in rats fed the cafeteria diet, but was not strongly affected by pre-existing obesity (see Fig. 1). The increase in non-foetal weight gain in cafeteria-fed rats consisted predominantly of fat. It is concluded that fatty acid composition of the food items in the cafeteria diet.

In the second part of the experiment, half of the rats, which had been fed just chow during pregnancy, were switched to the cafeteria diet during lactation, and the remainder continued to receive just chow. Similarly, half of the rats, which had been fed the cafeteria diet during pregnancy, were fed just chow during lactation, and the remainder continued to receive the cafeteria diet. The change in body weight during lactation was inversely related to the body weight at parturition and to the non-foetal weight gain during pregnancy. Therefore, the change in body weight during lactation compensated for the pre-existing obesity and for the enhanced non-foetal weight gain in pregnancy caused by cafeteria feeding. Furthermore, the type of diet available during lactation had little effect on body weight changes in lean lactating rats. Obese rats lost considerable amounts of weight during lactation, and this occurred even when the obese rats were fed a cafeteria diet (see Fig. 1). The results show that the consumption of a palatable, high-energy diet need not invariably lead to an increase in body weight.

Obese rats, provided with a cafeteria diet before parturition, showed an increased loss of body weight and a striking degree of hypophagia when they were given just chow during lactation. This decrease in energy intake resulted in reduced pup growth. The reduction in pup growth was probably due to diminished milk yield, since milk composition was not greatly altered in this group, compared with other chow-fed groups. Pup growth was directly related to maternal energy intake. The composition of the milk was significantly altered when rats were fed the high-fat cafeteria diet. Milk fat content was increased and the fatty acid composition of the milk lipid resembled the fatty acid composition of the food items in the cafeteria diet. Obesity per se and the diet available during pregnancy also affected milk composition, but to a lesser extent than the diet available during lactation.

Therefore, the changes in body weight during lactation appear to be regulated with respect to the body weight at parturition. The type of diet available may have a significant effect on body weight changes during lactation, but this effect is modulated by the degree of obesity. Both the type of diet available during lactation and the level of obesity can have a significant effect on milk composition.

Results are means of eight or nine observations; S.E.M.s are given for groups at mating, just before parturition and after 12 days of lactation.

Fig. 1. Body weights of lean and obese rats, fed on chow or a cafeteria diet, during pregnancy and lactation

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Obesity is associated with several alterations in the metabolic effects of insulin, and insulin plays a critical role in regulating metabolism in the lactating rat (Robinson et al., 1978). The possible role of insulin in the regulation of body weight during lactation was investigated in the second experiment. Obese and lean rats were fed either just chow or the cafeteria diet during lactation. Half the rats in each group were injected daily with insulin and the remainder were injected daily with saline. Obese animals catabolized much more body fat during lactation than their lean controls fed the same diet (see Table 1). Thus obese chow-fed rats lost three times as much body fat as lean chow-fed rats during lactation. The loss of body fat was partially reversed by daily injections of insulin, which also caused a 20% increase in energy intake. The anabolic effect of insulin appeared to be greater in obese chow-fed rats than in any other group. Cafeteria feeding increased the rate of pup weight gain in both obese and lean rats. However, the administration of insulin produced different effects on pup growth in chow-fed and cafeteria-fed rats. Pup growth was increased by insulin administration in cafeteria-fed rats and decreased by insulin administration in chow-fed rats. Pup growth was again related to maternal energy intake.

It is concluded that there is an exaggerated loss of body fat in obese rats during lactation, that this loss is response to insulin and that there may be significant differences in insulin responsiveness between obese and lean lactating rats. Furthermore, the response of mammary gland to exogenous insulin administration appears to depend on the type of diet available.

The physiological role of insulin in the regulation of body weight during lactation was investigated in the final experiment. Blood samples were collected from obese and lean rats fed just chow or the cafeteria diet during lactation. Plasma glucose and insulin concentrations in these animals were compared with the levels measured in their virgin controls. Lactation was associated with a larger decrease in plasma insulin in obese rats than in lean rats compared with their virgin controls. At peak lactation (day 12), obese and lean rats fed the two diets were infused with either insulin or saline. Plasma glucose concentrations did not fall to such an extent after infusion of insulin in obese rats as they did in lean rats. It is concluded that the increased catabolism of body fat, which occurs in the obese lactating rat, may be the result of the fall in plasma insulin coupled with an obesity-induced resistance to insulin. Further evidence implicating insulin in the regulation of body weight during lactation was provided by measurements of plasma glucose and insulin in cafeteria-fed rats. Cafeteria feeding not only reduced the weight loss of lactating rats, but was also associated with elevated plasma glucose and insulin concentrations.

The rate of lipogenesis in mammary gland, liver, brown and white adipose tissue was also determined in obese and lean, chow-fed and cafeteria-fed rats, infused with either saline or insulin. Mammary gland lipogenesis was increased in lactating rats, but this increase was reduced in cafeteria-fed rats compared with chow-fed rats. Cafeteria feeding stimulated brown adipose tissue lipogenesis in obese lactating rats, but reduced the rate in lean lactating rats. There were significant correlations between the rate of lipogenesis in mammary gland and liver and the concentration of insulin and glucose in the plasma. Thus, a high rate of lipogenesis in these two tissues was associated with reduced plasma insulin and glucose concentrations. It is suggested that, during lactation, lipogenesis in these two tissues is stimulated by insulin, and that an increased utilization of insulin and glucose results in a fall in plasma insulin and glucose concentrations.

In conclusion, obese rats display an exaggerated loss of body weight and fat during lactation compared with lean rats. This loss of body fat occurs even when the obese animals are fed a cafeteria diet, which normally induces body fat gain. Body fat catabolism during lactation is sensitive to insulin, and the administration of this hormone to the mother can have significant effects on the development of the neonate. These effects are modulated by the composition of the diet available during lactation. One reason why obese rats display an extensive catabolism of body fat during lactation is likely to be the fall in plasma insulin during lactation, coupled with insulin resistance in these animals. Further work is required to elucidate the mechanisms that signal the fall in plasma insulin during lactation in the obese rat.


### Table 1. Weight of fat extracted from the carcasses of lean and obese rats, fed on either chow or a 'cafeteria' diet, and injected daily with either saline or insulin (5, 10 and 15 i.u./kg body wt. for the first 5 days, the next 5 days and the last 11 days of lactation respectively), during lactation

<table>
<thead>
<tr>
<th>Diet during lactation</th>
<th>Agent injected</th>
<th>State</th>
<th>Lean</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chow</td>
<td>Saline</td>
<td></td>
<td>40.6 ± 3.7** (6)</td>
<td>74.9 ± 6.8** (5)</td>
</tr>
<tr>
<td>Chow</td>
<td>Insulin</td>
<td></td>
<td>56.4 ± 3.8 (5)</td>
<td>109.1 ± 9.5** (5)</td>
</tr>
<tr>
<td>Cafeteria</td>
<td>Saline</td>
<td></td>
<td>78.1 ± 3.3 (5)</td>
<td>110.9 ± 6.9** (5)</td>
</tr>
<tr>
<td>Cafeteria</td>
<td>Insulin</td>
<td></td>
<td>92.4 ± 7.2 (5)</td>
<td>131.6 ± 5.6** (5)</td>
</tr>
<tr>
<td>Killed at start of lactation</td>
<td></td>
<td></td>
<td>74.7 ± 5.5 (6)</td>
<td>174.0 ± 9.0 (6)</td>
</tr>
</tbody>
</table>

Body fat content of rats killed on the day of parturition is shown for comparison. Results are means ± S.E.M. with the number of observations (n) in parentheses. Value significantly different from that at start of lactation: *P* < 0.05, **P* < 0.01.