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Postprandial chylomicrons and adipose tissue lipoprotein lipase are altered in type 2 diabetes independently of obesity and whole-body insulin resistance

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Abstract *Background and aims:* Postprandial lipoprotein abnormalities in type 2 diabetes are associated with insulin resistance. The role of other diabetes-related factors is still not clear. The aim of this study is to differentiate the effects of whole-body insulin resistance, obesity, and type 2 diabetes on postprandial dyslipidaemia and lipoprotein lipase (LPL) in adipose tissue.

Methods and results: Ten subjects with obesity and diabetes (OD), 11 with obesity alone (O), and 11 normal-weight controls (C) — males, aged 26–59 years, with fasting normo-triglyceri-daemia underwent measurements of cholesterol, triglycerides, apo B-48 and apo B-100 concentrations in plasma lipoproteins separated by density gradient ultracentrifugation before and after a fat-rich meal. Fasting and postprandial (6 h) LPL activity was determined in abdominal subcutaneous adipose tissue biopsy samples. Insulin sensitivity was measured by hyperinsulinaemic euglycaemic clamp. OD and O subjects had similar degrees of adiposity (BMI, waist circumference, fat mass) and insulin resistance (insulin stimulated glucose disposal and M/I). They also showed a similarly higher postprandial increase in large VLDL lipids (triglyceride incremental AUC 188 ± 28 and 135 ± 22 mg/dl·6 h) than C (87 ± 13 mg/dl·6 h, $M \pm$ SEM, $p < 0.05$). OD had an increased chylomicron response compared to O (triglyceride incremental AUC 132 ± 23 *vs.* 75 ± 14 mg/dl·6 h, $p < 0.05$). OD had significantly lower fasting and postprandial adipose tissue heparin-releasable LPL activity than O and C.

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Conclusions: In insulin-resistant conditions of obesity, with and without diabetes, large VLDL are increased after a fat-rich meal. In addition, diabetic patients compared to obese subjects have an increased postprandial chylomicron response and a reduced adipose tissue LPL activity.

Introduction

Postprandial lipoprotein abnormalities are associated with an increased risk of coronary heart disease [1]. These abnormalities are more frequent in individuals with obesity, type 2 diabetes or other conditions characterized by insulin resistance [2–6].

Whether specific abnormalities of postprandial lipoprotein metabolism are present in patients with type 2 diabetes, however, is not clear [7]. These patients also exhibit postprandial abnormalities in the presence of fasting normo-triglyceridaemia [2,3]. Moreover, abnormalities concern both exogenous and endogenous triglyceride-rich lipoproteins, since the number of both apolipoprotein (apo) B-48 and apo B-100 particles in large VLDL fraction is increased after a fat-rich meal [3].

The cause/s of these abnormalities has not been defined. There are many indications that postprandial dyslipidaemia in type 2 diabetes is associated with insulin resistance. This is suggested by studies showing postprandial lipid abnormalities in insulin-resistant conditions, in first-degree relatives of type 2 diabetic patients [6], smokers [5], obese individuals [8] and non diabetic individuals with insulin resistance [4,9]. In patients with type 2 diabetes postprandial lipoprotein abnormalities were also present when the confounding effects of hyperglycaemia and hyperinsulinaemia were avoided by evaluating postprandial lipemia during a hyperinsulinaemic glycaemic clamp [10].

However, this remains to be confirmed in a chronic setting comparing diabetic patients with individuals with the same level of insulin resistance.

Mechanisms responsible for the altered postprandial lipoprotein profile in type 2 diabetes are also very much debated, with controversial results concerning the role of lipoprotein lipase (LPL), the key enzyme in the intravascular catabolism of triglyceride-rich lipoproteins. Discrepancies arise from differences in the type of sample, reflecting a different tissue origin of LPL, as well as from the confounding effect of the strict associations between diabetes, insulin resistance and obesity. Adipose tissue is central to these conditions and, at the same time, it has been suggested to be essential in postprandial removal and partitioning of exogenous fat [11].

Therefore, the aims of this study were to characterize postprandial dyslipidaemia of type 2 diabetes evaluating (a) the role of insulin resistance — comparing obese subjects with and without type 2 diabetes *vs.* normal-weight controls, (b) any additional effect of diabetes per se — comparing obese diabetic *vs.* only obese subjects, and (c) the role of adipose tissue LPL in the aetiology of these abnormalities.

Methods

Subjects

Ten patients with type 2 diabetes mellitus and obesity, 11 patients with only obesity, 11 normal-weight control subjects participated in the study. Their baseline characteristics are shown in Table 1. Subjects were males, aged 26–59 years, and had normal fasting plasma concentrations of both triglycerides (<150 mg/dl) and cholesterol (<210 mg/dl).

The subjects had no history or symptoms of any known disease, apart from diabetes, nor were they vegetarians or engaged in intensive physical activity. They were not taking

Table 1 Physical characteristics, fasting metabolic values, insulin sensitivity measures, and adipose tissue heparin-releasable LPL activity of the subjects participating in the study

	Diabetic obese	Obese	Controls
Male (*n*)	10	11	11
Age (years)	45.6 [6.4]	45.8 [8.7]	39.1 [8.3]
Anthropometrics			
BMI (kg/m^2)[a]	32.8 [2.0][b]	34.5 [2.7][b]	24.0 [1.3]
Waist circumference (cm)[a]	112 [8][b]	113 [7][b]	85 [4]
Body fat mass (kg)[a]	31.7 [4.4][b]	32.9 [4.9][b]	13.1 [1.4]
Fasting plasma values			
Cholesterol (mg/dl)	175 [24]	187 [35]	160 [24]
Triglycerides (mg/dl)	103 [24]	99 [34]	78 [27]
HDL cholesterol (mg/dl)[a]	35 [4][b,c]	43 [11]	47 [10]
Glucose (mg/dl)[a]	131 [36][b,c]	90 [9]	86 [9]
Hyperinsulinemic euglycemic clamp			
Glucose infusion rate (*M* value) (mg/kg b.w./min)[a]	4.1 [0.9][b]	4.5 [1.5][b]	8.2 [2.2]
M/I[a]	2.1 [1.1][b]	1.7 [0.8][b]	7.5 [3.2]
Adipose tissue LPL activity (nmol FA/g/h)[a]			
Fasting	99 [34][b,c]	217 [92]	252 [155]
6 h after meal	89 [51][b,c]	231 [99]	278 [130]

Data are presented as *M* [SD].
[a] $p < 0.05$ ANOVA.
[b] $p < 0.05$ *vs.* controls.
[c] $p < 0.05$ *vs.* obese.

any hypolipidaemic drug. Diabetic patients were in stable glycaemic control on diet alone (HbA1c = 6.5 ± 1.4%). The study protocol was approved by the Federico II University Ethics Committee and informed consent was obtained from all participants.

Experimental procedures

In the morning after a 12-h fast, anthropometric measurements and bioimpedentiometry were performed before subjects were given a standard meal. Before the meal and over the following 6 h blood samples were taken for determination of plasma levels of glucose, insulin, C-peptide, NEFA, lipids and lipoproteins, apo B-48 and apo B-100. Six hours after the meal a needle biopsy of abdominal subcutaneous adipose tissue was taken for the determination of LPL activity. A similar biopsy in the opposite side of lower abdomen was taken at fast 1—7 days apart. Subjects also underwent a hyperinsulinaemic euglycaemic clamp.

Anthropometry and body composition
Body weight, height, and waist circumference were measured according to standardized procedures [12]. Fat-free body mass (FFM) was determined by bioimpedentiometry [13]. Fat mass was calculated subtracting FFM from body weight.

Standard test meal
The standard meal (944 kcal; 31% carbohydrates, 57% fat (34% saturated), and 12% protein) consisted of a pie made of mashed potato, whole milk, egg, cheese, ham and butter, to be consumed in around 15 min.

Hyperinsulinaemic euglycaemic clamp [14]
Regular human insulin was administered intravenously at a constant rate of 1.5 mU kg body weight^{-1} min^{-1} for 2 h. Blood glucose concentrations were maintained around 90 mg/dl by adjusting the glucose infusion rate according to blood glucose measurements on an Accucheck analyser (Roche, Switzerland). As measures of whole-body insulin sensitivity, mean glucose infusion rate during the last 30 min of the clamp (M value) and M/I ratio (M value divided by the corresponding plasma insulin concentrations) were calculated.

Laboratory procedures

Lipoprotein separation
Samples were kept at +4 °C before, during and after centrifugation and treated to minimize proteolytic degradation of apo B [3]. Fasting and postprandial lipoprotein subfractions were isolated by discontinuous density gradient ultracentrifugation according to Refs. [15,16], as previously described [3]. Briefly, three consecutive runs were performed at 15 °C and at 40 000 rpm to float: chylomicrons (Svedberg flotation unit (Sf) >400), large VLDL (Sf 60—400) and small VLDL (Sf 20—60). IDL (Sf 12—20) and LDL (Sf 0—12) were recovered from the gradient after the Sf 20—60 particles had been collected. HDL was isolated by a precipitation method.

Apo B-48 and apo B-100
Concentrations of apo B-48 and apo B-100 were determined in chylomicrons, large VLDL and small VLDL fractions by SDS-PAGE on a self-made 3.5—20% gel gradient according to Karpe and Hamsten [17], as previously described [3]. The intra- and inter-gel coefficients of variation were 10.1% and 13.7% for apo B-48 and 6.9% and 12.3% for apo B-100, respectively.

Adipose tissue LPL activity
LPL heparin-releasable activity was determined as modified from Taskinen et al. [18]. Small pieces (5—10 mg) of frozen adipose tissue were incubated in duplicate in small vials for 45 min at 37 °C, 70 cycles/min, with 450 μl of 0.1 mol/l Krebs—Ringer Tris buffer, pH 8.4 (containing 1 g/100 ml bovine albumin and 45 μl pooled normal human serum) and 50 μl of beef lung heparin (50 units/ml saline). Thereafter, tissue pieces were removed and 100 μl eluate, in triplicate for each vial, were incubated with the same volume of a ^{3}H-trioleoylglycerol substrate emulsion stabilized by dioleoyl phosphatidyl choline [19] for 110 min at 37 °C. The ^{3}H-labelled oleic acid released was extracted by Belfrage and Vaughan mixture, shaken for 4 min and centrifuged at 3000 rpm, 20 min, 20 °C. 1.6 ml of the supernatant containing released oleic acid in 10 ml Instagel Plus was counted for 1 h in a Wallac 1410 Liquid Scintillation Counter.

Other measurements
Plasma concentrations of cholesterol, triglyceride and NEFA were assayed by enzymatic colorimetric methods (Roche Molecular Biochemicals, Mannheim, Germany), insulin and C-peptide by ELISA (Technogenetics, Milan, Italy).

Statistical analysis

Data are expressed as mean ± SEM, unless otherwise stated. Postprandial incremental area was calculated by the trapezoidal method as the area under the curve above baseline value (IAUC). Differences between the three groups were evaluated by ANOVA and by post hoc test between groups (LSD). Differences between the three groups at single time points after the meal were first evaluated by ANOVA for repeated measures. Variables not normally distributed were analyzed after logarithmic transformation or by nonparametric tests. Two-tailed tests were used and a $p < 0.05$ was considered statistically significant. Statistical analysis was performed using the Statistical Package for Social Sciences software (SPSS/PC, SPSS, Inc., Chicago, IL).

Results

Anthropometrics (Table 1)

Obese and diabetic obese subjects had similarly high BMI and abdominal circumference, with a similar body composition as shown by their fat mass.

Whole-body insulin sensitivity (Table 1)

Glucose infusion rate during the last 30 min of the euglycaemic hyperinsulinaemic clamp (M value) was similarly lower in the two obese groups compared to controls

($p < 0.001$). The impairment in insulin sensitivity was highlighted when M values were corrected for the concomitant plasma insulin levels (M/I ratios) ($p < 0.001$).

Fasting and postprandial glucose, insulin, C-peptide and NEFA concentrations (Fig. 1)

Blood glucose levels were higher in the diabetic subjects both at fasting and after the meal ($p < 0.01$ at all time points).

Fasting and postprandial plasma insulin levels were significantly higher in obese subjects with and without diabetes compared to controls ($p < 0.01$ at all time points). Compared to obese subjects, diabetic subjects showed a tendency to a blunted early insulin response (2 h after the meal). Plasma C-peptide concentrations showed a profile similar to insulin.

Fasting plasma NEFA levels were not significantly different between the three groups. NEFA levels were suppressed 2 h after the meal, with a tendency to a lower suppression in diabetic subjects.

Lipids and apo B concentrations

Whole plasma
Fasting plasma triglycerides and cholesterol concentrations were not significantly different between the three groups (Table 1). Postprandial IAUC for triglycerides was higher in diabetic subjects compared to obese and controls ($p < 0.05$) (Table 2). Cholesterol levels decreased postprandially, without differences between groups (Table 2).

Chylomicrons (Fig. 2)
Diabetic patients had higher levels of postprandial chylomicron lipids compared to the other two groups, the differences being significant at 6 h for both triglycerides and cholesterol ($p < 0.05$ vs. obese). Diabetic patients also showed significantly higher triglycerides IAUC ($p < 0.05$ vs. obese) and cholesterol IAUC ($p < 0.05$ vs. obese and controls) (Table 2). Apo B-48 levels at 6 h were also increased in diabetic subjects compared to the obese ones ($p < 0.05$). Apo B-100 levels, both before and after the meal, were not different between the three groups.

Large VLDL (Fig. 3, Table 2)
Fasting concentrations of triglycerides, cholesterol, and apo B-100 in this fraction were higher (albeit not significantly) in obese and diabetic obese compared to controls. After the meal, triglycerides, cholesterol, and apo B-100 concentrations increased more in the two obese groups, the differences being significant in the late postprandial phase. A greater IAUC was observed for triglycerides (188 ± 28 and 135 ± 22 in diabetic and obese subjects, respectively, vs. 87 ± 13 mg/dl·6 h in controls, ANOVA $p = 0.011$), and cholesterol (25.6 ± 3.9 and 19.2 ± 3.3 vs. 10.0 ± 2.0 mg/dl·6 h in controls, ANOVA $p = 0.006$). In contrast, apo B-100 IAUC was not significantly different in the three groups (ANOVA $p = 0.513$). There was a trend to higher postprandial apo B-48 in the diabetic subjects.

In the three groups combined, IAUCs of triglyceride and cholesterol large VLDL were inversely correlated with the insulin sensitivity index M/I ($r = -0.48$, $p = 0.009$ for both).
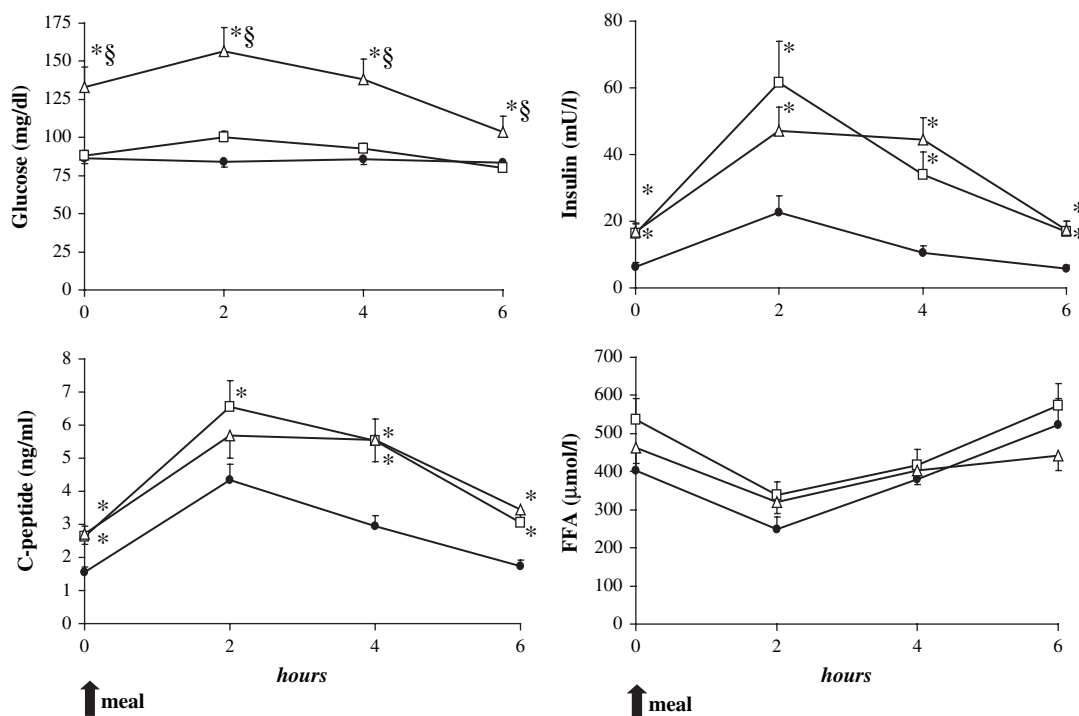

Figure 1 Plasma concentrations of glucose, insulin, C-peptide and FFA before and after a standard meal in obese (white squares), diabetic obese (white triangles), and normal-weight controls (black circles). $M \pm$ SEM; *$p < 0.05$ vs. controls, §$p < 0.05$ vs. obese.

Table 2 Incremental AUC for triglycerides (TG) (mg/dl·6 h), cholesterol (Chol) (mg/dl·6 h), apo B-48 (mg/l·6 h), and apo B-100 (mg/l·6 h) in whole plasma and lipoprotein fractions after a standard meal in diabetic obese, obese, and normal-weight control subjects

		Diabetic obese	Obese	Controls
Whole plasma	TG	343 [52][b,c]	222 [37]	208 [34]
	Chol	−8.7 [9.9]	−16.6 [9.7]	−14.3 [7.3]
Chylomicrons	TG	132 [23][c]	75 [14]	107 [20]
	Chol	5.1 [0.9][b,c]	3.1 [0.6]	3.1 [0.5]
	B-48	0.48 [0.22]	0.13 [0.04]	0.27 [0.12]
	B-100	1.5 [0.7]	0.78 [0.35]	0.42 [0.22]
Large VLDL	TG[a]	188 [28][b]	135 [22][b]	87 [13]
	Chol[a]	25.6 [3.9][b]	19.2 [3.3][b]	10.0 [2.0]
	B-48	5.0 [1.4]	3.3 [0.7]	3.0 [1.1]
	B-100	61 [23]	80 [18]	51 [12]
Small VLDL	TG[a]	−11.9 [5.3][b]	−2.9 [4.0]	3.5 [3.3]
	Chol	−5.2 [2.8][b]	−0.3 [1.3]	0.01 [1.6]
	B-48	0.9 [0.5]	2.2 [1.1]	1.0 [0.5]
	B-100	−10.8 [13.7]	33.6 [23.9]	15.6 [9.1]
IDL	TG	−3.0 [1.2]	−3.3 [1.3]	−0.9 [1.1]
	Chol	−1.8 [1.5]	−6.7 [2.3]	−1.8 [1.7]
LDL	TG	−5.7 [2.2]	−6.2 [2.3]	−2.1 [1.0]
	Chol	−24.1 [7.1]	−16.0 [12.3]	−16.9 [7.4]
HDL	TG	2.1 [4.9]	−0.2 [2.9]	−6.6 [7.3]
	Chol	−10.1 [2.3]	−12.3 [5.9]	−10.4 [3.1]

Data are presented as M [SEM].
[a] $p < 0.05$ ANOVA.
[b] $p < 0.05$ vs. controls.
[c] $p < 0.05$ vs. obese.

Small VLDL

Fasting lipids and apo B concentrations in this fraction were higher in the obese and diabetic obese compared to controls (data not shown). A slight postprandial decrease in triglyceride and cholesterol was present in the diabetic group, as shown by significantly lower IAUCs compared to controls (Table 2).

IDL, LDL and HDL

Fasting HDL cholesterol concentrations were significantly lower in subjects with diabetes compared to obese and control subjects (Table 1). The changes induced by the meal in IDL, LDL and HDL fractions did not significantly differ between the three groups (Table 2).

Adipose tissue LPL activity

Heparin-releasable LPL activity, expressed per gram of adipose tissue, was significantly lower in the diabetic subjects at fast (99 ± 11 vs. 217 ± 35 and 252 ± 51 nmol FA/g/h, in obese and controls, respectively, ANOVA $p < 0.05$) and after meal (89 ± 16 vs. 231 ± 31 and 278 ± 40 nmol FA/g/h, ANOVA $p < 0.01$) (Table 1). LPL activity was lower in subjects with diabetes, also when expressed per total fat mass. In the three groups combined, postprandial LPL activity was inversely correlated with postprandial IAUC of chylomicron triglycerides ($r = −0.42$, $p < 0.05$).

Discussion

While long being recognized, postprandial lipid abnormalities in diabetes, namely the specific types of lipoproteins affected and the mechanisms involved, are still not fully characterized. There are several reasons for these inconsistencies. Few studies have performed a thorough evaluation of postprandial lipoprotein fractions, including apo B-48 and apo B-100 measurements; fasting hypertriglyceridaemia has not always been taken into account as a confounding factor; patients with different degrees of blood glucose control and who were overweight have been studied, and insulin sensitivity has seldom been quantified. Paying attention to these factors, we have dealt with a relevant unsolved issue, i.e. the specific effects of diabetes per se, obesity per se and whole-body insulin resistance on individual postprandial lipoprotein alterations.

The first finding of this study defines the increase in large VLDL as the quantitatively most relevant postprandial alteration in obese and diabetic patients with fasting normo-triglyceridaemia. This abnormality was associated with insulin resistance since it was similarly observed in obese individuals with and without diabetes at comparable levels of whole-body insulin resistance. It mainly represented lipoproteins of endogenous origin, as shown by the higher postprandial levels of apo B-100, which completely
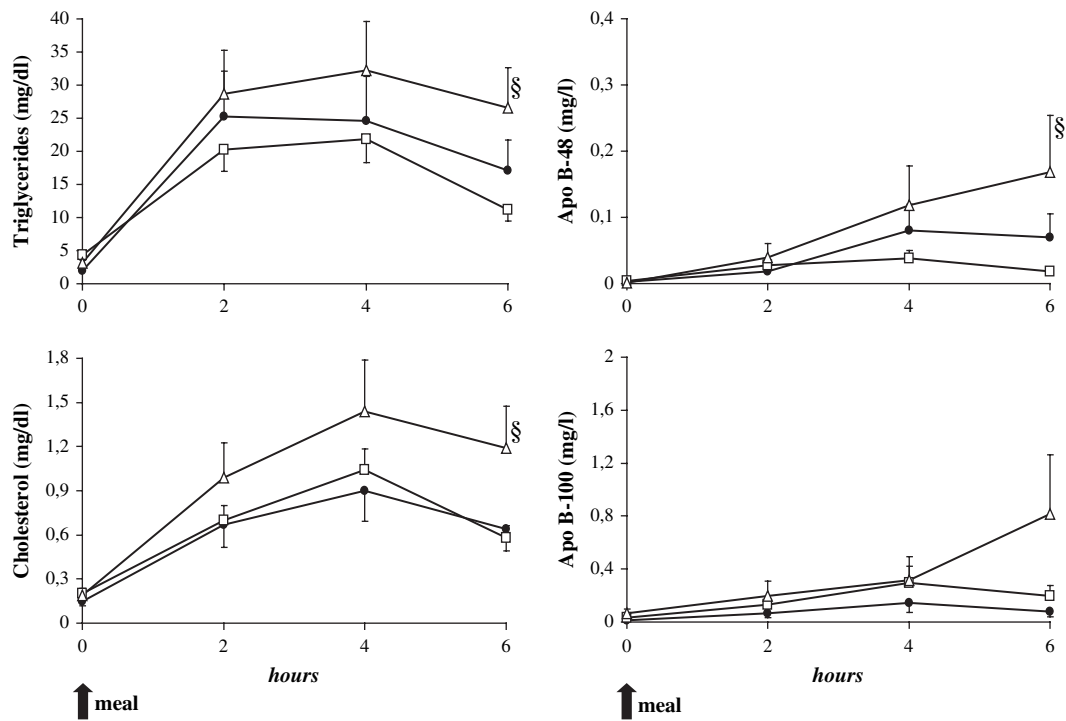
Figure 2 Concentrations of triglyceride, cholesterol, apo B-48, and apo B-100 in plasma chylomicrons before and after a standard meal in obese (white squares), diabetic obese (white triangles), and normal-weight controls (black circles). $M \pm$ SEM; §$p < 0.05$ *vs.* obese.
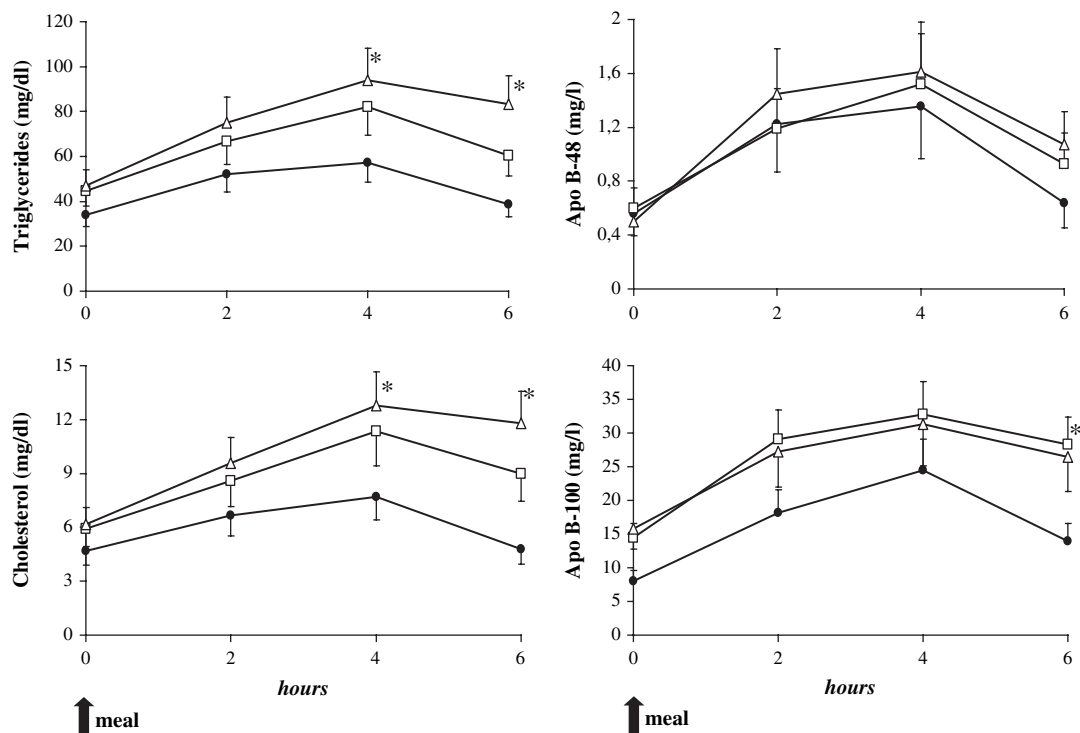

Figure 3 Concentrations of triglyceride, cholesterol, apo B-48, and apo B-100 in plasma large VLDL before and after a standard meal in obese (white squares), diabetic obese (white triangles), and normal-weight controls (black circles). $M \pm$ SEM; *$p < 0.05$ *vs.* controls.

overlapped in obese individuals with and without diabetes. The higher postprandial apo B-100 levels were not directly due to changes induced by the meal, as IAUCs only marginally differed in the three groups, but rather to the fact that apo B-100 levels were already higher in the fasting condition in insulin-resistant subjects compared with controls, confirming our previous observation [3]. This also indicates that in individuals with normo-triglyceridaemia, large VLDL postprandial alterations are related to fasting levels as well as to hepatic insulin resistance.

The second novel finding of this study is that, in addition to large VLDL abnormalities, diabetic patients had higher levels of exogenous triglyceride-rich lipoproteins than obese individuals without diabetes. The chylomicron increase was therefore related to diabetes ''per se'' and independent of whole-body insulin resistance. It is intriguing that the chylomicron response in simply obese individuals was even lower than that of normal-weight controls. This is nevertheless in agreement with previous studies showing similar/lower postprandial chylomicron lipids in normotriglyceridaemic obese individuals compared to normal-weight controls [20,21], and in line with the proposed ''buffering'' action of adipose tissue in the postprandial phase [11]. Adipose tissue could functionally act as a reservoir for the ingested fat, diverting it from other tissues where it wouldn't be necessary and therefore potentially deleterious. This process could be more active in individuals with simple obesity due to their prevailing higher peripheral insulin levels.

The higher chylomicron response in the diabetic subjects could be related to the lower LPL activity in adipose tissue we found in these patients. This possibility is supported by the inverse correlation observed between these two parameters. The role of LPL activity in the genesis of postprandial dyslipidaemia has been difficult to assess because of differences in type of meal and timing and, especially, source of sampling. In fact, there is a mixed contribution in plasma by tissues — mainly muscle and adipose tissue — with opposing postprandial behaviours [22]. In our study, diabetic subjects had a significant reduction of LPL activity in adipose tissue compared to subjects with a similar degree of adiposity, when the activity was expressed either per weight or per total body fat. This is in line with the results of a previous study in the fasting condition [23]. On the other hand, Eriksson et al. [24] showed that adipose tissue LPL activity was not significantly different between patients with type 2 diabetes and healthy controls, matched for age, gender and BMI. Reasons for this difference may be that in the latter study subjects were not obese and less homogeneous as for diabetes treatment and blood glucose control.

The LPL defective action in the diabetic subjects may also explain their slight reduction in small VLDL lipids after the meal, indicating a slower postprandial lipoprotein cascade also concerning the catabolism of larger particles to small VLDL.

We observed no changes in LPL activity between fasting and 6 h after the meal. Apart from the late postprandial sampling time, 6 h vs. 3.5—4 h as more often done, this may also be due to the type of stimulus, i.e., a fat-rich meal. In fact, an increased LPL activity is observed after glucose ingestion but not after fat ingestion [25]. In comparing fasting and post-meal LPL activities it must also be considered that fasting and postprandial biopsies were taken on different days, although all other conditions were kept unchanged between the two occasions.

Which factor/s may induce lower LPL activity is not known. LPL is an insulin sensitive enzyme, and in humans insulin increases adipose tissue LPL [26]. Therefore, it is possible that the higher plasma insulin levels in both insulin-resistant groups were unable to compensate in the case of diabetic subjects, who showed a blunted early postprandial insulin response compared to the only obese ones. Moreover, the first postprandial sample was taken 2 h after the meal and therefore we could have missed the largest difference between the two groups. As to the relevance of early insulin response, studies in rats have shown a central role of insulin in the postprandial response of adipose tissue LPL, that was also stimulated by early cephalically mediated insulin secretion [27].

The possible role of hyperglycaemia in the explanation of the lower LPL activity in diabetic patients must be considered, it being the main parameter discriminating between diabetic and obese subjects. As a matter of fact, LPL activity was increased in adipose tissue by improved diabetes control [28,29] and decreased in the circulation by hyperglycaemia [30].

In conclusion, this study elucidates types and possible mechanisms of postprandial lipid abnormalities in individuals with obesity and type 2 diabetes without fasting hypertriglyceridaemia. In these individuals the quantitatively most relevant alteration is an increase in hepatic large VLDL, which reflects the higher fasting levels of this fraction and is likely to be related to insulin resistance. In addition, diabetes per se is characterized by an increased postprandial chylomicron response, independent of obesity and whole-body insulin resistance, likely to be a consequence of the reduced adipose tissue LPL activity. Although the diabetic patients participating in this study do not represent the whole diabetic population, as they were selected in good glycaemic control and with fasting normotriglyceridaemia, it may be assumed that in the clinical setting these postprandial lipoprotein alterations will be even more evident.

Differences in postprandial abnormalities and related mechanisms imply that multiple therapeutic approaches be considered to correct the abnormal postprandial lipid metabolism in patients with obesity and diabetes mellitus, in order to potentially reduce their negative cardiovascular impact.

Acknowledgments

References

[1] Karpe F. Postprandial lipoprotein metabolism and atherosclerosis. J Intern Med 1999;246:341—55.

[2] Syvanne M, Hilden H, Taskinen MR. Abnormal metabolism of postprandial lipoproteins in patients with non-insulin-dependent diabetes mellitus is not related to coronary artery disease. J Lipid Res 1994;35:15—26.

[3] Rivellese AA, De Natale C, Di Marino L, Patti L, Iovine C, Coppola S, et al. Exogenous and endogenous postprandial lipid abnormalities in type 2 diabetic patients with optimal blood glucose control and optimal fasting triglyceride levels. J Clin Endocrinol Metab 2004;89:2153—9.

[4] Chen YD, Swami S, Skowronski R, Coulston A, Reaven GM. Differences in postprandial lipaemia between patients with normal glucose tolerance and noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab 1993;76:172—7.

[5] Eliasson B, Mero N, Taskinen MR, Smith U. The insulin resistance syndrome and postprandial lipid intolerance in smokers. Atherosclerosis 1997;129:79—88.

[6] Axelsen M, Smith U, Eriksson JW, Taskinen M-R, Jansson P-A. Postprandial hypertriglyceridemia and insulin resistance in normoglycemic first-degree relatives of patients with type 2 diabetes. Ann Intern Med 1999;131:27—31.

[7] Taskinen M-R. Diabetic dyslipidaemia: from basic research to clinical practice. Diabetologia 2003;46:733—49.

[8] Couillard C, Bergeron N, Prud'homme D, Bergeron J, Tremblay A, Bouchard C, et al. Postprandial triglyceride response in visceral obesity in men. Diabetes 1998;47:953—60.

[9] Panarotto D, Rémillard P, Bouffard L, Maheux P. Insulin resistance affects the regulation of lipoprotein lipase in the postprandial period and in an adipose tissue-specific manner. Eur J Clin Invest 2002;32:84—92.

[10] Annuzzi G, De Natale C, Iovine C, Patti L, Di Marino L, Coppola S, et al. Insulin resistance is independently associated with postprandial alterations of triglyceride-rich lipoproteins in type 2 diabetes mellitus. Arterioscler Thromb Vasc Biol 2004;24:2397—402.

[11] Frayn KN. Adipose tissue as a buffer for daily lipid flux. Diabetologia 2002;45:1201—10.

[12] Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults — the evidence report. National Institutes of Health. Obes Res 1998; 6(Suppl. 2) 51S—209S.

[13] Segal KR, Van Loan M, Fitzgerald PI, Hodgdon JA, Van Itallie TB. Lean body mass estimation by bioelectrical impedance analysis: a four-site cross-validation study. Am J Clin Nutr 1988;47:7—14.

[14] DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 1979;237:E214—23.

[15] Redgrave TG, Carlson LA. Changes in plasma very low density and low density lipoprotein content, composition, and size after a fatty meal in normo- and hypertriglyceridaemic man. J Lipid Res 1979;20:217—29.

[16] Karpe F, Steiner G, Olivecrona T, Carlson LA, Hamsten A. Metabolism of triglyceride rich lipoproteins during alimentary lipaemia. J Clin Invest 1993;91:748—58.

[17] Karpe F, Hamsten A. Determination of apolipoproteins B-48 and B-100 in triglyceride-rich lipoproteins by analytical SDS-PAGE. J Lipid Res 1994;35:1311—7.

[18] Taskinen MR, Nikkila EA, Huttunen JK, Hilden H. A micromethod for assay of lipoprotein lipase activity in needle biopsy samples of human adipose tissue and skeletal muscle. Clin Chim Acta 1980;104:107—17.

[19] Nilsson-Ehle P, Ekman R. Rapid, simple and specific assay for lipoprotein lipase and hepatic lipase. Artery 1977;3:194—209.

[20] Guerci B, Verges B, Durlach V, Hadjadj S, Drouin P, Paul JL. Relationship between altered postprandial lipemia and insulin resistance in normolipidemic and normoglucose tolerant obese patients. Int J Obes Relat Metab Disord 2000;24:468—78.

[21] Vansant G, Mertens A, Muls E. Determinants of postprandial lipemia in obese women. Int J Obes Relat Metab Disord 1999;23(Suppl. 1):14—21.

[22] Lithell H, Boberg J, Hellsing K, Lundqvist G, Vessby B. Lipoprotein-lipase activity in human skeletal muscle and adipose tissue in the fasting and the fed states. Atherosclerosis 1978;30: 89—94.

[23] Taskinen MR, Nikkila EA, Kuusi T, Harmo K. Lipoprotein lipase activity and serum lipoproteins in untreated type 2 (insulin-independent) diabetes associated with obesity. Diabetologia 1982;22:46—50.

[24] Eriksson JW, Buren J, Svensson M, Olivecrona T, Olivecrona G. Postprandial regulation of blood lipids and adipose tissue lipoprotein lipase in type 2 diabetes patients and healthy control subjects. Atherosclerosis 2003;166:359—67.

[25] Nilsson-Ehle P, Carlstrom S, Belfrage P. Rapid effect on lipoprotein lipase activity in adipose tissue of humans after carbohydrate and lipid intake. Scand J Clin Lab Invest 1975; 35:373—8.

[26] Sadur CN, Eckel RH. Insulin stimulation of adipose tissue lipoprotein lipase. Use of the euglycemic clamp technique. J Clin Invest 1982;69:1119—25.

[27] Picard F, Naimi N, Richard D, Deshaies Y. Response of adipose tissue lipoprotein lipase to the cephalic phase of insulin secretion. Diabetes 1999;48:452—9.

[28] Simsolo RB, Ong JM, Saffari B, Kern PA. Effect of improved diabetes control on the expression of lipoprotein lipase in human adipose tissue. J Lipid Res 1992;33:89—95.

[29] Yost TJ, Sadur CN, Eckel RH. Glycohemoglobin levels relate to the response of adipose tissue lipoprotein lipase to insulin/glucose in obese non-insulin-dependent diabetes mellitus. Metabolism 1995;44:1475—80.

[30] Kovar J, Fejfarova V, Pelikanova T, Poledne R. Hyperglycemia downregulates total lipoprotein lipase activity in humans. Physiol Res 2004;53:61—8.