

DIFFERING RESPONSE OF BODY WEIGHT GAIN TO HIGH FAT DIET TREATMENT IN THE MOUSE

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Abstract : Forty-eight mice maintained on a high fat diet supplement in addition to regular laboratory rodent chow responded differently in terms of body weight gain over a period of six weeks. Eleven mice gained weight that was comparable to body weights of mice given only chow for the same period of time while the others gained significantly higher body weights and became obese despite similar level of energy intakes. The increase in body weight was due to increase in body fat content as noted by carcass analysis. The differential response of the mice to identical dietary treatment in causing obesity or not in mice is discussed.

Key words : high fat diet obesity body fat mice

INTRODUCTION

Experiments in both humans and animals have demonstrated strong genetic factors in the development of obesity that express itself only under permissive conditions (1, 2). Increased energy intake and/or reduced components of energy expenditure such as basal metabolic rate, regulatory or facultative thermogenesis (e.g. diet-induced thermogenesis, non shivering thermogenesis) and physical activity, either singly or in combination are also factors that could result in obesity (3). Though, there is a large body of data available to support this claim, there has been a considerable and continuing interest in the extent to which the macronutrient part of the diet, particularly the fat, might affect the energy

balance causing excess fat stores in the body. This continuing interest in the subject matter is because of the diet induced obesity in animals have more similarities to spontaneous human obesity (4). Thus, it has become one of the prime goals of obesity research to explore in depth in that direction using animal models. Some strains of rats and mice will become obese while some remain lean when maintained on a high fat diet and such differences exist both across and within strains (4-9). The increase in body weight induced by feeding a high fat diet is primarily due to an increase in the body fat content in those animals. The mechanisms responsible for the differences in body weight gain are still not well understood although, several hypotheses are put forward. In the present study, body

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weight gain particularly in the form of fat accumulation to feeding a high fat diet supplement to CD₁ mice is investigated to find out whether the animals differ or not in response to such dietary treatment as claimed by other researchers using several other animal types and different diet treatment (4-9). The possible role of other factors that help to explain the development of obesity or not under such circumstances are also discussed.

METHODS

Male albino mice (CD₁ strain) were used for the study. After procuring them from the Animal Resource Center, they were housed in groups of six in plastic cages at 22°C for one week to get acclimatized to laboratory conditions. During this period, they were fed Purina rodent chow 5001. Subsequently for the next six weeks, 48 animals were offered a palatable high fat diet supplement (in addition to chow) to induce obesity. The composition of the high fat diet was as given by Richard et al (10)

TABLE I : Composition of diets.

High fat supplement (Ref. 10).			
Composition by weight (g)		Composition by calories (%)	
Peanut butter	500	Protein	19
Lard	250	Carbohydrate	12
Minerals	26	Fat	66
Vitamins	7.5	Energy content : 32.1 kJ/g	
Purina rodent chow 5001			
----	----	Protein	23.4
----	----	Carbohydrate	49.0
----	----	Fat	4.5
----	----	Energy content : 17.8 kJ/g	

and that of chow are shown in Table I. Another group of 36 mice given only chow throughout the study was included as controls. All animals had free access to food and tap water during the entire period of the experiment. Mice were matched for age and body weight (26-28 g) at the beginning of the study. The experiment was repeated 3 times and the results are pooled and presented.

Food intake measurements : Mice were placed individually in wire mesh bottom cages for 3 days before food intake measurements were begun. Weighed amounts of high fat diet supplement and chow were provided to animals in more than the required amounts in separate cups. Food intake was measured twice weekly for 6 weeks. Left over and spilled food was collected on a filter paper and was accounted for energy consumption.

Carcass analysis : Mice had their head, tail and gastrointestinal tract (GIT) removed. The adipose tissue associated with GIT was dissected away and returned to carcasses. Carcasses were autoclaved for 20 min at a pressure of 1.4 kg/cm² and homogenized in a blender with water to a final volume of 250 ml. A 10 ml aliquot was frozen and lyophilized to obtain the carcass dry weight. The fat content was then measured gravimetrically after a 24 hr extraction with 50 ml of chloroform:methanol (2:1; v/v) followed by a further 100 ml wash.

Statistics : NCSS software (Kaysville, UT, USA) was used for computation of data and one way analysis of variance for comparison of results. Differences between groups were considered statistically

significant when $P < 0.05$. All values are presented as means with their standard errors.

RESULTS

Obesity was induced in mice by offering a palatable diet rich in fat. Because of a large variation in body weight gain they were put in to two groups: a) 'Obese prone' mice defined by a weight gain of 15.4 ± 3.6

Weight gain in obese mice was mostly due to higher levels of carcass fat (50–60%) and water (10–15%) than non-obese or chow fed controls. Food intake was significantly higher in obese mice and was somewhat increased in non-obese mice. Out of the total daily energy intake, these mice derived only 10–12% of the energy from the chow diet indicating a high degree of choice they can make for the palatable diet when there is an option. However, there was no

TABLE II : Effects of 6 weeks feeding of high fat supplement on body weight and carcass of mice as compared to mice fed chow only.
(Values are mean \pm SE)

Diet	Chow+High fat supplement		Chow 5001 controls
	Obese prone	Non-obese	
Body weight (g)	$45.7 \pm 1.7^{**}$	37.8 ± 0.9	35.5 ± 0.9
Energy intake (kJ/day)	$111.7 \pm 7.6^*$	104.5 ± 7.5	87.2 ± 2.4
Carcass (g) :			
Weight	$35.8 \pm 1.6^{**}$	28.4 ± 0.7	26.4 ± 0.7
Fat	$9.7 \pm 0.8^*$	4.9 ± 0.6	3.8 ± 0.3
FFM	$8.0 \pm 0.3^{**}$	7.3 ± 0.2	7.3 ± 0.3
Water	$18.0 \pm 0.9^*$	16.2 ± 0.6	15.3 ± 0.5
n	37	11	36

n=number of animals

FFM = Fat Free Mass

*Indicates significant difference ($P < 0.05$) between mice fed chow only and those offered chow+high fat supplement.

†Indicates significant difference between obese prone and non-obese mice.

g and b) 'Obese resistant' or non-obese mice with a mean body weight gain of 8.5 ± 1.8 g. Body weight gain of non-obese mice was comparable to weight gain of chow fed mice. Out of 48 mice put on high fat diet supplement and chow, 11 mice did not become obese while others gained significantly higher body weights.

Food intake, body weight, carcass weight and other details are given in Table II.

significant differences in food intake between obese and non-obese mice although food consumption of chow fed controls was much less.

DISCUSSION

The basic knowledge of energy balance points out that either an increase in energy intake or reduction in any of the components of energy expenditure can result in excess

body weight gain (3). However, studies on obesity have indicated the very complex nature of this disorder.

Obesity is a heterogeneous disorder with the existence of differing sensitivity to diet induced obesity. Obesity was induced in the mice by offering a palatable diet rich in fat content. Some mice became hyperphagic and gained an average of 10 g body weight as fat compared to chow fed mice. But 20% of the mice included in the study did not gain excess weight than the chow fed mice.

Though different types of food (e.g. cafeteria diet, condensed milk) have been used in the laboratory to induce obesity in animals (5, 6, 11, 12), peanut butter and lard supplement used in the present study was shown to promote calorie intake in rats and mice and is not deficient in protein (10). Also, the fat content in this diet was higher than the fat in cafeteria diet. Though the degree of response to these different types of diet in the body weight gain by animals varies, the pattern in which some animals become obese while others do not remain the same.

We have taken care to include mice of comparable body weights at the start of the experiment in this study. It has also been argued that the initial body weight may not be a predictor of responsiveness to high fat diet feeding (13). The same is true of energy consumption i.e. it is possible that a mouse consuming less or equal amounts of energy than the other mouse might as well become obese while the excess energy consuming ones might not (13, 14, 15). In our study, there was no differences in energy intakes of mice maintained on high fat supplement though differences in body weight gain was

recorded. This excess weight gain was due to increased fat content of the body as revealed by carcass analysis.

In the obese mice, it has been suggested that higher appetite and low maintenance cost were factors underlying their obesity (16). Obese resistant mice may be able to maintain less positive energy balance by burning more fat and storing less than the obese prone mice. The propensity or otherwise to dietary obesity in mouse is also explained on the basis of a difference in the proliferative capacity of preadipocytes where the obese resistant mice will have a reduced proliferative capacity (17).

Other metabolic factors are also considered to play a role in the development of diet induced obesity. For example, lipoprotein lipase, an enzyme that responds to diet and hormones is located on the endothelial surface of capillaries in various extra-hepatic tissues including brown adipose tissue. This enzyme hydrolyses triglycerides and seems to play a key role (18). Differences in neuroendocrine aspects particularly of sympathetic nervous system activity in some strains of rat (19, 20), insulin resistance (9), changes in 3-hydroxybutyrate (8) that affect food intake do seem to play some role in the development of obesity. Brown adipose tissue, an energy buffer tissue has been widely considered to influence energy balance both in animals and humans thereby contributing to the development of obesity (3, 6, 21).

There are conflicting reports regarding the contribution of physical activity to obesity development (22). It has been argued that the energy spent on each of spontaneous activity is proportional to body

weight and the cost of activity therefore is more in the obese than the lean counterpart though there may be differences in the number of activity performed (23). Hence, measuring the cost of daily activity becomes essential in such studies to establish its role, but has several practical difficulties.

Some environmental conditions such as the preweaning and in utero (due to the metabolic status of the mother during pregnancy) are considered contributory to the development of obesity by some research workers (24). However, the postweaning conditions are not considered that important because it could be maintained constant and

identical for animals during this period.

In the light of the discussion made, it may be concluded that obesity is a multifactorial and a very complex disorder. High fat feeding in CD₁ mice produced a variable response within the strain where a greater proportion of the mice gained higher body weights by accumulating excess body fat while others did not even though they had similar energy consumption over a six week period. It would be possible to figure out the culprits causing obesity in each case by investigating in to all factors that would individually or in unison make a strong candidate for the development of obesity.

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