Obesity: Can Some Fat Cells Enlarge while Others Are Shrinking?

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ABSTRACT

CBA mice were made obese by injection with gold thioglucose (GTG). After receiving transplants of “lean” and “GTG-obese” fat under separate kidney capsules, the host mice were fed a restricted diet for three weeks. Over this period, the fat cells in the lean grafts enlarged whereas the fat cells in the GTG-obese grafts shrunk. Concurrent fat loss and fat gain can therefore take place.

INTRODUCTION

With increasing age, anterior leg fat thickness has been reported to diminish in both men and women, whereas trochanteric fat thickness increases (1). A photographic study of fat distribution in 90 women, aged between 13 and 69 years (2), showed older, fatter women were more likely to have a central type of fat distribution. Thus, both of these cross-sectional studies indicate that increasing age and/or obesity can produce a possible redistribution of fat among body depots. Cross-sectional studies such as these do not answer the question, “Can fat be lost from some sites at the same time as it is gained by others, or must the process of fat mobilization or fat storage be dominant at all sites at the same time?”

We have previously described a technique for transplanting small pieces of adipose tissue under the kidney capsule of mice (3). Here, we use this technique to look for concurrent fat loss and fat gain during dietary restriction in mice which had previously been made obese by injection with gold-thioglucose (GTG). GTG induces obesity probably via its ability to cause lesions in the ventromedial part of the hypothalamus (4,5) which consequently leads to overeating.

EXPERIMENTAL PROCEDURES

All mice were CBA strain females aged 6-7 weeks. They received an intraperitoneal injection (0.1 mL) of GTG (80 mg/mL in experiment I and 70 mg/mL in experiment II). In both experiments, a few mice that were not injected with GTG were kept as control “lean” mice. After six weeks, when the injected mice were approximately double the weight of the control lean mice, “GTG-obese” mice received transplants of lean gonadal fat under their left kidney capsule and “GTG-obese” gonadal fat under their right kidney capsule. Samples of donor fats and host gonadal fat were taken at this stage for the estimation of mean fat cell size by the method previously described (3,6). Immediately after transplantation, dietary restriction was begun and instead of free access to stock diet (ca. 3.8 g/day), the mice in experiment I were allowed an average of 2.2 g/day and the mice in experiment II were allowed ca. 3.3 g/day. Three weeks later, when their weights had reached a level which was intermediate between the original weights of GTG-obese and lean mice, the host mice (three in experiment I and 13 in experiment II) were killed by cervical dislocation. The kidneys plus fat grafts were removed and fat cell size was determined not only in these fat grafts but also in samples of the “slimmed” host mouse gonadal fat.

RESULTS

Donor Mice

Results are depicted in Table I and Figure 1. At transplantation, the body weights of the GTG-obese fat donors were 39 g (experiment I) and 41 g (experiment II) and the body weights of the lean fat donors were 20 g (experiment I) and 18 g (experiment II). Fat donors were not subjected to dietary restriction and neither their body weights nor fat cell weights changed significantly during the 3-week experimental period.

Host Mice

The mice in experiment II were subjected to less severe dietary restriction so that body weight and fat cell size decreased less than in Experiment I. However, the body weights of the host mice and their gonadal fat cell weights decreased significantly in both experiments (p<0.001, paired t-test).
Behavior of Grafted Fat

During the transplantation period, the lean grafts increased in fat cell size whereas the GTG-obese grafts decreased in fat cell size. The difference in behavior of the two types of grafts was significant. Fat cell size of the slimmed hosts and fat cell sizes of either of the grafts were not significantly different. Thus, dietary restriction resulted in equalization of graft fat cell sizes to a size typical of their hosts.

The smaller cells in the lean grafts were able to increase in weight even though the body weights of the host mice and the weights of the larger grafted cells were decreasing.

DISCUSSION

During dietary restriction of host mice, fat mobilization must have taken place with the overall effect of reducing body weight. Thus, it was not surprising that host gonadal fat cell size decreased during this period. However, it was less easy to predict the changes in fat cell size in the grafts. Results from in vitro experiments (7) have indicated that fat mobilization is greater from larger cells than from smaller cells. Indeed, in some of our preliminary experiments in which the host's fat cells shrank to a size even smaller than those of the lean donor, we observed that the fat cells in the lean grafts shrank less than the fat cells in the GTG-obese grafts.

Studies of fat mobilization in vivo have also shown that the decrease in fat cell size during starvation in animals (8,9) or dietary restriction in man (10) is proportional to initial cell size. When fat storage is induced in rats by insulin injection (11,12) or by hypothalamic ventromedial lesions (13), the greatest increase in fat cell size is seen in the region with the smallest cells. Thus, there is a general tendency during fat mobilization or fat storage for “fat cell size equalization” to take place and the only reported exceptions to this rule occur when fat changes are induced by hormones such as corticosteroids (14) or estrogens (9) which appear to exert specific regional effects.

The transplantation model is unique because it gives an opportunity to study changes in fat cell size at different fat sites in the same animal. Fat loss was greatest from the largest cells (in the GTG-obese grafts) and fat gain was greatest in the smallest cells (in the lean grafts). Our results have therefore not only confirmed the tendency to fat cell size equalization but are the first to demonstrate that it can be brought about by fat loss from some cells at the same time.