Variation in adrenergic regulation of lipolysis between omental and subcutaneous adipocytes from obese and non-obese men

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Abstract Regional variations in adipocyte lipolysis between subcutaneous and visceral fat may be important for obesity complications. In the present study, we compared adrenergic regulation of lipolysis in omental and subcutaneous adipocytes from obese (n = 15) and non-obese (n = 14) male subjects. Waist-to-hip ratio, blood pressure, plasma insulin, and plasma triglycerides were increased in obesity. No regional differences in adrenoceptor lipolytic function were observed in non-obese subjects with the exception of a slight increase in noradrenaline sensitivity in omental adipocytes ($P < 0.05$), because of increased β_1-adrenoceptor sensitivity ($P < 0.05$). In the obese subjects, the rate of noradrenaline-induced glycerol release was 2-fold higher ($P < 0.005$) and the noradrenaline sensitivity was 3-fold higher ($P < 0.05$) in omental versus subcutaneous adipocytes. These findings were mainly due to a 50-fold increase in omental β_3-adrenoceptor sensitivity ($P < 0.002$) and to a smaller 6-fold increase in omental β_1-adrenoceptor sensitivity ($P < 0.02$), accompanied by increased β_3- as well as β_1-adrenoceptor lipolytic rates at approximately 50% receptor subtype occupancy by the agonist ($P < 0.05$). In conclusion, minor regional differences in adipocyte lipolytic response to catecholamines are present in non-obese males. In contrast, catecholamine-induced lipolysis is markedly increased in omental as compared to subcutaneous adipocytes in obese males, mainly due to an increase in β_3-adrenoceptor function of visceral fat cells, in combination with a smaller increase in β_1-adrenoceptor function.—**Hoffstedt, J., P. Arner, G. Hellers, and F. Lönnqvist.** Variation in adrenergic regulation of lipolysis between omental and subcutaneous adipocytes from obese and non-obese men. *J. Lipid Res.* 1997. **38:** 795–804.

Supplementary key words adrenergic receptors • β_3-adrenoceptors • lipolysis • omental adipocytes • subcutaneous adipocytes

Human adipose tissue metabolism is subject to intense hormonal regulation. Catecholamines either stimulate or inhibit lipolysis in fat cells through their action on $\beta_{1,2,3}$- or α_2-adrenoceptors, respectively, while insulin has marked anti-lipolytic effects (1). However, adipose tissue is a heterogenous metabolic organ and, as reviewed (2–5), several differences in the rate of lipolysis have been observed among various fat depots. For example, visceral adipose tissue from subjects not selected for age or body weight has a higher lipolytic activity than subcutaneous adipose tissue due to a combination of increased β-adrenoceptor-mediated catecholamine-induced lipolysis and reduced antilipolytic action of insulin in the visceral fat depot. For obesity and related atherogenic complications, it is of particular importance to compare visceral and subcutaneous fat lipolysis as only the former depot is drained by the portal system to the liver. Therefore, increased FFA-release from the visceral fat depot may have a number of adverse effects including insulin resistance, glucose intolerance, dyslipidemia, and hypertension (6).

Site-specific variations in adipose tissue metabolism may thus be important for the pathogenesis of upper body obesity and related disorders. Consequently, recent work has demonstrated alterations in the lipolytic function in various conditions. Resistance to catecholamine-stimulated lipolysis in subcutaneous adipocytes, due to reduced β_2-adrenoceptor function, has been found in obese females (7), in subjects with hypertriglyceridemia (8), and in men with the metabolic syndrome (9). Lipolytic subcutaneous catecholamine resistance in obese males due to an increased α_2 adrenoceptor response has also been reported (10). In contrast, the lipolytic function in omental fat cells seems to be enhanced in subjects with upper-body obesity and the metabolic syndrome, mainly due to an increased β_3-adrenoceptor function (11, 12).

Abbreviations: EC_{50}, agonist concentration producing a half maximum effect; FCV, fat cell volume; FFA, free fatty acids; pD_2, −log mol EC_{50}; pl, picoliter = 10^{-12} l.

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Whether an obesity-related difference in lipid mobilization from the visceral and subcutaneous fat depots exists in the same individual remains to be established and, if so, the possible underlying mechanisms need to be explored. In a recent study (13), various differences in the regulation of adipose tissue metabolism between omental and subcutaneous fat cells were found in obese females. However, no normal-weight subjects were investigated, thus the impact of body weight on regional differences remains to be established. Bearing in mind the strong gender influence on complications to obesity, it is also of interest to elucidate regional differences in lipolysis between visceral and peripheral fat tissue in male subjects as well. The present study was therefore performed to investigate cathecolamine-induced lipolysis in omental and subcutaneous fat cells from nonobese and obese males and to investigate possible alterations in adrenoceptor subtype function.

MATERIAL AND METHODS

Subjects

The study group comprised 15 obese male subjects (with body mass indexes ranging from 29 to 53 kg/m^2) undergoing weight reduction surgery and 14 non-obese male subjects (body mass indexes ranging from 20 to 28 kg/m^2) undergoing elective cholecystectomy. All of the gallstone operations and half of the gastric binding surgeries were made through laparoscopic procedures, which limited the possibilities of obtaining large amounts of fat tissue for the experiments. The subjects were all Caucasians, aged between 23 and 59 years. Except for the surgery indication, all subjects were apparently healthy and not receiving any medication. None had a history of alcohol overconsumption. The fasting blood glucose levels of five obese patients were increased (>7.0 mmol/l). However, these subjects had no diabetic symptoms and were not on any form of antidiabetic diet.

The waist-to-hip ratio (WHR), the sagittal diameter, and the systolic and diastolic blood pressures were measured in the supine position the day before surgery. The sagittal diameter was obtained by measuring the distance from the examination table to a horizontal crossbar placed over the abdomen of the recumbent subject at the level of the crista. The systolic and diastolic pressures were determined using phases I and V of the Korotkoff sounds. Each value was taken as the mean of three consecutive measurements after a 10-min rest. After an overnight fast, the study subjects rested in bed for 15 min, then venous blood samples were obtained that were analyzed by the hospital's routine chemistry laboratory, except for insulin which was measured with a radioimmunoassay kit (Pharmacia, Uppsala, Sweden).

General anesthesia was induced at 8 AM by propofol in a fat emulsion (Diprivan, Zeneca, Bristol, UK) in combination with fentanyl and midazolam and maintained by propofol and a mixture of oxygen and air. Muscle relaxation was induced by suxamethonium and maintained by abracurium. Intravenous saline was administered prior to the fat biopsies, which were taken from the major omentum, at the beginning of the operation. The study was approved by the ethics committee of Karolinska Institute, Stockholm, and all the patients gave informed consent to participate in the study.

Lipolysis

For technical reasons, it was not possible to obtain specimens larger than 0.3–1.0 g of omental or subcutaneous fat during the laparoscopic operations. The omental and subcutaneous adipose tissue biopsies were immediately transported to the laboratory in saline at 37°C and isolated fat cells were prepared by collagenase treatment, as previously described (14). The cells were kept in an albumin solution, as described below, and the cell density of the fat cell suspension was kept constant by slow stirring. Direct microscopic determination of the fat cell diameter, as performed according to the method of Di Girolamo, Mendlinger, and Fertig (15), was calculated by using 200 cells from each subject. The mean fat cell volume and weight were determined, taking into account the skewness in the distribution of the cell diameter and using the method described by Hirsch and Gallian (16). The total lipid content in each incubation was determined gravimetrically after organic extraction. Assuming that lipids constitute >95% of the fat cell weight, the number of fat cells was then calculated by dividing the total lipid weight by the mean cell weight.

A detailed description of the lipolysis assay has been reported elsewhere (17). In brief, 0.2 ml of diluted suspensions of isolated fat cells (5,000–10,000 cells/ml) was incubated in duplicate for 2 h with or without increasing concentrations of either the natural catecholamine noradrenaline, the selective β_1-adrenoceptor agonist dobutamine, the selective β_2-adrenoceptor agonist terbutaline, the selective partial β_3-adrenoceptor agonist CGP 12177 (18) or the selective α_2-adrenoceptor agonist UK 14304 (19). All incubations were performed at 37°C in Krebs-Henseleit phosphate buffer (pH 7.4), supplemented with glucose (1 g/L), bovine serum albumin (20 g/L) and ascorbic acid (0.1 g/L), with air as the gas phase. The agents were added simultaneously at the start of the incubation. The concentration range for each agent ranged overall from 10^{-12} to 10^{-4} mol/L.

As discussed in detail previously (20), adenosine leaking out from isolated fat cells may interfere with the α_2-adrenoceptor-mediated anti-lipolytic effects of catecholamines. In our dilute incubation system there is minimal influence of adenosine contamination. However, in the α_2-adrenoceptor experiments, adenosine deaminase (1 mU/ml) was added to prevent anti-lipolytic interactions with traces of adenosine that might still be present and might induce additional inhibitory effects (20) in the diluted cell suspensions. The influence of adenosine on lipolysis in a fat cell system like ours is, on the other hand, negligible when adipocytes are stimulated with lipolytic drugs, as discussed previously (21). Therefore, we chose not to add adenosine deaminase in the remaining concentration-response experiments. In the experiments with UK 14304, the incubation medium was also supplemented with 10^{-3} mol/L 8-bromo cyclic AMP to increase the initial (basal) rate of lipolysis, which otherwise might be too low to be inhibited by UK 14304. We have shown previously that 8-bromo cyclic AMP-induced lipolysis can be fully inhibited by anti-lipolytic agents in human fat cells (22). There was no difference in sensitivity to 8-bromo cyclic AMP between obese and nonobese subjects. After 2 h of incubation, a cell-free aliquot was removed for determination of the glycerol concentration, using a bioluminescence method (23).

All agonists caused a concentration-dependent stimulation of glycerol release that reached a plateau at the highest agonist concentrations. Consequently, it was always possible to determine the concentration of agonist that produced a half-maximum effect on glycerol release, which in turn is an indirect measure of adrenoceptor sensitivity (24). These EC_{50} values (expressed as log mol/l) were determined by linear regression analysis of log-logit transformation of the ascending (β-agonists) or descending (α_2-agonist) parts of the individual concentration-response curves (25). The negative logarithms of the EC_{50} values were used in the calculations, as this value is a pharmacological representation of receptor sensitivity (pD_2). Differences in pD_2 were expressed either as a difference of log units or as a fold difference. In this regard, 0.3 log unit represents a 2-fold difference. Lipolysis rates in the presence of concentrations near the half-maximum (EC_{50}-related lipolysis rate) and maximum effective agonist concentrations were related to fat cell number.

Drugs and chemicals

Bovine serum albumin (fraction V, lot 63F-0748), *Clostridium histolyticum* collagenase type I, glycerol kinase from *E. coli* (G4509), and adenosine deaminase were obtained from Sigma (St. Louis, MO). Terbutaline sulfate came from Draco (Lund, Sweden), dobutamine hydrochloride from Lilly (Indianapolis, IN), CGP (±)12177 ((−)-4-(3-*t*-butylamino-2-hydroxy-propoxy)-benzimidazole-2-one) from Ciba Geigy (Basel, Switzerland) and UK 14304 tartrate from Pfizer (Sandwich, UK). Noradrenaline was purchased from Hässle (Mölndal, Sweden). ATP monitoring reagent containing firefly luciferase came from LKB Wallac (Turku, Finland). All other chemicals were of the highest grade of purity commercially available. The same batches of collagenase and albumin and the same stock solutions of adrenoceptor agonists were used throughout the study.

Statistical analysis

Values are given as the mean ± standard deviation (SD) or standard error of the mean (SEM) in the figures for illustrative reasons. The Student's two-tailed paired or unpaired *t*-tests were used for statistical comparisons. All statistical calculations were performed with a software package for statistics (Abacus Concepts, Inc., Berkeley, CA).

RESULTS

The clinical data for the non-obese and obese subjects used in the present study are presented in **Table 1.**

TABLE 1. Clinical data of obese and non-obese subjects

	Obese	Non-obese	*P*
Age (years)	39 ± 10	43 ± 10	NS
Smoking (yes/no)	6/15	4/14	NS
Body mass index (kg/m^2)	41 ± 7	25 ± 2	
Waist-hip-ratio	1.05 ± 0.04	0.97 ± 0.05	0.0001
Sagittal diameter (cm)	32 ± 4	22 ± 2	0.0001
Systolic blood pressure (mm Hg)	143 ± 15	134 ± 17	NS
Diastolic blood pressure (mm Hg)	91 ± 12	79 ± 8	<0.01
Plasma insulin (mU/l)	28 ± 15	11 ± 5	<0.01
Plasma glucose (mmol/l)	7.7 ± 3.9	5.5 ± 0.04	NS
Plasma triglycerides (mmol/l)	2.9 ± 1.4	1.8 ± 1.0	<0.05
Cholesterol (mmol/l)	5.5 ± 1.1	5.6 ± 0.9	NS
HDL-cholesterol (mmol/l)	1.1 ± 0.3	1.1 ± 0.3	NS

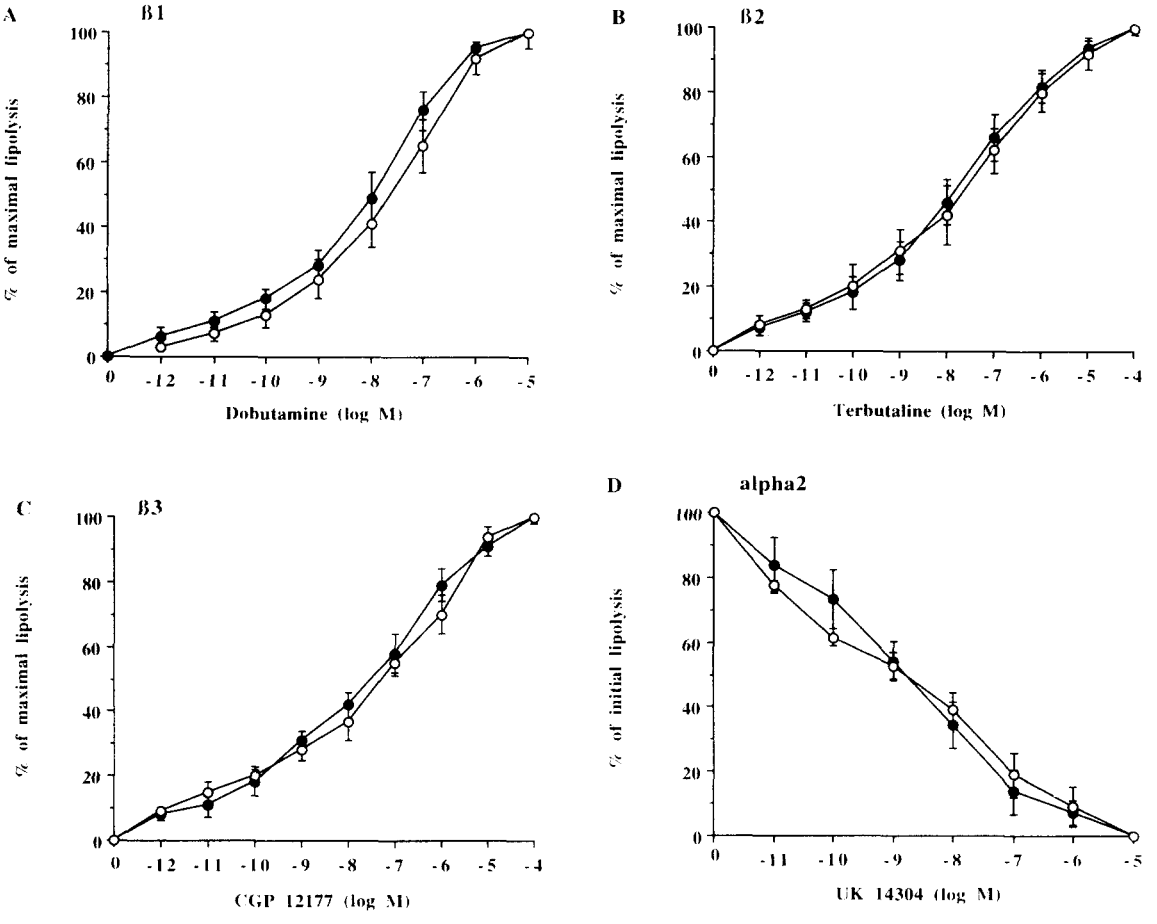

Fig. 1. Mean concentration response curves of selective adrenergic agonists in omental and subcutaneous fat cells from non-obese subjects. Omental (filled boxes) and subcutaneous (open boxes) fat cells from non-obese subjects were incubated with increasing concentrations of dobutamine (β_1) (A), terbutaline (β_2) (B), CGP 12177 (β_3) (C), and UK 14304 (α_2) (D). The adrenoceptor effect is expressed in percent of the maximum stimulatory or inhibitory effect. Values are means ± SEM.

There were no differences in age or smoking habits between the two groups. However, increased WHR, sagittal diameter, blood pressure, plasma insulin and triglyceride levels were found in the obese subjects indicating an upper-body fat distribution with associated metabolic complications.

The adrenoceptor functions in non-obese and obese subjects were investigated by measuring the sensitivities to lipolysis induced by dobutamine (β_1), terbutaline (β_2), CGP 12177 (β_3) and UK 14304 (α_2) in omental compared to subcutaneous adipocytes. **Figure 1** shows the mean-concentration response curves for $\beta_{1,2,3}$- and α_2-adrenergic agonists in non-obese subjects. In this group, only dobutamine-stimulated lipolysis showed significant, albeit small, difference in lipolytic sensitivity between omental and subcutaneous fat cells. The sensitivity of terbutaline, CGP 12177 and UK 14304 did not differ between the two fat depots. In **Table 2,** the mean pD_2 values of adrenoceptor agonists in the two regions in the non-obese group are shown. The mean pD_2 value for dobutamine in non-obese subjects was increased in omental adipocytes by about 0.5 log units ($P < 0.05$).

The mean-concentration response curves for the various adrenoceptor agonists in obese subjects are depicted in **Fig. 2.** There were no differences between the groups for the sensitivity of terbutaline-stimulated or UK 14304-inhibited lipolysis. However, the concentration-response curves for dobutamine and, in particular, CGP 12177 were clearly shifted to the left in the omental fat cells. The mean pD_2 values for dobutamine and CGP 12177 were approximately 0.5 ($P < 0.02$) and 1.5 ($P < 0.002$) log units, respectively, higher in omental than in subcutaneous adipocytes (**Table 3**).

To investigate whether there were any alterations in catecholamine-induced lipolysis, noradrenaline sensitivity and maximum rate of noradrenaline-induced glycerol release were calculated in non-obese and obese subjects. As shown in Tables 2 and 3, the pD_2 value for

TABLE 2. Lipolytic sensitivity (EC_{50}) to adrenergic agonists in non-obese subjects (n = 14)

	pD_2		
	Omental Fat cells	Subcutaneous Fat Cells	*P*
	−log mol/liter		
Noradrenaline	7.97 ± 0.69	7.67 ± 0.83	<0.05
Dobutamine (β_1)	7.99 ± 0.82	7.56 ± 1.00	<0.05
Terbutaline (β_2)	7.87 ± 1.11	7.82 ± 1.26	NS
CGP 12177 (β_3)	7.62 ± 1.19	7.31 ± 0.86	NS
UK 14304 (α_2)	8.83 ± 0.88	8.78 ± 0.66	NS

TABLE 3. Lipolytic sensitivity (EC_{50}) to adrenergic agonists in obese subjects (n = 15)

	pD_2		
	Omental Fat cells	Subcutaneous Fat Cells	*P*
	−log mol/liter		
Noradrenaline	8.34 ± 0.66	8.07 ± 0.62	<0.05
Dobutamine (β_1)	8.43 ± 1.16	7.77 ± 0.71	<0.02
Terbutaline (β_2)	7.19 ± 0.68	6.96 ± 0.85	NS
CGP 12177 (β_3)	9.08 ± 0.92	7.57 ± 1.32	<0.002
UK 14304 (α_2)	8.18 ± 0.79	8.46 ± 0.95	NS

noradrenaline was increased in omental versus subcutaneous adipocytes in non-obese as well as obese subjects, although to a small extent (about 0.3 log units, $P < 0.05$). However, the maximum noradrenaline-stimulated lipolysis rate (μmol of glycerol/10^7 cells/2 h) was almost twice as high in omental adipocytes compared to subcutaneous fat cells in the obese subjects (21.8 ± 10.3 vs. 12.4 ± 7.9, $P < 0.005$), while no difference was observed in the non-obese group (13.0 ± 7.1 vs. 11.9 ± 6.9), as shown in **Fig. 3.**

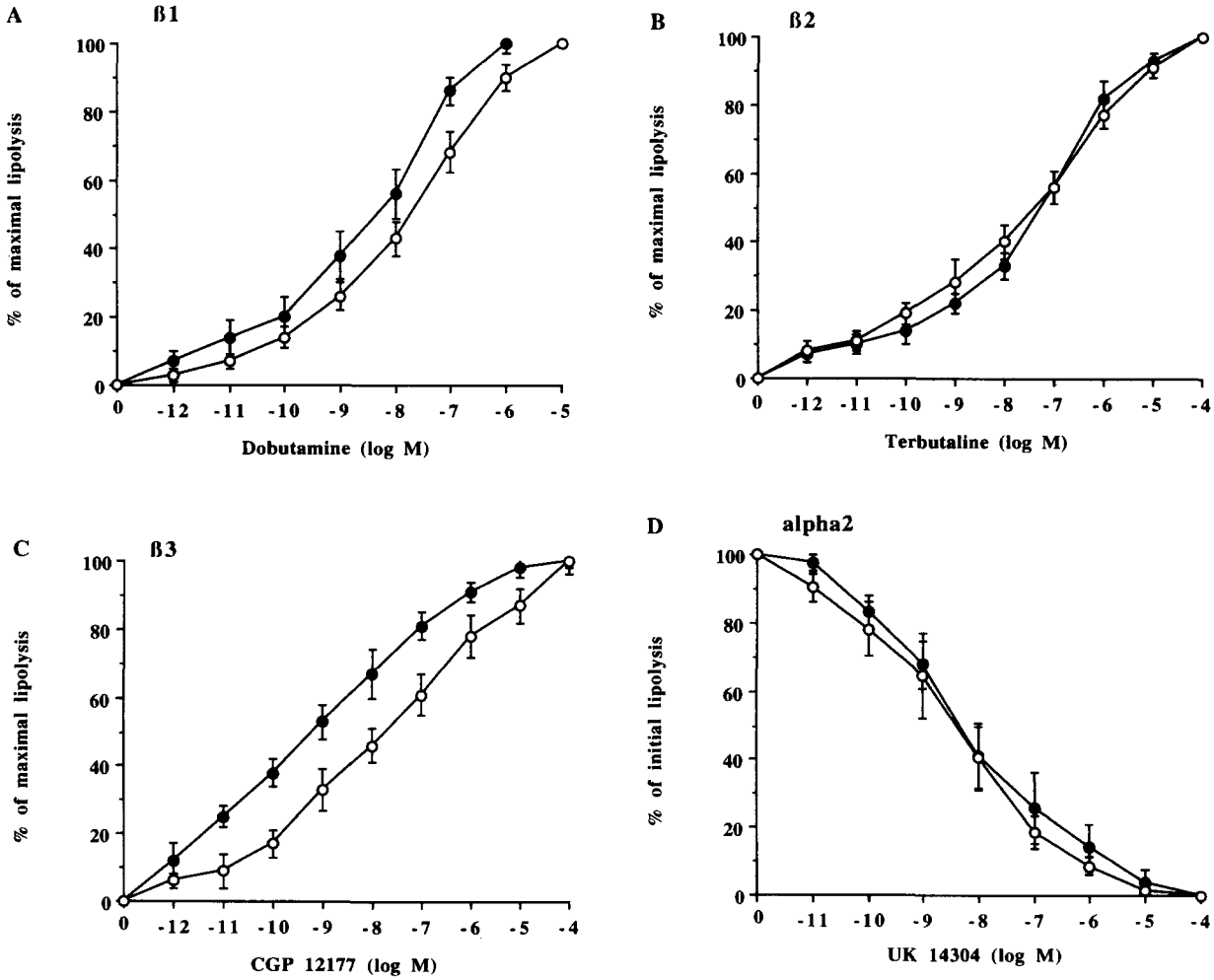

Fig. 2. Mean concentration response curves of selective adrenergic agonists in omental and subcutaneous fat cells from obese subjects. Omental (filled boxes) and subcutaneous (open boxes) fat cells from obese subjects were incubated with increasing concentrations of dobutamine (β_1) (A), terbutaline (β_2) (B), CGP 12177 (β_3) (C), and UK 14304 (α_2) (D). The adrenoceptor effect is expressed in percent of the maximum stimulatory or inhibitory effects. Values are means ± SEM.

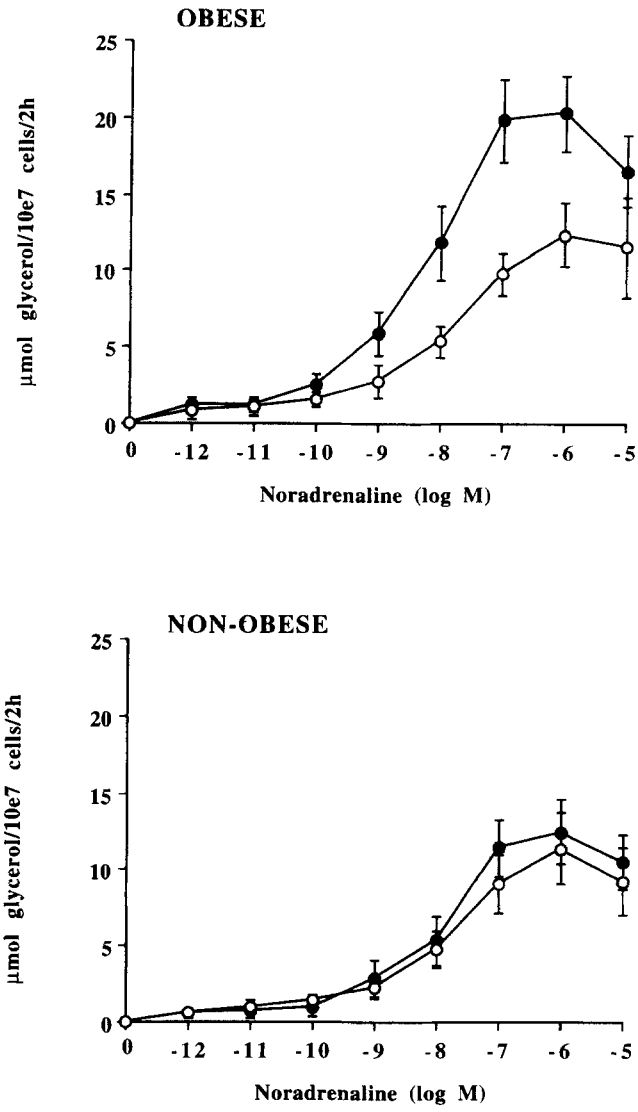

Fig. 3. Maximum lipolytic response induced by noradrenaline in omental and subcutaneous fat cells from obese and non-obese male subjects. Lipolytic responses at maximum-effective concentrations were determined after subtraction of basal lipolysis from omental (filled boxes) and subcutaneous (open boxes) fat cells. The maximum-effective noradrenaline concentrations varied interindividually and were 10^{-8} to 10^{-6} mol/L. The values are means ± SEM.

We also examined whether the observed alterations in noradrenaline- and β-adrenoceptor-induced lipolysis were related to the lipolytic rate by investigating the release of glycerol in agonist concentrations near the EC_{50} value, which is characterized by a 50% occupancy of the total number of receptors that need to be occupied in order to give a full response, as discussed in detail (24). As shown in **Fig. 4,** there were no differences observed in EC_{50} lipolytic rate between omental and subcutaneous fat cells of non-obese subjects either for noradrenaline or the various β-adrenoceptor agonists. In contrast, in obese males, the noradrenaline as well as the dobutamine and the CGP 12177 lipolytic rates in agonist concentrations close to the EC_{50} value were increased (**Fig. 5**). However, no significant difference was observed for terbutaline.

The maximal lipolytic responses of the various β-adrenoceptor agonists and the basal rate of lipolysis were also examined, as illustrated in **Table 4.** There was a tendency towards an increased maximal lipolytic rate in subcutaneous versus omental fat cells of the non-obese subjects, though significant only regarding terbutaline and CGP 12177. The opposite finding, i.e., a higher maximal responsiveness in omental as compared to subcutaneous adipocytes, was found in terbutaline-induced maximal lipolytic rate in the obese males. As regards the basal lipolysis rate, this value was higher in subcutaneous fat cells of both non-obese and obese subjects.

Fat cell volume (FCV) in omental and subcutaneous adipocytes of non-obese and obese males was also measured. In non-obese males, FCV was about 100 pl higher in subcutaneous as compared to omental fat cells (482 ± 152 vs. 380 ± 170, $P = 0.002$). In contrast, no significant differences between subcutaneous (832 ± 176) and omental (711 ± 183) adipocytes were found in the obese subjects.

DISCUSSION

In the present study, we have for the first time examined regional differences in the lipolytic function of visceral versus subcutaneous fat cells in men. In non-obese subjects, there was only a marginal difference in catecholamine-induced lipolysis between the two regions. Noradrenaline sensitivity was slightly increased in omental fat cells because of a 3-fold difference in β_1-adrenoceptor sensitivity. However, no differences in lipolytic rate were observed. In obese males, there was an increase in noradrenaline sensitivity as well as lipolytic action in omental fat cells. This finding was mainly due to a pronounced increase in β_3-adrenoceptor sensitivity (50-fold) in omental as compared to subcutaneous fat cells. The slightly higher β_1-adrenoceptor sensitivity in omental as compared to subcutaneous fat cells observed in non-obese males was also present in obese subjects. No differences in α_2- or β_2-adrenoceptor sensitivity between omental and subcutaneous fat cells were found in obese males or in non-obese subjects. Thus, we found regional differences in catecholamine-induced lipolysis that were markedly augmented in obese as compared to non-obese males favoring a higher lipolytic activity in omental fat cells, mainly explained by a higher β_3-adrenoceptor activity in these cells.

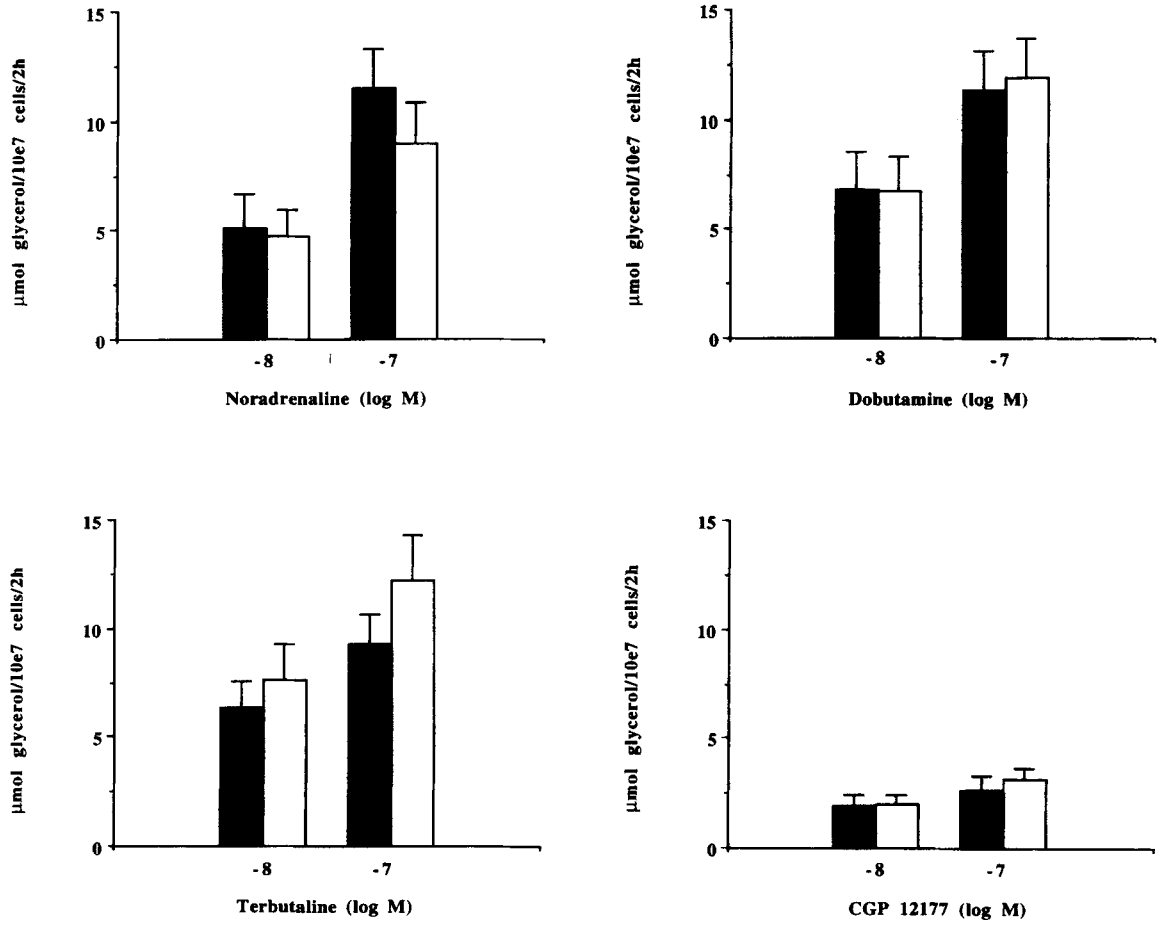

Fig. 4. Half-maximum lipolytic responses induced by noradrenaline, dubutamine, terbutaline, and CGP 12177 after subtraction of basal lipolysis from non-obese male subjects. Omental (filled boxes) and subcutaneous (open boxes) fat cells. The values are means ± SEM. No significant site differences were observed.

In a recent study, the lipolytic activity in human adipocytes from visceral and abdominal subcutaneous tissue of obese females was studied (13). As regards adrenoceptor function, a higher β-adrenergic sensitivity in omental compared to subcutaneous adipocytes was found. Furthermore, an increased omental β_2-adrenoceptor sensitivity and a lack of regional variation in α_2-adrenergic sensitivity was also reported, the former in contrast with the results of the present study. Finally, an increased sensitivity to BRL 37344 in omental adipocytes was found, which in turn was interpreted as a finding of increased β_3-adrenoceptor sensitivity. However, we have in a recent study shown that BRL 37344 does not have β_3-adrenoceptor selective properties in human omental fat cells, but instead significant β_1- as well as β_2-adrenoceptor-mediated effects on lipolysis (26). Thus, the regional importance of β_3-adrenoceptor-mediated lipolysis in females needs to be further clarified.

Increased β-adrenoceptor function in omental versus subcutaneous adipocytes thus may be a common feature of obese males as well as obese females. In this regard, β_3-adrenoceptor function may be of particular pathophysiological importance, at least in male subjects. In non-obese males, the role of the β_3-adrenoceptor appears to be more or less the same in omental as in subcutaneous fat cells. However, as the intra-abdominal fat depot increases in size, β_3-adrenoceptor function becomes more pronounced, resulting in an increased lipolytic activity. The findings of β_3-adrenoceptor function are in contrast with the role of the β_1-adrenoceptor in omental versus subcutaneous adipocytes. Although omental β_1-adrenoceptor sensitivity is increased in non-obese male subjects, as previously demonstrated (27), β_1-adrenoceptor function seems to be less affected by obesity. In the present study, this was also true for noradrenaline sensitivity, whereas the lipolytic response of noradrenaline was markedly influenced by the accumulation of upper-body fat.

The difference in the rate of noradrenaline-stimulated lipolysis between omental and subcutaneous fat

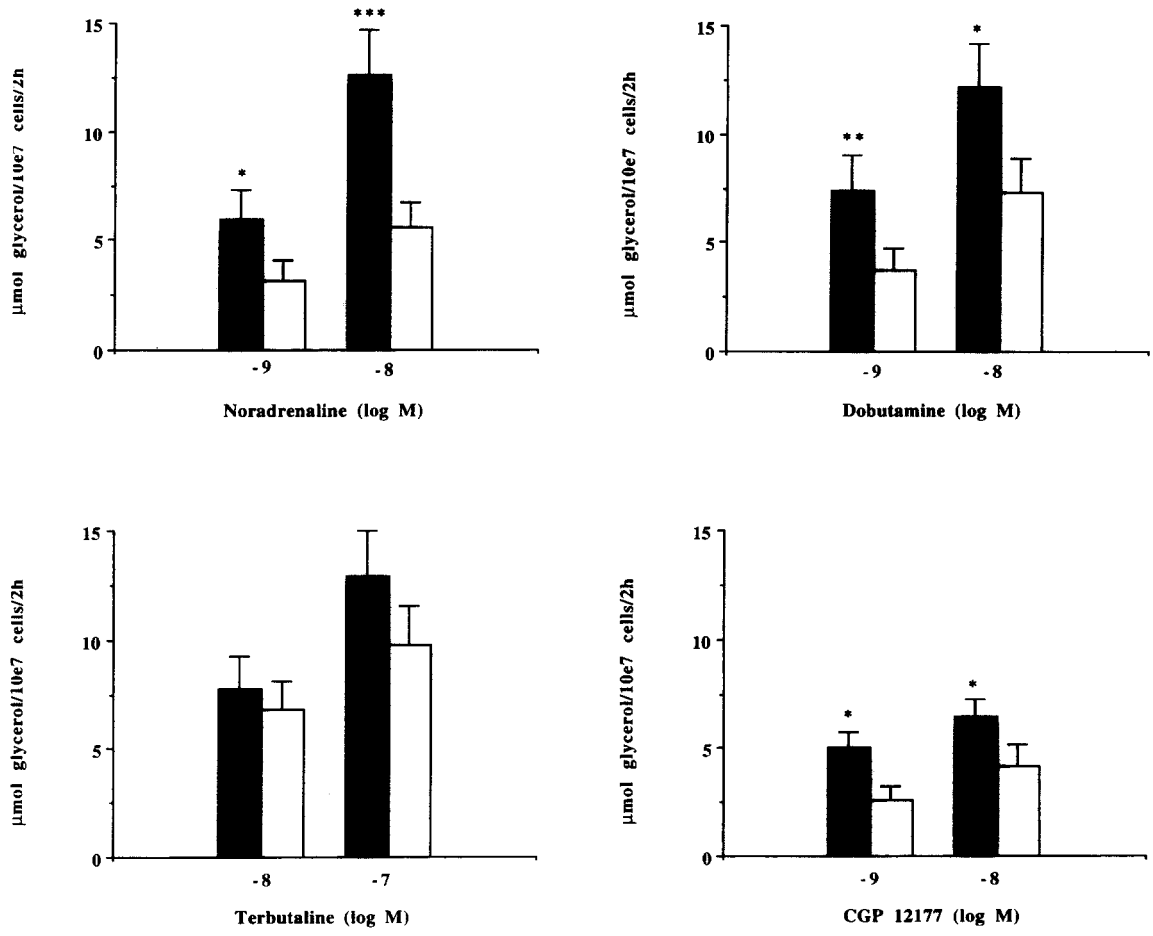

Fig. 5. Half-maximum lipolytic responses induced by noradrenaline, dobutamine, terbutaline, and CGP 12177 after subtraction of basal lipolysis from obese male subjects. Omental (filled boxes) and subcutaneous (open boxes) fat cells. The values are means ± SEM. Significant site differences are indicated in the graph as * = $P < 0.05$, ** = $P < 0.01$, and *** = $P < 0.005$.

cells of the obese males could also be explained by mechanisms other than alterations in adrenoceptor function. This is especially true for the maximal lipolytic response, which is mainly influenced by various postreceptor mechanisms such as coupling to Gs/Gi-proteins, the activities of the hormone-sensitive-lipase and phosphodiesterase, etc. (1). For example, some of the site variations in maximum-induced rate of lipolysis found with the β-adrenoceptor agonists (Table 4) could be explained by such mechanisms. Because of limited access to omental fat cells, due mostly to the use of laparoscopic surgical procedures, we were not able to make a more detailed examination of lipolysis regulation.

In the present study, we also investigated the half-maximum lipolytic rate, i.e., the release of glycerol in a state where only 50% of the amount of receptors needed to give a full response is occupied by a ligand, as discussed in detail (24). The EC_{50}-related lipolytic rate

TABLE 4. Maximal lipolytic activity and basal lipolysis rate in omental and subcutaneous fat cells of non-obese and obese subjects

	Non-Obese			Obese		
	Omental	Subcut	*P*	Omental	Subcut	*P*
Dobutamine	14 ± 7.0	17 ± 7.2	NS	23 ± 12	17 ± 7.8	NS
Terbutaline	15 ± 6.3	19 ± 6.9	<0.01	25 ± 13	18 ± 9.1	<0.05
CGP 12177	3.7 ± 2.6	5.5 ± 3.2	<0.05	9.0 ± 3.2	7.0 ± 4.2	NS
Basal lipolysis	2.2 ± 2.1	5.2 ± 4.3	0.01	7.0 ± 3.2	12.9 ± 4.8	<0.001

Values given as µmol glycerol/10^7 cells per 2 h (means ± SD).

contrasts the maximal lipolytic rate, which in turn is a situation where 100% of the amount of receptors needed for a full response are bound by a ligand. Under normal physiologic, in vivo, conditions it is more likely that only about 50% of the receptors (or less) are occupied during stimulation. Therefore, the half-maximum lipolytic rate may be a more physiologic measure of the lipolytic response than is the maximal lipolytic response and may thereby also reflect a possible significance of alterations in receptor sensitivity among various fat depots. As regards the present results on EC_{50}-related lipolysis, no regional variation in catecholamine-induced lipolysis was demonstrated in non-obese subjects. In contrast, noradrenaline- as well as dobutamine- and CGP 12177-stimulated half-maximum lipolysis was markedly increased in omental as compared to subcutaneous fat cells of obese males, thus further enhancing a possible pathogenic role of the β_1- and β_3-adrenoceptors in obesity regarding regional fat lipolysis.

The basal lipolysis rate was increased in subcutaneous adipocytes of non-obese as well as obese subjects. It is well known that the basal lipolysis rate is higher in large than in small fat cells (28, 29). However, as the further significance of and the mechanisms for the maintainance of basal lipolysis are poorly understood, as discussed (30), the physiologic importance of this finding is not easy interpreted. Therefore, we chose to subtract all the basal lipolytic values from the stimulated values.

The metabolic complications of upper-body obesity, characterized by intra-abdominal fat accumulation, should also be considered. The obese males in the present study had several signs of the metabolic syndrome such as increased WHR, sagittal diameter, plasma insulin and triglyceride levels as well as elevated blood pressure. Although the underlying mechanisms of this syndrome are not fully understood, enhanced lipolysis from visceral adipocytes could have direct effects on the liver, as discussed previously (6).

In conclusion, minor regional differences in catecholamine-induced lipolysis are present in non-obese males favoring lipolysis in visceral versus subcutaneous fat cells owing to a slightly higher β_1-adrenoceptor function in the former cells. These differences are markedly increased in obese males because of an additional improvement mainly in β_3-adrenoceptor function of omental adipocytes. Thus, regional variations in adrenergic lipolysis regulation may be important for the development of atherogenic complications to male obesity.

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