ADRENAL GLUCOCORTICOIDS (GC) are important modulators of energy balance. Removal of GC by adrenalectomy (ADX) attenuates or prevents the development of obesity in the majority of genetic and experimental rodent models of obesity (35), an effect that is reversed by administration of corticosterone (18). GCs act on energy metabolism both at the central level, where they affect neuronal pathways involved in the regulation of food intake and energy expenditure, and at the periphery, where they modulate metabolic pathways that accommodate changes in energy balance (7, 8, 38). The metabolism of lipid substrates undergoes alterations that adjust its various components to the lipid flux imposed by energy intake and expenditure, and several of these components are directly modulated by GC. Indeed, the steroids positively modulate hepatic lipid synthesis and secretion (2, 6, 41) and potentiate the positive modulation by insulin of adipose tissue lipoprotein lipase (LPL) (1, 19, 31), the enzyme responsible for the tissue uptake of fatty acids derived from circulating triglycerides (TG). GCs also tend to stimulate insulin secretion through several mechanisms (5, 39), and insulin shares with corticosterone most of its actions on lipid production and storage.

The respective contribution of central and peripheral actions of GC on overall lipid metabolism remains to be fully determined. The centrally mediated anorectic and thermogenic effects of GC removal, for instance through ADX, obviously result in decreased TG synthesis in the liver, secretion and transport into the circulation, and deposition into lipid stores. Changes in determinants of TG metabolism brought by manipulation of the GC status have indeed been found to correlate with the concomitant alterations in energy intake (9, 25). However, this relationship is partial, and direct peripheral actions of GC may be involved in the establishment of some of the adaptations of TG metabolism to centrally mediated alterations in energy intake.

The present study, therefore, aimed to verify the hypothesis that ADX exerts actions on TG metabolism that are independent of those on energy intake. This was verified by comparing rats having undergone ADX to intact animals whose energy consumption was matched to that of their ADX counterparts. The consequences of altering the GC status on energy and TG metabolism are strongly dependent on diet composition (22, 25, 35, 36). We have indeed shown that the impact of GC on TG metabolism is minimal when diet composition maintains a low lipid flux but becomes highly significant when diet increases lipid flux (25). Therefore, a diet that maintains a low lipid flux (rodent chow) was compared with a diet high in sucrose and fat (HSF), which maintains a high lipid flux and produces alterations in glucose and lipid metabolism (25) that are reminiscent of those observed in the human dyslipidemic insulin resistance syndrome (11). This comparison allowed testing of the secondary hypothesis that
the energy intake-independent, peripheral actions of GC on TG metabolism are modulated by diet composition.

**MATERIALS AND METHODS**

**Animals and Treatments**

Two cohorts of 32 male Sprague-Dawley rats each (Charles River; St. Constant, Quebec, Canada) initially weighing 225–250 g were housed individually in stainless-steel cages in a room maintained at 24 ± 1°C, with a 12:12-h light-dark cycle (lights on at 0000). The animals were cared for and handled in compliance with the Canadian Guide for the Care and Use of Laboratory Animals, and the experimental procedures were approved by our institutional animal care committee. In each of the two cohorts, the animals were randomly assigned to four groups according to a 2 × 2 factorial design. The factors were the adrenal status with two levels (intact and ADX) and diet with two levels (chow and HSF).

Bilateral removal of the adrenals was performed in two groups of each cohort, whereas the remaining two groups underwent a sham operation. The bilateral removal of the adrenals was achieved through two small lateral skin incisions performed under isoflurane anesthesia. The adrenals were pulled out through the incision by holding the periadrenal fat and were severed with scissors. After each excision surgery, incisions were appropriately sutured. Sham-operated animals were handled in the same way as ADX animals except that the adrenals were not excised.

All rats were given 0.15 M NaCl in lieu of water to drink throughout the experiment and were fed either a commercial, high-carbohydrate nonpurified diet (Charles River rodent chow #5075), with an energy density of 14.4 kJ/g, or the HSF diet that contained 41% of energy as carbohydrate (sucrose), 39% as lipid (1:1, corn oil to lard), and 20% as protein (casein), supplemented with vitamins, minerals, and fiber, with a gross energy content of 19.44 kJ/g. Food intake and body weight were recorded daily during the experimental period. Throughout the experiment, food intake of the intact animals was measured so as to avoid the strong effects on lipid metabolism of the acute nutritional status, which would have differed between intact and ADX animals. An additional group of five intact animals was fed the chow diet ad libitum throughout the experiment and was used for comparison of food intake and body and tissue weights with the pair-fed and ADX groups fed chow.

Variables of TG Metabolism

VLDL-TG secretion rate. An initial blood sample (0.15 ml) was withdrawn through the venous catheter, and rats were injected through the catheter with 300 mg/kg body wt of Triton WR-1339 (Sigma, St. Louis, MO), a detergent that prevents intravascular TG catabolism (32). Blood samples (0.15 ml) were then taken 20, 40, and 60 min after the Triton injection. The rate of VLDL-TG secretion into the circulation was determined from regression analysis of TG accumulation in plasma versus time. Secretion rate was calculated by multiplying the slope of the regression line by plasma volume estimated from body weight and was expressed as micromoles per minute.

Postheparin plasma lipases. Approximately 0.5 ml of blood was drawn from the jugular catheter 10 min before and 10 min after the rapid intrajugular administration of 200 IU/kg body wt of sodium heparin (porcine intestinal mucosa, 1,000 USP/ml, Sigma) (23). Blood was centrifuged at 1,500 g, 4°C for 15 min, and plasma was stored at −70°C for later biochemical measurements.

Blood and tissue harvesting. Rats were killed by decapitation. Blood collected from the neck wound was centrifuged at 1,500 g, 4°C for 15 min. Serum was stored at −70°C for later biochemical measurements. Retroperitoneal and inguinal white adipose tissues (WAT) as well as the vastus lateralis muscle (VLM) were excised and weighed. Approximately 50 mg were taken from WAT and the red portion of the VLM, and tissue samples were homogenized using all-glass tissue grinders (Kontes, Vineland, NJ). WAT were homogenized in 1 ml of a solution containing 0.25 M sucrose, 1 mM EDTA, 10 mM Tris-HCl, and 12 mM deoxycholate, pH 7.4. The VLM was homogenized in 1 ml of a solution containing 1 M ethylene glycol, 50 mM Tris-HCl, 3 mM deoxycholate, 10 IU/ml heparin, and 5% (vol/vol) aprotinin (Trasylo, Miles Pharmaceuticals, Rexdale, Ontario, Canada), pH 7.4. These homogenizing media were found to yield optimal LPL activities in the individual tissues. Homogenates of the VLM were quickly frozen and stored at −70°C until measurement of LPL activity. WAT homogenates were centrifuged at 12,000 g, 4°C for 20 min. The fraction between the upper fat layer and the bottom sediment was removed after tube slicing, diluted with four volumes of the homogenization solution without deoxycholate, and stored at −70°C until later measurement of LPL activity.

Serum variables. Insulin was quantitated by radioimmunoassay using a reagent kit from Linco Research (St. Charles, MO) with rat insulin as standard. Serum corticosterone was determined by a competitive protein-binding assay (sensitivity: 0.058 nmol/l; interassay coefficient of variation: 9.0%) using plasma from a dexamethasone-treated female Rhesus monkey as a source of transcertin (27). Serum glucose was determined by the glucose oxidase method using the Beckman glucose analyzer (Beckman, Palo Alto, CA). TG concentrations were assayed by an enzymatic method using a reagent kit from Boehringer Mannheim (Montréal, Quebec, Canada), which allows correction for free glycerol. Plasma nonesterified fatty acids (NEFA) were determined with a reagent kit from Wako Chemicals (Richmond, VA).

Postheparin plasma lipases and tissue LPL activities. LPL activity was measured in postheparin plasma and tissue homogenates as described earlier (33). Samples of 100 µl of postheparin plasma diluted 1:50 with saline and of WAT and VLM homogenates were incubated for 1 h at 28°C under gentle agitation with 100 µl of a substrate mixture consisting of a 0.2 M Tris-HCl buffer, pH 8.6, which contained 10 MBq/ml carboxyl-14C linoleate and 2.52 mM cold linoleate emulsified in
5% gum arabic, as well as 2% fatty-acid free bovine serum albumin, 10% human serum as a source of apolipoprotein C-II, and either 0.1 or 2 M NaCl. Free oleate released by LPL was then separated from intact triolein using a liquid partition system (3) and mixed with Universal (New England Nuclear, Montreal, Canada), and sample radioactivity was determined. LPL activity was calculated by subtracting non-LPL lipolytic activity determined in a final NaCl concentration of 1 M from total lipolytic activity determined in a final NaCl concentration of 0.05 M. Postheparin plasma hepatic TG lipase (PHHL) activity was directly evaluated in plasma samples to which 25 mM sodium dodecyl sulfate was added before incubation with the TG emulsion to inhibit LPL activity (42). Tissue LPL activity was expressed as microunits (1 µmol NEFA released per hour of incubation at 28°C), and PHLPL and PHHL activity was expressed as microunits per milliliter of plasma. The interassay coefficient of variation was 4.8% and was determined using bovine skim milk as a standard source of LPL. Protein content of the tissue extracts was determined by the method of Lowry et al. (24). Tissue LPL activity was expressed per total tissue (total activity) and per unit tissue protein (specific activity).

Statistical analysis. Data are expressed as means ± SE. Main treatment effects and treatment interactions were analyzed using factorial analysis of variance (ANOVA). Comparison between intact ad libitum, intact pair fed, and ADX groups fed chow (Table 1) was performed by one-factor ANOVA. When significant, individual means were then compared pairwise using Fisher’s protected least squares difference (PLSD) post hoc test. All other comparisons were performed by two-factor ANOVA. The factors were the adrenal status with two levels (intact, ADX) and diet with two levels (chow, HSF diet). When justified by a significant treatment interaction, comparisons between individual group means were performed using Fisher’s PLSD test. Data were log transformed before analysis when group variances were not homogeneous (O’Brien’s test), but untransformed values are presented below. Differences were considered statistically significant at P < 0.05.

RESULTS

The effects of ADX on food intake and of pair feeding and ADX on body and tissue weights of chow-fed rats are shown in Table 1. ADX induced a 25% reduction in ad libitum food intake, which was reflected in body weight that was 11% smaller than that of intact rats fed ad libitum. Final body weight of intact, pair-fed rats was identical to that of ADX animals. The mass of the three adipose depots that were considered was decreased almost by one-half in ADX compared with intact animals. In contrast, pair feeding intact animals did not result in any significant change in adipose tissue weight compared with their ad libitum-fed counterparts. Vastus lateralis weight remained unaltered by either pair feeding or ADX.

As expected, surgery to remove the adrenals resulted in a slight loss of body weight (Fig. 1, days 0-2), which was followed by resumption of weight gain. Therefore, the present experimental conditions resulted in an initial weight loss that was followed by a phase of weight recovery and stunted growth compared with intact animals fed chow ad libitum (Fig. 1, inset). The ADX animals appeared to be more sensitive in terms of weight gain to subsequent surgery and 12-h fasting [cannulation (day 6) and fasting (day 8) before postheparin plasma lipase procedure] than their intact pair-fed counterparts. However, neither the adrenal status nor the type of diet significantly affected final body weights (see below) after 12 days of treatment.

The impact of the adrenal status and diet on energy intake, final body weight, and plasma variables is depicted in Table 2. ADX rats fed the HSF diet ingested slightly (+6%), but significantly, more energy than those fed chow, which did not translate into a significant difference in final body weight. Final body weights were similar in intact pair-fed and ADX groups regardless of diet. Fasting plasma corticosterone levels were similar in intact rats of both dietary cohorts and undetectable in ADX animals. The adrenal status and diet affected neither fasting plasma levels of TG and NEFA nor the activity of PHLPL, whereas ADX exerted an overall lowering action on PHHL.

As depicted in Fig. 2A, liver TG content, an index of long-term hepatic TG production, was more than twofold higher in HSF- than in chow-fed rats, whereas it remained unaffected by the presence or absence of corticosterone. In contrast, ADX reduced hepatic VLDL-TG secretion rate by 41% in chow-fed rats, an effect that was abolished in HSF-fed animals (adrenal status × diet interaction; Fig. 2B). Diet did not affect VLDL-TG secretion rate in intact pair-fed rats. Despite equal energy intakes, ADX rats displayed lower insulinemia than intact pair-fed animals (Fig. 3A). The difference related to the adrenal status was attenuated in HSF-fed rats, as ADX reduced fasting insulinemia less in the latter than in their chow-fed counterparts (adrenal status × diet interaction). Plasma insulin was identical in intact pair-fed rats regardless of diet. Fasting serum glucose was reduced in ADX compared with intact pair-fed rats but remained unchanged by diet (Fig. 3B).

The effects of the adrenal status and diet on retroperitoneal WAT are depicted in Fig. 4. ADX resulted in lower retroperitoneal WAT weight than pair feeding in both dietary cohorts, whereas depot weight was higher in HSF- than in chow-fed rats (Fig. 4A). Although the ADX effect was relatively smaller in HSF- than in chow-fed animals (~33% vs. ~58%), treatments did not interact significantly with each other. Total protein

| Table 1. Average daily energy intake, final body weight, WAT and muscle weights of intact rats fed the nonpurified diet ad libitum or pair-fed, and of ADX rats fed the nonpurified diet ad libitum for 12 days |
| --- | --- | --- | --- |
| | Intact Ad Libitum | Intact Pair-Fed | ADX Ad Libitum |
| Energy intake, kJ/day | 337 ± 13* | 259 ± 2† | 254 ± 8† |
| Final body weight, g | 339 ± 6* | 302 ± 3† | 302 ± 7† |
| Retroperitoneal WAT, g | 1.26 ± 0.13* | 1.21 ± 0.17* | 0.61 ± 0.12† |
| Epididymal WAT, g | 1.94 ± 0.18* | 1.56 ± 0.14* | 1.08 ± 0.09† |
| Inguinal WAT, g | 1.27 ± 0.07* | 1.17 ± 0.12* | 0.72 ± 0.05† |
| Vastus lateralis, g | 1.06 ± 0.02 | 1.09 ± 0.03 | 1.02 ± 0.05 |

Values are means ± SEM of 5-8 animals. WAT, white adipose tissue; ADX, adrenalectomized. Means not sharing a common superscript are different from each other at P < 0.05.
content closely reflected depot mass, and both were highly correlated ($r = 0.89, P < 0.0001$), indicating that the extra depot weight loss induced by ADX included both lipid and protein mass (Fig. 4B). Despite treatment effects on depot weight, total LPL activity was comparable in all groups (Fig. 4C). However, when expressed relative to total protein, LPL activity was higher in ADX than in intact pair-fed animals, whereas it remained unaffected by diet (Fig. 4D). Globally, similar observations were made in the subcutaneous inguinal depot (Fig. 5). Despite the absence of a significant treatment interaction, examination of Fig. 5 indicates that the reducing effect of ADX on WAT weight was clearly stronger in chow- than in HSF-fed rats. Here again, protein content of the depot was reduced in ADX rats compared with the intact pair-fed animals (Fig. 5B). Total tissue LPL activity was comparable in all groups (Fig. 5C), but LPL was higher in ADX than in pair-fed rats when expressed as specific activity (Fig. 5D). In both WAT depots, insulinemia was positively correlated with weight ($r = 0.67, P < 0.0001$) but not with total or specific activity of LPL.

The slight reduction in VLM weight (Fig. 6A) and protein content (Fig. 6B) in ADX compared with intact pair-fed animals did not reach statistical significance, and these variables were not affected by the type of diet. Lipoprotein lipase activity was significantly reduced in ADX compared with intact pair-fed animals when expressed per total muscle (Fig. 6C), but not when expressed per unit protein (Fig. 6D). Diet did not affect muscle LPL in any substantial manner.

**DISCUSSION**

The present study confirms that in the presence of reduced energy intake, corticosterone contributes to the maintenance of adipose stores and that the consequences of its absence tend to be attenuated when a high-energy diet is fed. The study further shows that contrary to ad libitum feeding conditions, most determinants of TG metabolism, such as hepatic TG stores, triglyceridemia, PHLPL, and adipose tissue LPL are minimally affected by GCs when consumption of a high-energy diet is restricted, suggesting that GCs affect TG metabolism mostly indirectly through their central action on ingestive behavior.

It is well established that pair feeding brings about changes in energy balance that are not identical to those produced by ADX. Food restriction reduces sympathetically activated thermogenesis (13). In contrast, ADX lowers energy intake, but thermogenesis is maintained at higher levels than in pair-fed animals, because corticosterone no longer inhibits sympathetically mediated thermogenesis (13). An additional unknown metabolic component, independent of GC action and sympathetically mediated thermogenesis, also contrib-

<table>
<thead>
<tr>
<th>Energy intake, kj/day</th>
<th>Chow</th>
<th>HSF Diet</th>
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<tr>
<td>Intact ADX</td>
<td></td>
<td></td>
</tr>
<tr>
<td>259 ± 2 254 ± 8</td>
<td>276 ± 3 270 ± 6</td>
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<tr>
<td>Body weight, g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>303 ± 3 302 ± 7</td>
<td>318 ± 4 309 ± 9</td>
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<tr>
<td>Corticosterone, µmol/l</td>
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<tr>
<td>0.71 ± 0.09 ND</td>
<td>0.77 ± 0.08 ND</td>
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<tr>
<td>Triglycerides, mmol/l</td>
<td></td>
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<tr>
<td>0.51 ± 0.04 0.55 ± 0.04</td>
<td>0.40 ± 0.03 0.57 ± 0.10</td>
<td></td>
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<tr>
<td>NEFA, mmol/l</td>
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<tr>
<td>0.47 ± 0.03 0.43 ± 0.03</td>
<td>0.44 ± 0.02 0.45 ± 0.04</td>
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<tr>
<td>PHLPL, µU/ml</td>
<td></td>
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<tr>
<td>60 ± 6 50 ± 5</td>
<td>56 ± 4 53 ± 5</td>
<td></td>
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<tr>
<td>PHHL, µU/ml</td>
<td></td>
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<tr>
<td>42 ± 3 30 ± 3</td>
<td>41 ± 4 37 ± 4</td>
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</table>

Values are means ± SE of 7 or 8 animals, except for corticosterone (14 or 15 animals pooled from the two cohorts). ND, not detectable (intact means compared by Student's t-test); NEFA, nonesterified fatty acids; PHLPL, postheparin plasma lipoprotein lipase; PHHL, postheparin plasma hepatic lipase; NS, not significant.
utes to the conservation of energy stores during restricted feeding (14, 15). In the present study, such energy-conserving adaptations explain the larger adipose depots of pair-fed animals, which were only slightly below those of ad libitum-fed rats, compared with ADX rats despite identical energy intake. The findings also confirm the contribution of GC to these adaptations. On the other hand, diet composition, particularly a high fat content, has also been shown to promote the conservation of lipid stores during recovery from undernutrition in normal rats (12) and to attenuate the effects of ADX on fat stores of obese ob/ob mice (20, 22, 36). These effects are partly related to the lower cost of storing dietary fat compared with carbohydrate or protein (12). The sucrose component of the HSF diet was also likely involved, because dietary carbohydrates have been shown to influence the effects of ADX on energy balance (22, 35). The findings of the present study on the effects of the adrenal status and diet composition on adipose tissue mass are, therefore, congruent with these diet-GC interactions on energy balance.

Liver TG content, which reflects long-term endogenous TG production, was much higher in the HSF- than in chow-fed rats and was not affected by the presence or absence of corticosterone. This indicates that in situations of reduced energy intake, hepatic lipid production remains very sensitive to the amount of lipogenic substrates provided by the diet, as is the case in ad libitum feeding conditions (4, 25). Sucrose, particularly its fructose moiety, is highly lipogenic in rats (4, 10), which explains the higher hepatic TG content of rats fed the HSF diet compared with those fed chow. A larger uptake of dietary fatty acids, either nonesterified or within lipoprotein remnants, may also have contributed to a greater lipid input to the liver. In addition, the findings indicate that, although GCs clearly favor de novo lipid production by the liver (4) in animals fed ad libitum, their contribution becomes insignificant, regardless of diet composition, when energy intake is low. This is in sharp contrast to what we have observed in ad libitum-fed rats, in which marked effects of the adrenal status were noted on hepatic lipids, particularly in animals fed the HSF diet (25). It can therefore be concluded that corticosterone alters liver lipid production mainly through its central modu-

Fig. 2. Liver triglyceride (TG) content (A) and hepatic TG secretion rate (TGSR, B) in intact pair-fed (INT) and ADX rats fed chow or HSF diet for 12 days. Bars represent means ± SE of 4–8 animals. The ANOVA table presents the level of significance of main and interactive treatment effects on the variables as determined by two-factor ANOVA, 1 factor being the adrenal status with 2 levels (INT, ADX), and the other being diet with 2 levels (chow, HSF diet). Because factorial ANOVA revealed a treatment interaction on hepatic triglyceride secretion rate, pairwise comparisons between individual means were carried out to locate the interaction. Bars not sharing a common superscript are different from each other, P < 0.05; NS, not significant.

Fig. 3. Serum concentrations of insulin (A) and glucose (B) in INT pair-fed and ADX rats fed chow or HSF diet for 12 days. Bars represent means ± SE of 5–8 animals. Bars not sharing a common superscript are different from each other, P < 0.05. See Fig. 2 legend for significance of ANOVA table.
lation of nutrient intake rather than through a direct action on hepatic TG synthesis.

Fasting rates of hepatic VLDL-TG secretion in chow-fed, ADX animals were approximately one-half of those of their intact pair-fed counterparts, confirming the positive modulation of hepatic VLDL secretion by GC (4). In vitro studies have shown that GCs affect the intracellular fate of apolipoprotein B (41), which underlies their modulation of VLDL-TG secretion. Therefore, in the presence of a reduced supply of dietary energy, corticosterone contributes directly to approximately one-half of the hepatic output of TG into the circulation in the fasted state. However, this contribution of corticosterone to VLDL-TG secretion was no longer evident when the HSF diet was fed, as the HSF diet and the presence of corticosterone did not exert an additive effect on VLDL-TG secretion. It may be that corticosterone contributes to VLDL-TG secretion when hepatic TG stores are low, such as in rats pair fed the chow diet, but that this contribution is masked when hepatic TG stores are larger, as was the case in HSF-fed animals. In the chow-fed rats, adrenal status-related changes in hepatic TG secretion rates did not impact fasting triglyceridemia. This is likely because endothelium-bound LPL, which remained unchanged by treatments, was in sufficient amount to metabolize the larger mass of TG secreted in the intact rats, thereby maintaining their triglyceridemia to levels similar to those of ADX animals.

Adipose tissue LPL is generally modulated in concomitance with the flux of fat deposition. Indeed, LPL tends to be increased when energy metabolism favors fat accretion and is decreased with fat mass loss (16, 17, 29, 34). In the present conditions, however, adipose tissue LPL specific activity was higher and total tissue LPL similar in ADX than in intact pair-fed rats despite the smaller size of their fat depots. Moreover, higher adipose LPL in ADX rats compared with intact pair-fed animals was not congruent with the hormonal milieu created by ADX. In rats fed ad libitum, adipose LPL was greatly reduced by ADX in rats fed the HSF diet in concomitance with the effects of the adrenal status and diet on insulinemia (25). In the ADX rats of the present study, lower insulinemia and the absence of corticosterone, two positive modulators of the enzyme, as well as the possible activation of the sympathoadrenal system (13) should all have tended to decrease adipose tissue LPL activity relative to intact animals. Pairing the latter for food intake of ADX animals revealed that in conditions of reduced energy intake, adipose LPL appears to escape the endocrine modulation characteristic of ad libitum feeding conditions. This phenomenon perhaps manifests itself below a certain threshold of fat mass and would be akin to what is observed in well-

![Fig. 4. Weight (A), total protein content (B), and total (tot, C) and specific activity (spec, D) of lipoprotein lipase (LPL) in retroperitoneal adipose tissue of INT and ADX rats fed chow or HSF diet for 12 days. Bars represent means ± SE of 6–8 animals. See Fig. 2 legend for significance of ANOVA table.](http://ajpregu.physiology.org/10.1210/an00603.532)
trained athletes whose low fat reserves are associated with paradoxically high adipose LPL activity (26, 28). Such an adaptation, established by as yet unknown mechanisms, may serve to render a depleted adipose tissue ready for an eventual replenishment of fat stores. Finally, the fact that higher LPL activity was present in adipose tissues of ADX compared with pair-fed animals demonstrates that modulation of LPL is not part of the metabolic adaptations that favor the sparing of fat reserves elicited by GC.

In contrast to adipose LPL, muscle LPL was reduced by ADX, independently of the type of diet. Whether corticosterone directly influences muscle LPL activity has not yet been systematically investigated, and a lack of effect of ADX has been previously observed in ad libitum-fed male and female rats (25 and Y. Deshaies, A. Dagnault, and D. Richard, unpublished observations). The present results suggest however, that in conditions of reduced energy intake, the hormone may contribute to the maintenance of muscle LPL, which would constitute a useful adaptation to ensure an adequate supply of lipid substrates to the muscle. Inasmuch as LPL activity measured in tissue homogenates is proportional to the fraction of the enzyme pool available at the endothelial surface (30), it is worthy of noting that the divergent changes in LPL of adipose and muscle tissues tended to cancel each other, because total endothelium-bound LPL measured in postheparin plasma remained unchanged by treatments.

Despite identical food intake, fasting insulinemia diverged widely between intact and ADX animals, and the difference was greatly attenuated by consumption of the HSF diet. The present findings show that for a given level of energy intake, fasting insulin levels are maintained at a higher level in the presence than in the absence of corticosterone. This is in agreement with the notion that GCs tend to stimulate insulin secretion through several mechanisms (5, 39), including GC-induced peripheral insulin resistance (39) that is compensated by hypersecretion of insulin. The dampening of the hypoinsulinemic effect of ADX by consumption of the HSF diet is also congruent with the presence of insulin resistance associated with dietary sucrose and fat (37, 43). The present findings indicate that the development of insulin resistance induced by such diets is at least partly independent of GC. The effects of the adrenal status and diet on insulinemia, which correlated with those on fat mass, suggest an involvement of the hormone in treatment effects on body fat. This corroborates the well-known lipogenic actions of insulin, but the degree of involvement of insulin in treatment effects remains to be determined directly, as high-fat diets have been shown to dampen the effects of ADX on energy balance without concomitant changes.
in insulinemia (22). As to determinants of TG metabolism, our findings do not suggest an involvement of insulin in treatment effects. Indeed, given the known actions of insulin on TG metabolism (21, 40), changes in fasting insulinemia could not explain treatment differences in hepatic lipid content, hepatic TG secretion rates, or tissue LPL activity. This again contrasts with the ad libitum-feeding condition, in which insulinemia was strongly associated with most determinants of TG metabolism (25).

**Perspectives**

The present study confirmed that corticosterone participates in the maintenance of fat reserves in situations of decreased energy intake and that a high-energy diet complements this action. However, with the exception of hepatic TG secretion in chow-fed rats, corticosterone appeared to have little direct impact on determinants of TG metabolism, including hepatic TG stores, triglyceridemia, postheparin plasma lipases, and adipose tissue LPL. Although diet composition did influence some determinants of TG metabolism, it did not modulate the impact of corticosterone thereupon. Whether such a lack of impact of the adrenal status extends to the postprandial period remains to be determined. We have previously shown in rats fed ad libitum that the impact of corticosterone on TG metabolism is minimal in rats fed a diet (rodent chow) that maintains a low lipid flux but that it greatly affects TG metabolism in animals fed a diet (HSF) that increases lipid flux. The present study extends these findings by showing that corticosterone influences TG metabolism only minimally when consumption of the high-energy diet is restricted. On the other hand, the mechanisms by which GCs exert their fat-sparing action remain unclear. The present results indicate that modulation of the availability of LPL in adipose tissue is not part of the adaptations that allow for the fat-sparing action of GCs. Together with our previous findings of a strong, diet-dependent impact of the presence of corticosterone on determinants of TG metabolism in ad libitum feeding conditions, the present studies demonstrate that determinants of TG metabolism, as assessed after an overnight fast, are affected in the long term to a much greater extent through the central modulation of energy intake by GC than by their direct peripheral actions on TG metabolism.

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