Body Fat Distribution With Long-Term Dietary Restriction in Adult Male Rhesus Macaques

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Dietary restriction (DR) is the only intervention that has been shown to increase both average and median life span in laboratory rodents. The effect of long-term, moderate DR on body composition and fat distribution was evaluated in male rhesus monkeys.Thirty animals (8–14 years of age) fed either 30% less than baseline intake (R, n = 15) or allowed to eat to satiety (C, n = 15), have been assessed semiannually using somatometrics and dual-energy x-ray absorptiometry (DXA) for 7.5 years. R subjects have reduced body weight (p < .0001), total body fat (p < .0001), and percentage body fat located in the abdominal region (p < .05). In addition, there has been a sustained reduction in plasma leptin concentrations (p < .001). These findings suggest reduced risk for common morbidities, such as insulin resistance, dyslipidemia, and type 2 diabetes mellitus, that are associated with advancing age and increased levels of body fat, especially in the visceral depot.

Dietary restriction (DR), or undernutrition without malnutrition, is the only intervention that has been shown to increase both average and median life span in laboratory rodents (1–3). The ability of DR to increase life span is also seen in spiders, fish, water fleas, and other animals (1). In the field of body composition, DR studies are able to address two points, the effects of the intervention and normal aging. Alteration in body composition, mainly a decrease in fat mass, is among the first changes seen with the initiation DR. In rodents, 40% DR results in rapid and dramatic decreases in fat mass (4–7). Studies of DR in rhesus monkeys at the National Institute on Aging (males and females in three age groups, 1–2 years of age, 3–5 years of age, and > 15 years of age at the onset of DR) (8, 9) and the Wisconsin Regional Primate Research Center (males and females, 6–14 years of age at the onset of DR) (10–12) both similarly show reduced body weight and body fat in DR compared to control animals.

Studies in rodents have shown that percent survival and maximal life span are related to degree of DR (13). These results show that the DR effect on life span does not simply involve prevention of obesity. Furthermore, genetically obese mice on DR maintain high levels of body fat and show a similar degree of life extension as DR lean mice (14). These results suggest that the life-extending action of DR is not simply the result of the prevention of obesity or the maintenance of an extremely thin body composition. However, prevention of obesity does confer health benefits in the realm of metabolism and cardiovascular health.

Accumulation of excess body fat has long been known to have adverse effects on health, and severe obesity is clearly associated with increased mortality (15). Mortality among obese women (bone mass index [BMI] ≥ 29) is more than twice that among the leanest (BMI ≤ 19) women (16). In addition to overall obesity, body fat distribution has long been known to differentially affect health (17), and more recently, studies have shown that excess abdominal adiposity is a risk factor for, among other things, cardiovascular disease (18–20) and glucoregulatory impairments (21,22). The distinction between visceral and subcutaneous fat is also informative of general health and disease prediction. There is substantial evidence to link visceral fat to increased risk for diabetes and coronary heart disease (23).

Nonhuman primates make excellent models for human health and aging due to their close phylogenetic relationship to humans, and their largely shared anatomy, physiology, and behavior (24,25). In particular, the rhesus monkey (Macaca mulatta) is an excellent model in large part due to the extensive knowledge of this species. Although body composition information for rhesus monkeys is less extensive than for humans, studies have shown similar age-related trends. Specifically, there is a reduction in the percentage of lean mass and an increase in the percentage of fat mass with age leading to middle age animals having generally higher percent body fats than old animals (26). Rhesus monkeys have been shown to be susceptible to spontaneous obesity (27–31), as well as obesity-related glucoregulatory impairments (29,31), hypertension, and cardiovascular disease (32,33).

Body composition is regularly assessed (by somatometric measurements and dual-energy x-ray absorptiometry) as part of a long-term study of DR and aging in male rhesus monkeys (10). In addition, plasma leptin levels, known to positively correlate with body fat content in rodents (34), rhesus monkeys (35) and humans (36), have also been evaluated.

The aim of the present study is twofold. First, the effect of DR on parameters of body composition, particularly fat distribution, is evaluated. Second, the longitudinal effect of aging on these parameters is explored within a paradigm of undernutrition without malnutrition, or DR. This work adds to the literature regional assessment of body composition and new insights into the actions of DR.

METHODS

Subjects and Design

The effects of aging and DR were analyzed longitudinally in a group of adult male rhesus monkeys, ranging in age from 8 to 14 (average 9.3) years at the beginning of the study. A more de-
The 30 rhesus monkeys (Macaca mulatta) used in this study have lived their entire lives at the Wisconsin Regional Primate Research Center. Prior to the start of this experiment, no animals in the study group had any clinical or experimental history that would be expected to affect body composition. All animals were individually housed, to allow for the accurate assessment of daily food intake (10), and grouped into two rooms. Within rooms, individuals had extensive visual and auditory contact with each other and were provided with an enriched environment consisting of perches, branches, and small noninjurious toys which were rotated on a regular basis. Animals rooms were maintained at an approximate temperature of 21°C and humidity of 50–65%. Room lighting was automatically controlled on a 12-hour light, 12-hour dark schedule.

Animals were monitored daily for general health by animal care and research staff and semiannually by veterinary staff. Since the onset of the study in 1989, five animals have died (two control [C], three dietary restricted [R]). The two C animals died from anesthesia complications (following the 36-month assessment) and bloat (following the 72-month assessment). The three R animals died from anesthesia complications (following the 18-month assessment), cardiomyopathy (following the 54-month assessment), and aspired vomitus (following the 60-month assessment). The remaining animals were in relatively good health as evidenced by normal complete blood count and serum chemistry values (with the exception of elevated triglyceride levels in the C animals). Additionally, some C animals began to show indications of altered glucose regulation (elevated basal insulin and glucose) by the 30-month assessment and asymptomatic hypertriglyceridemia (38).

Animals were monitored for individual baseline food intakes of a purified diet (Teklad #85387, Madison, WI [10]) for a period of 3 months prior to the start of the study. Animals were then randomized to either C (n = 15) or R (n = 15) groups based on their baseline intake values of the Teklad diet.

All animals had 24-hour access to water and were supplied with food for approximately 6–8 hours per day. C animals were fed approximately 20% more than their average daily intake, and R animals were fed their allotted 30% reduction from individual baseline intake values. Each animal was fed their individually weighed portion of food in the morning. In the late afternoon, any food remaining in the food hoppers was collected and weighed. In addition, food left in the cage, or on the screen below the cage was counted and the weight determined. The weight of this spillage was estimated by the average weight of a piece of food and not by actual weight, avoiding overestimation caused by wet food. Very few animals scattered food outside their cages. When an animal was found to do this consistently, a cover was placed over the food hopper to prevent the animal from throwing food. At the time food was removed in the evening, each animal received a piece of fresh fruit. This method of calculating food intake has been fully described previously (10).

Procedures

Body size and composition.—Body weight and somatometric assessments of body composition were performed semiannually beginning at baseline. For these analyses, measurements from baseline through 90 months were used. Body weight (BW; kg) and somatometric measurements were taken while the animals were sedated with ketamine HCl (10 mg/kg, intramuscularly [IM]). Somatometric measurements included circumferences of the abdomen (AbCirc, cm), chest (ChCirc, cm), upper arm (ArmCirc, cm), and upper leg (LegCirc, cm) taken with a nonelastic tape measure while the animal was in lateral recumbency; skin fold thicknesses (indications of subcutaneous fat depth) taken at the triceps (ChF; mm), pectoral (ArmF; mm), and two abdominal sites (5 cm above and below the umbilicus summed as AbF; mm) taken with the animal in a supine position with Lange calipers; and crown-rump length (CR; cm) measured with the animal in a supine position on a board with a calibrated rule and a fixed headrest. Derived indices of adiposity and fat distribution, bulge (AbCirc/CR), and sag (AbCirc/ChCirc) were calculated.

Body composition was measured by dual-energy x-ray absorptiometry (DXA; Model DPX-L, Pediatric software version 4.0a, Lunar Corp., Madison, WI) yearly from 12 months of DR through the 60-month assessment period and then every six months from the 66–90-month assessments. At baseline, the DXA technology was unavailable. Body composition as measured by DXA yields results for fat mass (total), lean mass, bone mineral content, and bone mineral density for the total body and definable regions of interest. Total body scans were performed following somatometric measurements under additional ketamine HCl (7 mg/kg, IM) and xylazine (0.6 mg/kg, IM) for maintenance of anesthesia and muscle relaxation. Each total body scan took ~15 minutes with the animal in the supine position. Analyses were conducted on total body, as well as defined regions of interest (abdomen, chest, arms, legs). The regions of interest were defined based upon bony landmarks. The abdominal region includes from the first lumbar vertebrae through the first sacral vertebrae, the chest was defined as from the level of the shoulders until immediately above the first lumbar vertebrae, and the upper and lower legs were divided at the interface of the femur and tibia. DXA is a safe, noninvasive, precise method of analyzing soft tissue and bone mass; the precision, (mean/standard deviation) × 100, of total body composition and regional analysis by DXA was less than 5% (Table 1).

Table 1. DXA Scan Precision

<table>
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<tr>
<th>Region</th>
<th>Compartment</th>
<th>Precision* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total body</td>
<td>Lean mass</td>
<td>0.8</td>
</tr>
<tr>
<td>Total body</td>
<td>Fat mass</td>
<td>1.8</td>
</tr>
<tr>
<td>Total body</td>
<td>Percent fat mass</td>
<td>1.4</td>
</tr>
<tr>
<td>Abdominal</td>
<td>Fat mass</td>
<td>3.6</td>
</tr>
<tr>
<td>Abdominal</td>
<td>Percent fat mass</td>
<td>1.9</td>
</tr>
<tr>
<td>Arms</td>
<td>Fat mass</td>
<td>3.5</td>
</tr>
<tr>
<td>Chest</td>
<td>Fat mass</td>
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<tr>
<td>Upper leg</td>
<td>Fat mass</td>
<td>3.8</td>
</tr>
<tr>
<td>Lower leg</td>
<td>Fat mass</td>
<td>4.7</td>
</tr>
</tbody>
</table>

*Precision = coefficient of variation determined as the average of the CVs of five repeated scans taken from five monkeys.
DXA analysis of fat tissue mass has also been shown to be accurate to within 6% by comparison with chemical analysis (39).

**Leptin.**—Fasting plasma leptin levels were measured in all animals yearly from the 12-month through the 72-month assessment period. Basal samples acquired during a frequently sampled intravenous glucose tolerance test (FSGTT), performed as a regular part of the semiannual assessment period (10,37), were analyzed at the Wisconsin Regional Primate Research Center Assay Laboratories, using a radioimmunoassay kit developed and validated for rhesus monkeys (LINCO Research Inc., St. Louis, MO). The inter- and intrasay coefficients of variation for this assay in our laboratories were 10.48% and 4.53%, respectively.

**Statistics.**—All data were initially analyzed cross-sectionally at each individual time point using two-tailed t tests in Systat (Systat Inc., Evanston, IL). All variables were then tested for time-by-treatment interactions in SAS (SAS Institute, Cary, NC). If the interaction was significant, the treatment groups were compared using simple-effect t tests at the .05 level. For the analysis with no baseline value, a repeated-measures analysis of variance (ANOVA) was used, and when baseline values were available, analysis of covariance (ANCOVA) was used to account for initial values. The statistical software used for this analysis (SAS, SAS Institute, Cary, NC) allows the user to choose the best matrix by giving information as to how appropriate each matrix is for the given data set. In both cases, an appropriate covariance structure was used (either unstructured or Toeplitz). At the 72-month assessment, the relationship between plasma leptin values and body composition, basal glucose, basal insulin, and insulin sensitivity parameters derived from the minimal model analysis (10,37) were examined with scatterplots, Pearson product moment correlations, and stepwise multiple regression analysis in Systat (Systat Inc., Evanston, IL). Data for animals that have died since the onset of the study were included in the data set until their time of death.

**Results**

**Body weight.**—Body weight, somatometrics, and total body composition as measured by DXA have previously been reported for this study through the 36-month assessment period (10,11,37). The data presented here extend the analysis through 90 months of DR and add the assessment of new somatometric measurements, regional body composition by DXA and leptin.

**Somatometrics**

Body weight, which did not differ at baseline between C and R animals, showed a significant \(p < .0001\) time-by-treatment interaction and was different \(p < .05\) between groups from 12 through 90 months of study (Figure 1). This difference in overall size was also apparent in regional measurements of body composition. The C and R animals did not differ at baseline in AbCirc; however, there were a significant \(p < .0001\) time-by-treatment interaction and a significant \(p < .05\) treatment effect in AbCirc from 12 through 90 months of study (Figure 2). Other circumference data (ChCirc, ArmCirc, LegCirc) showed similar results (data not shown). AbF, representing abdominal subcutaneous fat mass, did not differ at baseline between groups, and similar to other variables, had a significant \(p < .0001\) time-by-treatment interaction and a significant \(p < .05\) treatment effect from 24 through 90 months (Figure 3). Results for ChF and ArmF, representing subcutaneous fat mass from the chest and arm regions, respectively, were similar (data not shown). Derived indices of adiposity and fat distribution, bulge and sag, differed between groups as well (Figure 4). Both variables had a significant \(p < .0001\) time-by-treatment interaction and a significant \(p < .05\) treatment effect beginning at either 12 (bulge) or 24 (sag) months and were maintained through 90 months.

**DXA**

Total body fat (TBF) and lean (TBL) mass measured by DXA showed significant \(p < .0001\) time-by-treatment interactions. TBF was significantly \(p < .05\) different at 12 months and this

![Figure 1. Influence of dietary restriction on body weight. Filled squares represent control (C) and open diamonds represent restricted (R) means for each time point. Bars represent standard errors. Time-by-treatment interaction was significant \(p < .0001\) and there was a significant treatment effect on body weight from 12 through 90 months. Asterisks (*) represent timepoints at which simple-effect \(t\) tests between C and R animals were significant \(p < .05\).](https://academic.oup.com/biomedgerontology/article-abstract/54/7/B283/541331/541331)

![Figure 2. Influence of dietary restriction on abdominal circumference. Filled squares represent control (C) and open diamonds represent restricted (R) means for each time point. Bars represent standard errors. Time-by-treatment interaction was significant \(p < .0001\) and there was a significant treatment effect on abdominal circumference from 12 through 90 months. Asterisks (*) represent timepoints at which simple-effect \(t\) tests between C and R animals were significant \(p < .05\).](https://academic.oup.com/biomedgerontology/article-abstract/54/7/B283/541331/541331)
difference was maintained through the 90-month assessment (Figure 5). The difference in TBF represents the largest portion of the difference in BW between C and R groups. TBL first became different between groups at 36 months and this difference was maintained through the 90-month assessment (Figure 5).

Regional body fat analysis (legs, chest, arms) showed similar trends as those seen for TBF (Figure 6). Total fat mass in the abdominal region, analyzed as a percentage of TBF (ABF%), showed a significant time-by-treatment interaction ($p < .05$) and this variable was significantly different between C and R groups at the 36-month assessment and then continually from the 66- through 90-month assessment periods (Figure 6). This indicates a difference in total fat mass, as well as in the distribution of body fat with DR.

**Leptin**

Fasting plasma leptin levels at the 72-month assessment period were found to correlate highly with indicators of body size and composition, whereas correlations with glucoregulatory parameters (10,37) were not as high (Table 2). All body size variables correlated positively with leptin levels, with the highest correlations being between leptin and percent fat ($r = .906, p < .0001$) and fat mass ($r = .898, p < .0001$). Changes in individual leptin concentrations were positively correlated with changes in body fat mass. A scatterplot representing the relationship between plasma leptin levels and percent body fat at the 72 month assessment period is shown in Figure 7, confirming the strong relationship between leptin and body fat. Differences in fasting plasma leptin values over time with DR mimicked the difference in body fat between C and R groups. There were a significant ($p < .001$) time-by-treatment interaction and a significant ($p < .05$) treatment difference from the 24-month assessment periods that were maintained through all other periods in which these effects were measured (through the 72-month assessment period, Figure 8).
Figure 7. Relationship between fasting plasma leptin levels and percent body fat at the 72-month assessment period. Each point represents data for an individual animal. Filled squares represent control (C) and open diamonds represent restricted (R) animals.

Figure 8. Influence of dietary restriction on fasting plasma leptin levels. Filled squares represent control (C) and open diamonds represent restricted (R) means for each time point. Bars represent standard errors. Time-by-treatment interaction was significant \( (p < .001) \). There was a significant treatment effect from 24 through 90 months. Asterisks (*) represent timepoints at which simple-effect \( t \) tests between C and R animals were significant \( (p < .05) \).

Table 2. Pearson Product Moment Correlations With Fasting Plasma Leptin Values at the 72-Month Assessment Period

<table>
<thead>
<tr>
<th>Region</th>
<th>Correlation</th>
</tr>
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<tbody>
<tr>
<td>Body weight</td>
<td>.868*</td>
</tr>
<tr>
<td>Fat mass</td>
<td>.898*</td>
</tr>
<tr>
<td>Percent fat</td>
<td>.906*</td>
</tr>
<tr>
<td>Lean mass</td>
<td>.712†</td>
</tr>
<tr>
<td>Basal insulin</td>
<td>.564†</td>
</tr>
<tr>
<td>Basal glucose</td>
<td>.344</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>(-.608^*)</td>
</tr>
<tr>
<td>Glucose effectiveness</td>
<td>(-.309)</td>
</tr>
<tr>
<td>Glucose disappearance rate</td>
<td>(-.260)</td>
</tr>
<tr>
<td>Acute insulin response</td>
<td>.389</td>
</tr>
</tbody>
</table>

Note. \( n = 26 \).

\(^* p < .0001; ^† p < .01; \) correlations with no superscript are \( p > .05 \).

DISCUSSION

In humans, body composition is known to change as a function of age, with some individuals showing an increase in body fat in middle age and a late-life reduction in fat (40,41). As part of this increase in percent body fat, there is an increase in the percent of fat in the abdominal region with age (42). The body composition literature for nonhuman primates is less extensive than the human literature; however, the data available indicate that nonhuman primates follow age-related trends similar to humans. For example, nonhuman primates lose lean mass and gain fat mass with increasing age, leading to an increase in percent body fat in older compared to younger animals (26,43,44). In addition, rhesus macaques are susceptible to spontaneous obesity (27–31) and the associated glucoregulatory impairments (29,31) as well as hypertension and cardiovascular disease (32,33).
Our monkeys are currently middle-aged and some C animals are showing the human-like increase in body fat associated with this age group. However, we do not have baseline DXA body composition data, and our food intake and body weight data suggest that food intake was greatest in the C animals during the first year of study (10). In Figure 1, there appeared to be a rapid increase in body weight between 6 and 12 months of study. It is likely that much of this weight gain reflects fat mass, as indicated by the somatometric measurements; however, we do not have DXA data to address this question. Therefore, the changes we see in body fat mass probably underestimate the actual changes that have occurred since the beginning of this study. Other studies in rhesus monkeys also show an increase in body fat mass with age (26,43,44). At this point, the animals are not yet old enough to begin to show the late-life reduction in body fat characteristic of human aging. These changes in body composition, in conjunction with alterations in energy intake and energy expenditure, are closely tied to many of the diseases of aging.

In addition to overall obesity, body fat distribution has long been known to differentially affect health. In 1956, Vague (17) first published his observations of the effect of the different patterns of body fat distribution found in males (android, or upper body obesity) and females (gynoid, or lower body obesity). He discovered that women with upper body obesity (the pattern more often found in men) were more likely to suffer from atherosclerosis and diabetes than women with the more common gynoid pattern of fat distribution (17). More recently, studies of regional adiposity, those that emphasize the location of fat rather than the whole body fat mass, have shown that excess abdominal adiposity (matching Vague's android or male type obesity) is a risk factor for, among other things, cardiovascular disease and glucoregulatory impairments.

Our data have shown that adult onset DR can be safely initiated (10,11,37), and maintained long-term (7.5 years), in a non-human primate, the rhesus monkey. The results discussed here agree with other studies of DR in rodents (4-7) and nonhuman primates (9,12) in that the main treatment effect upon body composition, in conjunction with alterations in energy intake and energy expenditure, are closely tied to many of the diseases of aging.

Obesity is a strong predictor for the risk of developing glucoregulatory impairments and, eventually, diabetes mellitus (45). Hyperinsulinemia is associated with overall obesity (23,46-48), upper-body obesity, (21,22) and with visceral fat accumulation (23). In patients with non-insulin-dependent diabetes mellitus (NIDDM), obesity diminishes the insulin sensitivity of both hepatic and peripheral tissues (49) and increases insulin resistance and fat metabolism (45). To this end, weight loss improves insulin sensitivity and glycemic control in obese NIDDM patients (50,51).

Obesity is also a known risk factor for cardiovascular disease (52); however, evidence is now leaning more toward regional fat being a more important predictor of susceptibility to disease mortality and morbidity than overall body fat (18-20). Men with little body fat, but with fat located primarily in the abdominal region, were at highest risk for ischemic heart disease, whereas obese men with fat distributed evenly over the body were at the lowest risk (19). In women, the same association was found but it was even more pronounced (20). A recent autopsy study of young men found that abdominal fatness, assessed by the waist-hip ratio, was associated with mild cardiac hypertrophy and the severity of coronary lesions of atherosclerosis-prone regions of the coronary tree in men under 40 years of age, without any signs of cardiovascular disease in their lifetime (53). Further, upper body obesity, especially fat localized to the abdominal visceral compartment, has been shown to be a significant and independent predictor of cardiovascular disease, associated with hypertension (34), dyslipidemia (35), and increased cardiovascular disease (36).

In addition to the glucoregulatory and cardiovascular risks associated with obesity and excessive abdominal and visceral adiposity, body fat distribution has been associated with increased risk from cerebrovascular disease. An elevated waist-hip ratio, indicating abdominal obesity, was found to be a risk factor for cerebrovascular disease (57), and recently, a strong association has been found between abdominal obesity (by waist-hip ratio and waist circumference) and stroke (58).

Based upon the decrease seen in the percent of the TBF that was localized in the abdominal region (Figure 6), DR may be improving health not only by decreasing the total fat mass and preventing the spontaneous obesity of adulthood, but by altering the distribution of fat away from the more medically dangerous abdominal distribution.

TBF was also evaluated indirectly through measurements of plasma leptin. Plasma leptin concentrations were significantly lower in R compared to C animals at each assessment period. These results agree with studies in rodents (59) and humans (59-61) which have shown that food restriction results in a significant decrease in circulating leptin concentrations. Our study suggests that the initial decrease in blood leptin concentration with food restriction is maintained as long as DR is continued. Because leptin is secreted by adipocytes and should change with alterations in the size of the body fat store, the changes in leptin concentration with DR appear to reflect changes in body fat content. Studies have shown that leptin is strongly correlated with measures of body fat in rodents (34), humans (36), and rhesus monkeys (35). In agreement with these studies, we found that total body fat or percent body fat were the best predictors of plasma leptin concentration. Inclusion of insulin or glucose in the model did not improve the prediction of leptin. These results show that leptin is a good indicator of fat mass and changes in leptin and body fat content occur in parallel.

As in humans, the relationship between body weight and plasma leptin concentrations becomes more variable with increasing body weight (36). Most leptin studies, however, present data from extremely obese individuals and leptin values are highly variable in these subjects. The relatively low leptin variability in our study probably reflects the fact that none of the animals were grossly obese, and we saw no evidence for extremely high leptin levels, as seen in morbidly obese humans, in our heaviest monkeys. Also, environmental variables, such as diet and opportunity for exercise, were controlled.
BODY FAT DISTRIBUTION AND DIETARY RESTRICTION

In addition to indicating the size of body fat stores, it is also possible that decreases in leptin concentration contribute to the antiaging action of DR. It has recently been proposed that the major function of leptin may be to regulate the neuroendocrine response to fasting (62). Studies have shown that leptin levels decrease rapidly during fasting in rodents (62) and humans (63,64). Similarly, changes in blood leptin concentrations appear to be among the most rapid of the sustained hormonal changes with DR. In our experiment, plasma leptin concentrations differed at 12 months and became highly significant by the 24-month assessment period, whereas significant differences in insulin did not occur until the 30-month assessment (37). It is possible that decreases in plasma leptin levels with DR play a role in regulating changes in insulin, adrenal hormones, thyroid hormones, and energy expenditure, similar to the role leptin may play in regulating changes in these parameters during short-term fasting. Leptin has been proposed to play a major role in regulating insulin secretion (65) and energy expenditure (66,67). Decreases in both of these processes have been postulated as major contributors to the effects of DR. It is possible that a decrease in leptin is crucial towards regulating the changes in energy expenditure and insulin, as well as other endocrine changes, that occur with DR.

In conclusion, DR led to the expected decreases in body weight and body fat mass. DR also led to decreases in fasting plasma leptin concentrations and abdominal body fat. These changes are all indicative of improved health, potentially leading to a decrease in morbidity and mortality and extension of life span. Future use of methods, such as computer tomography and ultrasound, that provide more accurate assessment regional body fat, particularly subcutaneous and visceral fat mass, may allow for further elucidation of how DR positively affects body fat distribution.

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