Regional variation in adipose tissue lipolysis in lean and obese men

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Abstract Biopsies of adipose tissue were obtained from two subcutaneous regions (abdominal and femoral) in a sample of 54 men (32 obese and 22 lean subjects). Clonidine-induced antilipolysis in femoral adipose cells was similar in both groups, whereas subcutaneous abdominal adipocytes of obese individuals showed a higher α2-adrenergic response than did subcutaneous abdominal adipose cells from lean subjects. In addition, epinephrine had a biphasic effect in subcutaneous abdominal adipocytes from obese individuals, as it induced antilipolysis at low concentrations, and a net lipolytic response at higher doses. In contrast, the physiological amine promoted lipolysis in subcutaneous abdominal adipose cells of lean subjects. Epinephrine- and clonidine-induced antilipolysis of subcutaneous abdominal adipocytes was positively associated with the level of subcutaneous abdominal fat measured by computed tomography (CT). Finally, men with a high α2-adrenergic response of subcutaneous abdominal fat cells were fatter than those with a low α2-adrenergic component. These results suggest that, in men with a wide range of body fatness, variations in the lipolytic response of subcutaneous abdominal adipose cells to epinephrine appear to involve changes in the functional balance between α2- and β-adrenoceptors.—**Mauriège, P., J. P. Després, D. Prud'homme, M. C. Pouliot, M. Marcotte, A. Tremblay, and C. Bouchard.** Regional variation in adipose tissue lipolysis in lean and obese men. *J. Lipid Res.* 1991. **32:** 1625–1633.

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Earlier studies of body fat topography have demonstrated a significant sex dimorphism in adipose tissue distribution and morphology, in both normal and obese individuals. In men, an increased adiposity is generally associated with a preferential accumulation of upper body fat whereas in women, a high proportion of the adipose mass is generally located in the lower body, especially, in the gluteal and femoral regions (1, 2). Associations between regional fat distribution, namely abdominal fat deposition, and aberrations in metabolism have been well documented through the last decade (3–10). It has also been proposed by several groups of investigators that the regional variation in storage and/or mobilizing potencies of fat cells may contribute to local differences in adiposity (see reference 11 for a detailed review). Adipocytes from various deposits respond differently to lipogenic or lipolytic stimuli, although the origin of such differences remains partly unknown (12–15). Recent studies have indicated that variation related to site of adipose tissue sampling and to gender exists in the response of fat cells to catecholamines (16, 17). Moreover, subcutaneous fat cells from the abdominal region are more responsive to epinephrine and norepinephrine than those from peripheral depots (14, 18, 19), suggesting that human adipose tissue is not homogeneous from a functional point of view. Several mechanisms may be responsible for these regional differences in fat cell responsiveness to catecholamines. Human adipose cells possess both β- and α2-adrenoceptors coupled antagonistically to plasma membrane adenylate cyclase, controlling cAMP production, and thus, lipolytic activity through hormone-sensitive lipase activation (20). Although large adipocytes have been associated with a high adipose cell α2-adrenergic response (21), we do not know how levels of total fat and of regional adipose tissue distribution are related to the α2/β-adrenoceptor balance, in men.

Moreover, as numerous investigations have dealt with non-obese individuals (15–18) and since altered adrenergic effects on the adrenergic control of lipolysis have already been reported in obesity (21), the present study investigated more particularly the influence of variations in the level of body fatness on the lipolytic response of subcutaneous abdominal and femoral adipocytes obtained from obese and lean men.

Abbreviations: KRBA, Krebs-Ringer bicarbonate buffer with albumin; ADA, adenosine deaminase; CT, computed tomography; WHR, waist-to-hip ratio.

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MATERIAL AND METHODS

Subjects

Fifty-four healthy male volunteers, aged 36 ± 3 years (mean ± SD) (range: 29–42 yr) were recruited through the media and gave their written informed consent to participate in this study, which was approved by the Laval University Medical Ethics Committee. All participants were subjected to a physical examination by a physician, which included a medical history. Subjects with cardiovascular disease, diabetes, or other endocrine disorders, or those on medication were excluded. All men had been sedentary for the last months and were non-smokers. They also had a moderate alcohol consumption and none of them was on a diet or involved in a weight-reducing program.

Body composition and regional fat distribution

Body density was determined by the underwater weighing technique (22) and percent body fat was derived from body density (23). Fat mass was determined by multiplying percent body fat by body weight. Pulmonary residual volume was measured using the helium dilution method (24). Waist and hip girths were measured according to the procedures recommended at the Airlie Conference (25). Computed tomography was used to measure adipose tissue areas on a Siemens Somatom DRH scanner (Erlangen, Germany), according to the methodology described by Sjöström et al. (26).

Adipose tissue biopsy procedure

After an overnight fast, men were subjected to biopsies of subcutaneous fat, one performed in the periumbilical region (abdominal site) and the other at the mid-thigh level (femoral site). Local anesthesia (xylocaine 1% without epinephrine) was performed in such a way that it did not influence the metabolic activity of the excised adipose tissue (27). A small cutaneous incision (1 cm) was made in both sites and about 200 mg of subcutaneous adipose tissue was surgically removed from the two adipose depots.

Adipocyte isolation

Adipocytes were isolated according to the method of Rodbell (28) in a Krebs-Ringer bicarbonate buffer (pH 7.4) containing 4% bovine serum albumin (KRBA) and 5 mM glucose, plus 1 mg/ml collagenase, as previously described (29). Digestion took place in a shaking water bath under a gas phase of 95% O_2 and 5% CO_2, for 40 min at 37°C. The suspension was then filtered and the cellular filtrate obtained was rinsed three times with 5 ml of KRBA. Isolated adipocytes were finally resuspended in KRBA, to obtain a final concentration of approximately 500 cells per 50 μl.

Measurement of adipocyte lipolysis

Extracellular glycerol release was used as the indicator of adipocyte lipolysis. Fifty-μl aliquots of the continuously stirred cell suspension were placed in 1.5-ml conical tubes. Two of these tubes were used for cell counting and sizing; two others containing 10 μl KRB were immediately placed on ice and provided an evaluation of the initial concentration of glycerol in the medium. Agents for lipolysis stimulation or inhibition were added just before the beginning of the assay in 10-μl portions in order to obtain the desired final concentration. After a 2-h incubation at 37°C in a shaking water bath, under a gas phase of 95% O_2 and 5% CO_2, 50 μl HCl (1 N) was added to all tubes to stop the reaction, then 50 μl NaOH (1 N) was added to neutralize the medium. All tubes were stoppered and stored at −20°C until glycerol determination according to Kather, Schroder, and Simon (30). NADH concentration was measured by bioluminescence with a luciferase solution, using a 1251 LKB Wallac luminometer (30, 31). For each concentration of stimulator or inhibitor, the amount of glycerol was taken as the average of the quantities obtained from the two incubated tubes. Glycerol measurement by bioluminescence is very sensitive and especially well adapted when only small amounts of adipose tissue are available (31).

The lipolytic activity of the isolated fat cells was tested with isoproterenol (β-agonist), clonidine (α2-agonist) and the physiological amine, epinephrine, which is a mixed agonist (α2/β) with a higher affinity for α2 sites (19, 32). Ascorbic acid (0.1 mmol/l) was included in the incubation medium to prevent catecholamine degradation. Some experiments were also conducted with forskolin (a direct activator of adenylate cyclase) (33), theophylline (an inhibitor of phosphodiesterase) (34), and dibutyryl-cAMP (a potent stimulator of the protein kinase hormone-sensitive lipase system). When anti-lipolytic effects were investigated, the incubation buffer was supplemented with 5 μg/ml adenosine deaminase (ADA) to remove adenosine released in the incubation medium by the isolated fat cells; this procedure allows for more accurate investigations of α2-mediated anti-lipolytic effects (32).

Drugs and chemicals

Collagenase, bovine serum albumin, adenosine deaminase, and enzymes for glycerol assays were obtained from Boehringer (Mannheim, Canada). Ascorbic acid (−)isoproterenol bitartrate, (−)epinephrine bitartrate, clonidine hydrochloride, theophylline, forskolin, dibutyryl-cAMP, and N^6-(l-2-phenylisopropyl)-adenosine were purchased from Sigma Chemical Co. (St. Louis, MO). All other chemicals were of the highest purity grade commercially available.

Statistical methods

Values presented in tables are given as means ± SD (standard deviation) and values shown in figures are means ± SE (standard error). The Student *t*-test was utilized for comparisons between lean and obese subjects. Associations between two variables were quantified using Pearson product-moment correlation coefficients. The effects of obesity (lean vs. obese) and of regional variation (abdomen vs. mid-thigh) were tested by a two-way analysis of variance for paired observations on one factor (adipose depot).

RESULTS

Table 1 shows the physical characteristics of the subjects. Mean age was 36 ± 3 years, and percentage of body fat ranged from 16 to 33% (not shown). Although mean age was similar among the two groups, significant differences were obviously observed between lean and obese men for all the morphological variables tested ($P < 0.001$). Average fat cell weights from both adipose depots were also significantly greater in obese subjects, as compared to lean inividuals ($0.05 > P < 0.001$). However, adipocytes were smaller in the abdominal than in the femoral site of lean controls ($P < 0.001$), whereas such regional variation was not found in obese subjects.

The basal lipolytic rate in subcutaneous abdominal adipocytes was significantly higher ($P < 0.05$) in obese as compared to lean men, but no significant difference was found for basal lipolysis in femoral fat cells between the two groups. On the other hand, when the incubation buffer was supplemented with adenosine deaminase (ADA) at 5 μg/ml, lipolysis increased by about onefold, with no further increment at higher doses of ADA. The level of lipolysis reached with ADA was similar for femoral fat cells in both groups of subjects, but it was significantly greater ($P < 0.005$) for subcutaneous abdominal adipocytes in obese men. Results were essentially the same when lipolytic activity was expressed on a per cell basis or corrected for variation in adipocyte surface area (not shown).

The action of epinephrine, which is known for its mixed agonist ($\alpha 2$ and β) properties on lipolysis was determined in the presence of ADA. As shown in **Fig. 1**, the physiological amine initiated a similar biphasic responsiveness in femoral adipocytes from both groups: antilipolysis was observed at the lowest concentrations, this effect being completely reversed at higher doses. It must be noted that the antilipolytic effect was less pronounced in lean men than in obese individuals. The profile of epinephrine response was quite different for subcutaneous abdominal fat cells: in obese men, the catecholamine promoted an inhibition of lipolysis at low concentrations (10^{-9}–10^{-7} M) but exerted a lipolytic action at higher doses (10^{-6}–10^{-5} M). In contrast, in lean individuals, epinephrine acted exclusively as a lipolytic agent. The maximal antilipolytic response, observed at 10^{-7} M, was also significantly different in abdominal adipocytes between obese and lean men ($P < 0.005$), as well as in femoral adipose cells ($P < 0.05$). There was no variation between sites for the maximal antilipolysis to epinephrine, either in obese or in lean men. Moreover, the maximal values of epinephrine-induced lipolysis (at 10^{-5} M) were quite similar, whatever the site or the level of fatness of the subjects.

TABLE 1. Physical characteristics of the subjects

	Lean Men (n = 22)	Obese Men (n = 32)
Age (yr)	36 ± 3	36 ± 3
Anthropometric variables		
Weight (kg)	70 ± 7	90 ± 8*
BMI (kg/m²)	23 ± 1.5	30 ± 2*
Fat mass (kg)	14 ± 3	26 ± 5*
Fat-free mass (kg)	55 ± 5	63 ± 5*
WHR	0.87 ± 0.05	0.96 ± 0.04*
Regional fat cell weight (μg lipid/cell)		
Abdominal	0.43 ± 0.11	0.55 ± 0.10*
Femoral	0.50 ± 0.11[a]	0.58 ± 0.13**
Adipose tissue areas measured by CT (cm²)		
Abdomen (L4–L5)		
Subc	149 ± 42	305 ± 81*
Deep	85 ± 30	139 ± 46*
Midthigh		
Subc	137 ± 33	232 ± 63*

Values are means ± SD; BMI, body mass index; WHR, waist-to-hip ratio; subc, subcutaneous; n, number of subjects. Statistical significance at $^*P < 0.0005$ and $^{**}P < 0.05$.
[a]Indicates the significant regional difference in the lean group.

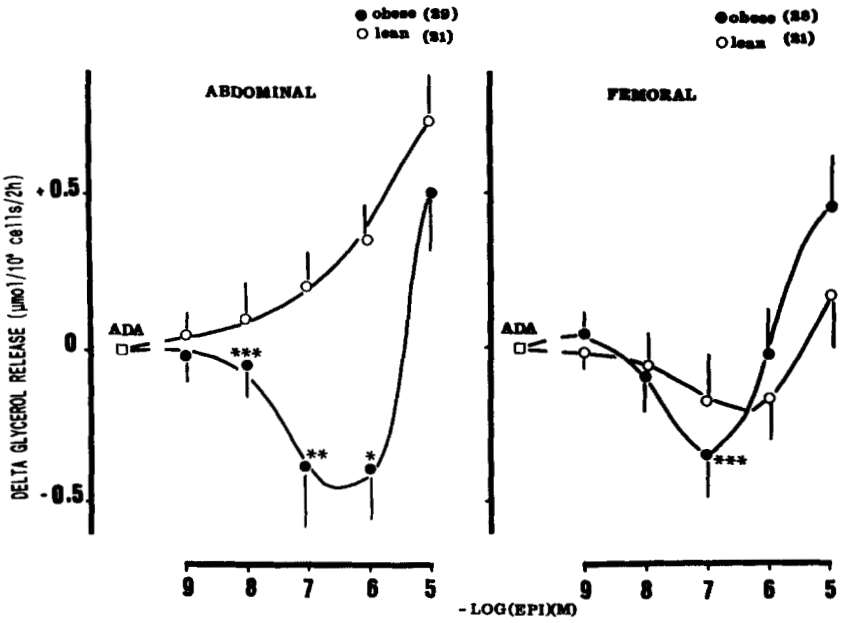

Fig. 1. Effect of epinephrine on ADA-stimulated lipolysis in abdominal (left) and femoral (right) adipocytes obtained from obese (●) and lean (○) men. Values are means ± SE and the number of subjects is shown in parentheses. Glycerol release was expressed as the difference between stimulated (with epinephrine) and basal values. Negative values reflect inhibition of lipolysis. Fat cells were incubated in the presence of 5 μg/ml of adenosine deaminase (ADA). Significant difference between the obese and lean groups at $^{*}P < 0.0005$, $^{**}P < 0.005$, and $^{***}P < 0.05$.

As shown in **Fig. 2**, the relative lipolysis initiated by isoproterenol was not strikingly different among regions and between lean and obese men. However, an increased β-adrenergic sensitivity, defined as the concentration of agonist required for half-maximal lipolysis, was observed in subcutaneous abdominal adipocytes from obese as compared to lean individuals (33 ± 10 vs. 150 ± 35 nM; $P < 0.001$). Moreover, no difference in sensitivity to isoproterenol was observed among obese and lean men for the femoral adipose cells (187 ± 16 nM and 131 ± 42

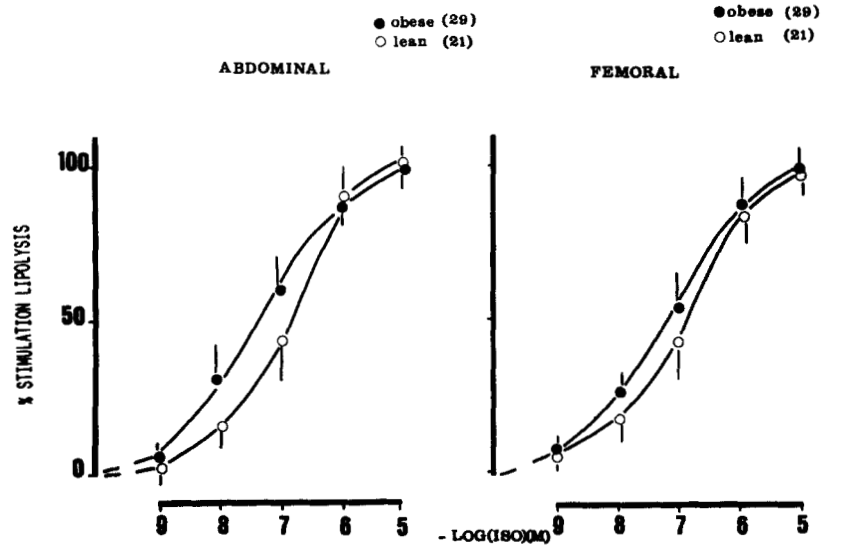

Fig. 2. Isoproterenol-induced lipolysis in abdominal (left) and femoral (right) adipocytes obtained from obese (●) and lean (○) subjects. Values are means ± SE and the number of subjects is shown in parentheses. Fat cells were incubated without ADA and the lipolytic effect was expressed on a percent value of maximal response. Agonist concentrations required for half-maximal stimulation of lipolysis (EC50) were determined from these curves.

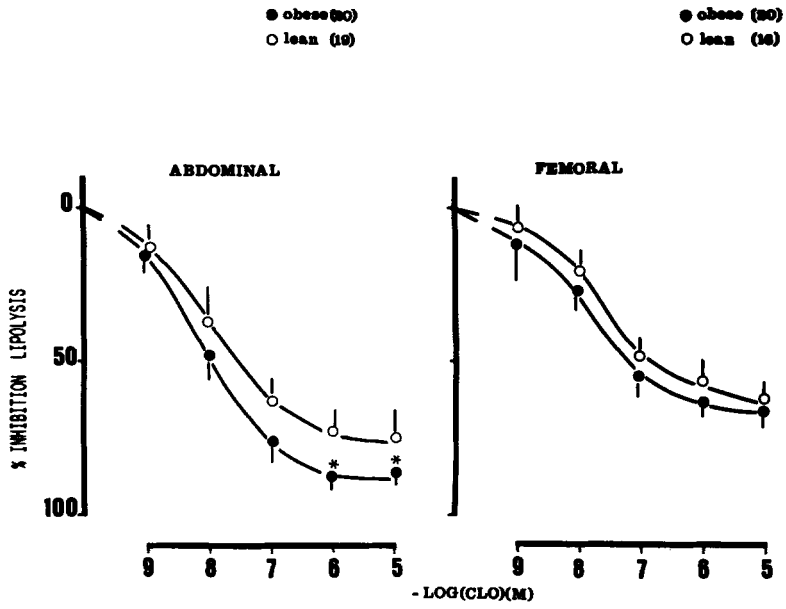

Fig. 3. Clonidine-induced inhibition of ADA-stimulated lipolysis in abdominal (left) and femoral (right) adipocytes obtained from obese (●) and lean (○) subjects. Values are means ± SE and the number of subjects is shown in parentheses. The antilipolytic effect is given as percent inhibition of ADA-stimulated lipolysis in each group, i.e., (ADA minus CLO/ADA) × 100. Agonist concentrations required for half-maximal inhibition of lipolysis (EC50) were determined from these curves. Fat cells were incubated in the presence of ADA (5 μg/ml). *$P < 0.01$ compared to the corresponding value for the abdominal or femoral site.

nM, respectively). On the other hand, the β-adrenergic sensitivity was significantly greater in subcutaneous abdominal than in femoral adipose cells of obese individuals (33 ± 10 vs. 187 ± 16 nM; $P < 0.001$), whereas such regional variation was not found for lean subjects.

To characterize the α2-adrenoceptor component, the selective α2-agonist clonidine was tested on ADA-stimulated lipolysis. To control for variations in the level of stimulated lipolysis achieved, results were expressed on a percentage basis. Clonidine exerted an antilipolytic effect in both groups and adipose sites (**Fig. 3**). However, although the maximal antilipolytic effect noted at 10^{-5} M was identical for lean and obese femoral adipose cells, maximal antilipolysis was slightly but significantly greater in subcutaneous abdominal adipocytes of obese men, suggesting a stronger α2-inhibitory component. A clear and significant regional difference was also observed in obese subjects for the maximal antilipolytic response to clonidine ($P < 0.005$), whereas such variation was not found in lean men. α2-Adrenergic sensitivity estimated as the half-maximal antilipolysis induced by clonidine was similar in both depots and groups and clustered around 20 nM in all cases. Similar results were obtained for epinephrine-, isoproterenol-, or clonidine-stimulated lipolyses when expressed per cell surface area (not shown).

On the other hand, when lipolysis was inhibited through A1-adenosine receptors with phenyl-isopropyladenosine (PIA), an ADA-resistant adenosine analogue, no variation among adipose sites nor between lean and obese men was found (not shown).

In an attempt to investigate the physiological relevance of the differences observed in the antilipolytic effect of epinephrine, the maximal inhibition of lipolysis produced either by the hormone itself or by the selective α2-agonist clonidine was plotted against total fatness and fat distribution variables. In subcutaneous abdominal adipocytes, maximal antilipolyses induced by both agents were significantly and positively related to the fat mass ($0.42 \leq r \leq 0.49$; $P < 0.01$), the WHR ($0.36 \leq r \leq 0.42$; $P < 0.05$) and the subcutaneous abdominal fat area measured by CT ($0.39 \leq r \leq 0.48$; $0.05 > P < 0.005$), (**Figs. 4A**, **4B**, and **4C**, respectively). However, such associations were not found between the maximal antilipolytic responses of femoral adipose cells to these agents and neither fat mass, WHR, nor subcutaneous femoral CT-scan area (not shown).

Finally, subgroups of men with the lowest and highest maximal subcutaneous abdominal antilipolytic response to the α2-agonist clonidine were also compared (**Table 2**). Despite a similar age, men with a high α2-adrenergic component were fatter than subjects with a low α2-adrenergic response. In contrast, when comparing men with the highest and lowest femoral α2-adrenergic component, no statistical difference was found between the two subgroups for the total body fat and adipose tissue distribution variables studied (not shown).

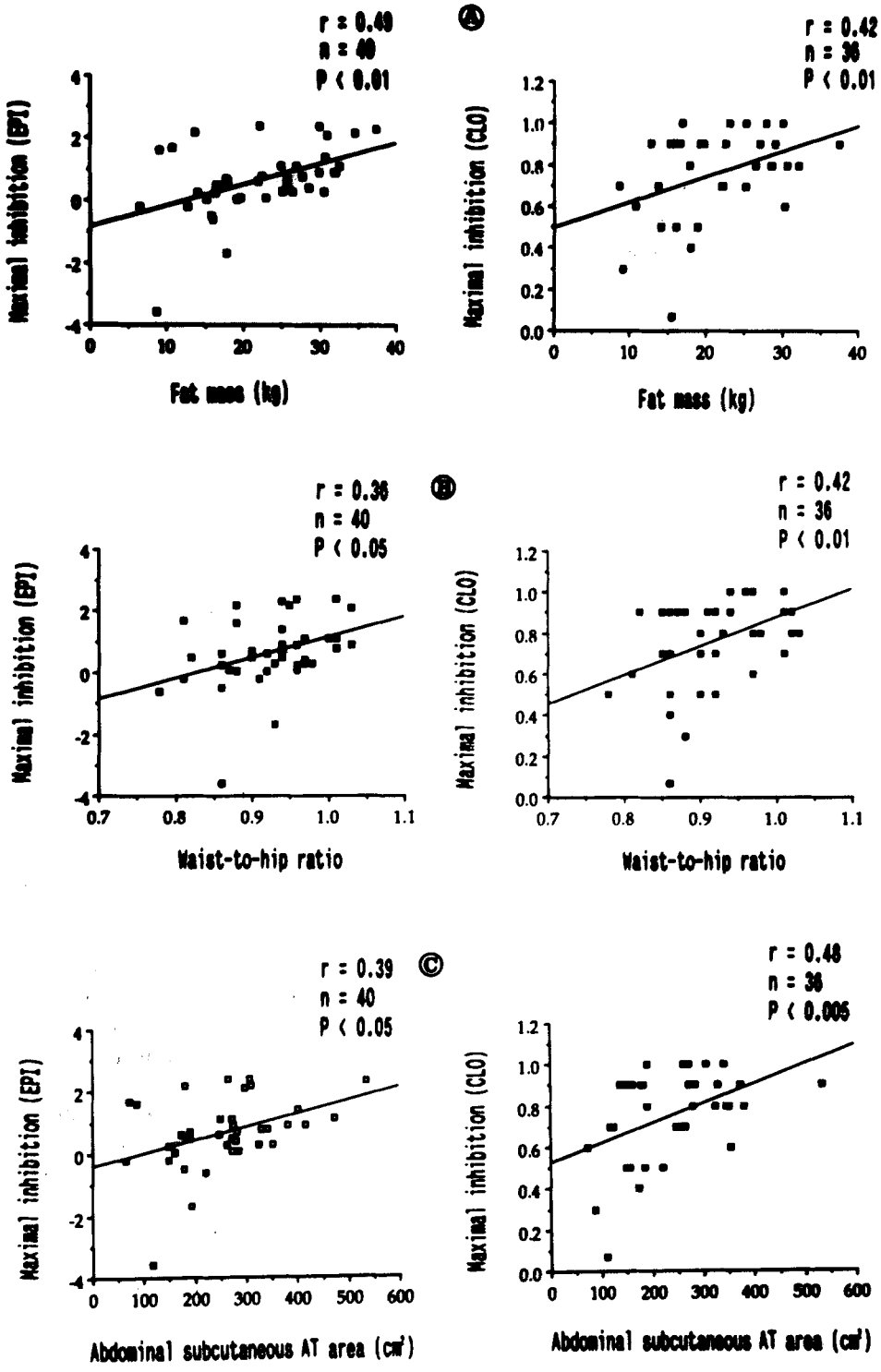

Fig. 4. Relationships between the maximal abdominal antilipolytic effects of epinephrine (EPI) and clonidine (CLO) and the fat mass (panel A), the waist-to-hip ratio (panel B), and the subcutaneous abdominal adipose tissue (AT) area measured by computed tomography (panel C).

TABLE 2. Indices of body fatness and of regional adipose tissue distribution in subgroups of 10 subjects with lowest and highest values of maximal antilipolytic response to clonidine, Imax (CLO), in abdominal adipose cells

Variable	Low Imax (CLO)	High Imax (CLO)
Age (yr)	36.2 ± 2.3	36.8 ± 3.6
Weight (kg)	73.1 ± 10.2	90.5 ± 8.2*
BMI (kg/m²)	23.6 ± 2.9	29.0 ± 2.6*
Fat mass (kg)	16.3 ± 5.8	25.0 ± 6.8**
Waist girth (cm)	85.8 ± 10.2	101.4 ± 11.4*
WHR	0.87 ± 0.05	0.95 ± 0.06**
Abdominal subc (cm²)	163.1 ± 81.2	305.6 ± 106.5*
Midthigh total (cm²)	159.8 ± 53.9	247.2 ± 89.9**
Abdominal FCW	0.43 ± 0.14	0.50 ± 0.08
Femoral FCW	0.51 ± 0.09	0.55 ± 0.09

Values are means ± SD; FCW, fat cell weight (μg lipid/cell); Imax (CLO), maximal inhibition of lipolysis at 10^{-7} M of clonidine was expressed as the ratio (ADA minus CLO/ADA minus basal). For other abbreviations, see legend to Table 1.

Statistical significance at $^{*}P < 0.005$ and $^{**}P < 0.05$.

As any step in the lipolytic cascade may be responsible for the site differences observed in catecholamine responsiveness, the effects of agents acting at different post-adrenoceptor levels were also investigated. There was no regional variation, nor difference between lean and obese men, when lipolysis was stimulated with maximal concentrations of either forskolin (10^{-5} M), theophylline (10^{-3} M), or dibutyryl-cyclic AMP (10^{-3} M) (not shown). On the other hand, when the maximal lipolytic responses of subcutaneous abdominal adipose cells to these post-adrenoceptor agents were plotted against the subcutaneous abdominal fat area, there was no statistical evidence of any significant association. In contrast, the maximal lipolyses of femoral adipocytes to either theophylline or dibutyryl-cyclic AMP displayed a positive and significant relationship with the subcutaneous femoral fat area ($r = 0.48$ and $r = 0.49$, respectively; $P < 0.05$). These correlations remained significant when lipolysis was controlled for fat cell surface ($r = 0.51$ and $r = 0.53$, respectively; $P < 0.01$).

DISCUSSION

The present investigation was conducted to provide further information on the mechanisms underlying regional variation in lipolysis in men. As prior experiments have dealt with non-obese individuals (15–18), we have compared obese and lean men, and we have also studied the influence of the level of fatness on these site differences.

Epinephrine responsiveness in obese abdominal and femoral adipose cells probably reflects the interaction of the hormone with both types of adrenoceptors and supports the notion of a differential recruitment initially of α2- then β-sites, as previously reported (19, 32). The more pronounced antilipolysis in abdominal and femoral adipocytes from obese men reveals a stronger α2-adrenergic component, compared to lean individuals. The "biphasic" appearance of the epinephrine dose-response curve in abdominal fat cells from obese men could be partly explained by an enhancement of the α2-adrenergic component, whereas the exclusive lipolytic action of the hormone in lean individuals could be due to either a weaker α2-adrenergic activity or to its full suppression by a greater β-adrenergic component. Furthermore, subcutaneous abdominal adipocytes exhibited a greater maximal antilipolytic response to clonidine in obese than in lean men, but this difference was not found in femoral adipose cells. The lower α2-adrenergic effect in abdominal adipocytes of lean men is concordant with the exclusive lipolytic response to epinephrine in these adipose cells.

Regional differences reported for normal weight subjects have also been observed in markedly obese individuals (14). As we found no regional variation in the maximal antilipolytic response to epinephrine in both lean and obese men, it is still difficult to draw a firm conclusion relative to the persistence of regional variations in lipolysis in obesity. Conflicting results have shown either an increased (14, 35) or a similar (36) responsiveness to catecholamines in abdominal as compared to femoral fat cells in obesity. This question is still a matter of debate since, with the exception of one study (3), no attempt was made to classify obese subjects according to the regional body fat distribution (i.e., gynoid vs android obesity). However, to the best of our knowledge, our study is the first that included obese and non-obese men for the measurement of regional variation in adipose cell lipolysis. Whether the potential mechanisms underlying the regional differences in the α2-adrenergic effect are either at the α2-adrenoceptor step itself or at the level of the inhibitory GTP-sensitive coupling Gi protein (37) remains unknown, but a minor role of G proteins as modulators of clonidine has been previously suggested (17).

The subcutaneous abdominal adipose tissue area was positively related to both epinephrine- and clonidine-induced maximal antilipolyses in subcutaneous adipose cells, whereas no significant relationship was found between the CT-femoral fat area and the maximal antilipolytic responses to these agents. Moreover, not only was there a significant obesity × site interaction for clonidine-maximal antilipolysis ($F = 8.17$, $P < 0.01$), but the significant differences in body fatness observed between subgroups of men with low and high maximal antilipolytic responses to the selective α2-adrenergic agonist also support the view that a reduced subcutaneous abdominal adipose cell lipolytic response to catecholamines in obesity is probably due to a greater α2-adrenoceptor component presumably related to α2-adrenoceptor density in this region. This hypothesis is largely confirmed by the clear adiposity effect (obese vs. lean) observed for epinephrine lipolytic response of subcutaneous abdominal adipose cells ($F = 8.86$, $P < 0.005$). Our results indicate that the WHR was related to abdominal fat cell α2-adrenergic

response, but so were the total body fat mass and the level of subcutaneous abdominal fat measured by CT. Therefore, at least in men, the relation of the WHR to the antilipolytic effect of epinephrine in abdominal adipose cells is not independent from variation in body fatness. Although WHR provides an anthropometric estimate of regional fat deposition, its variation depends partly upon variation in the level of deep abdominal fat (38). As lipolytic activity was measured on subcutaneous abdominal adipose cells, it is therefore not surprising that the WHR only displayed a moderate association with subcutaneous abdominal fat cell antilipolytic response to epinephrine.

Furthermore, within-site analyses revealed no significant difference between lean and obese men in the lipolytic response of neither abdominal or femoral adipocytes to isoproterenol, suggesting that the β-adrenoceptor pathway plays a minor role in explaining the regional differences in adipose cell lipolysis, as opposed to the α2-adrenergic component. However, the higher sensitivity of β-adrenoceptors to isoproterenol in abdominal adipocytes of obese men seems to reflect a more efficient β-adrenergic component in obesity. This point of view is supported by the fact that a high affinity of the β-adrenergic pathway of abdominal adipose cells has already been reported not only in obese women (14) but also in healthy men and women (15, 18).

Despite the lack of statistically significant difference among adipose sites or between groups when lipolysis was stimulated with post-adrenoceptor agents, correlational analyses showed positive relationships between the femoral adipose cell maximal lipolytic response to either theophylline or dibutyryl-cyclic AMP and the subcutaneous femoral fat area. The fact that such associations have not been found between abdominal adipocyte lipolysis and the amount of subcutaneous abdominal fat may suggest that post-receptor events located at the phosphodiesterase or at the protein kinase level) are linked to variation in femoral adipose cell lipolytic response observed between obese and lean men.

CONCLUSION

To the best of our knowledge, our study documents for the first time that the α2-adrenergic component of subcutaneous abdominal fat cells is directly proportionate to the level of total body fat in men. However, these findings, essentially based on correlational analyses, should be interpreted with caution, as cross-sectional comparisons of lean and obese men cannot clarify whether a high α2-adrenergic component increases the risk of fat accumulation, or whether such a high α2-adrenergic response is a consequence (rather than a cause) of the obese state. Therefore, further longitudinal studies are needed to address this issue.

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