Real-time assessment of postprandial fat storage in liver and skeletal muscle in health and type 2 diabetes


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It is not known whether the increased tissue triglyceride levels in type 2 diabetes is a consequence of decreased lipid oxidation or of increased tissue uptake. It is also unclear whether the triglyceride pools in liver and muscle are relatively static or turn over rapidly. Defects in mitochondrial fatty acid oxidation have been reported in type 2 diabetes (13), insulin-resistant offspring of type 2 diabetic subjects (25), and older normal subjects (24). However, to date there has been no technique to permit observation of real-time dynamics of postprandial liver and muscle triglyceride storage in humans. This will be important in understanding the pathogenesis of tissue triglyceride accretion. We have developed a method to allow real-time tracking of ingested fatty acids in humans by use of 13C magnetic resonance spectroscopy (MRS) and have quantified the postprandial dynamics of liver and muscle fat storage in normal and type 2 diabetic subjects.

MATERIALS AND METHODS

Subjects

Subjects with diet-controlled type 2 diabetes (≥2 yr duration, HbA1c <7.5%, no history of weight loss or ketonuria at time of diagnosis) and age- and body mass index-matched healthy volunteers with no family history of diabetes were recruited. Athletes in training and subjects with other metabolic disease were excluded. Subjects were also excluded if they were taking any medication that might affect carbohydrate or lipid metabolism or if they had hepatic or renal impairment. Ethical permission was obtained from the Newcastle and North Tyneside Local Research Ethics Committees. Informed consent was obtained from each subject before commencement of studies. Anthropometric measurements were documented after an overnight fast. Bioimpedance was performed using a Holtain BC Analyser (Holtain, Dyfed, UK), and the percentage of body fat was derived.

The subjects' characteristics are shown in Table 1.

Study Design

Subjects abstained from alcohol or vigorous exercise for 3 days before the study. During this period, they kept a food diary to record all food intake and were given a list of foods naturally rich in 13C, which they were instructed to avoid. Both groups reported similar calorie intake (1,923 ± 207 kcal/day for diabetic and control subjects, respectively) and similar food composition (carbohydrate, 256 ± 36 g vs. 232 ± 72 g; fat, 69 ± 8 vs. 72 ± 9 g; protein, 83 ± 5 vs. 69 ± 5 g). They fasted from 1800 on the previous evening before the study, although water was permitted. On the morning of the study, subjects were transported to the magnetic resonance center by taxi.
The subject was placed in a comfortable supine position. The liver coil was held firmly by a waist vest and rested across the right hypochondrium, positioning the liver optimally in the region of sensitivity of the coil. The soleus muscle was placed directly over the muscle coil. Vacuum pillows were used to ensure reproducibility of the position of the subject for repeated measurements on both the liver and soleus muscle.

Manual shimming was performed on the water resonance peak. The shimmmed signal was localized to the volume of interest by using either the $^{13}$C coil (muscle coil) at the proton frequency or the $^1$H coil (liver coil). Water line-widths of 20–50 Hz were achieved for both liver and leg. Each coil was tuned and matched before each lipid measurement with a Network Analyser (HP model 8751A, 5–500 kHz).

$^{13}$C spectra were acquired according to the following pulse sequence. A 100–μs rectangular pulse was used for $^{13}$C excitation, with a peak power of 390 ± 10 W at a resonant frequency of 32.154973 MHz. CYCLOPS phase cycling was used to cancel any phase-coherent noise. Broadband proton decoupling was performed using three WALTZ-8 (31) cycles during acquisition with a peak power of 68 ± 2 W. A repetition time of 0.72 s was used, and spectra were collected in blocks of 500 scans, giving a temporal resolution of 6 min. The sampling time was set to 142 μs, and 512 data points were collected during the acquisition period. Radio frequency power values were monitored throughout the acquisition to ensure that they stayed well below the maximal values allowed according to specific absorption rate (SAR) guidelines recommended by the National Radiological Protection Board (21). The repetition rate of 0.72 s ensured that the SAR limits were not exceeded and also allowed for sufficient T1 recovery of $^{13}$C lipid magnetization.

### Analyses of $^{13}$C Spectra

The peaks at 128–130 ppm were analyzed to identify alkenes double bonds, 14 ppm to identify methyl carbon, and 20–40 ppm to identify methylene carbons (Fig. 1, A and B). Uptake of unsaturated fatty acids by the liver and muscle is seen as an overall increase in signal with a concomitant change in the peaks of the alkene carbon. This was more apparent with a resolution enhancement filter, TRAF (transform of reverse added FIDS). The increase in saturated fatty acids is seen as an increase and broadening of the peaks in the methylene carbon (20–40 ppm) (Fig. 1, A and B). Results are shown for the increase in $^{13}$C alkenes carbons in both groups. The change in $^{13}$C methylene carbon was identical (data not shown).

All spectra were analyzed using the Matlab version of the MRUI software package (40). The data were first converted using a conversion routine written in-house to an MRUI-compatible format. The spectra were zero-filled to 4 K and apodized using an exponential decay weighting of 5 Hz, and the baselines were corrected. Three spectra acquired at each time point were added to improve the signal-to-noise ratio. The AMARES algorithm was used to fit each selected peak to Lorentzian line shapes. During the fitting, the noise level was estimated from the last 50 data points. The integral of the peaks was expressed as a fraction of that from the formate peak, derived from a phantom containing $^{13}$C formate and placed at the center of the $^{13}$C coils. Liver- and calf-shaped phantoms were constructed using 5.33 mmol/l labeled algal lipid mixture dissolved in deuterated chloroform. Again, the integral from the peaks was expressed as a fraction of that from the formate peak. The incorporated labeled fatty acid concentration into hepatic triglyceride or muscle triglyceride was then calculated using the formula

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\frac{(R_{lipid(S)} - R_{lipid(S=0)}) \times \text{[labeled lipid concentration (mmol/l)]}}{R_{lipid(ph)}}
\]

where $R_{lipid(S)}$ is the ratio of the lipid to formate peaks in the subject at time $t$, and $R_{lipid(ph)}$ is the ratio of the lipid to the formate peaks in the phantom. Due to broadening of liver and muscle spectra in one
control subject and three diabetic subjects, spectroscopy data are shown only for seven control subjects and nine diabetes subjects.

**Plasma Lipid and Breath Gas Analysis**

Lipoprotein fractionation was performed by sequential ultracentrifugation as described (6). Briefly, serum was overlayed with sodium chloride solution, 1.006 density (0.195 M), and spun in a Beckman L8–70 ultracentrifuge with a 70.1 Ti rotor at 7,000 g at 4°C for 30 min. The upper chylomicron layer was pipetted off and washed with 4 ml of 1.006 density saline followed by ultracentrifugation (16 h at 85,000 g). Simultaneously, the remaining plasma with a layer of 1.006 density saline was spun for 16 h at 85,000 g to isolate a triglyceride-rich lipoprotein (TRL) fraction (very-low-density lipoproteins and chylomicron remnants). The remaining plasma was then adjusted to a final density of 1.21 with NaCl-NaBr solution and spun for 16 h at 100,000 g to isolate the cholesterol-rich lipoproteins (CRL), comprising intermediate-, low-, and high-density lipoproteins. The remaining lipoprotein-depleted plasma was subjected to nonesterified fatty acid (NEFA) analysis. Triglyceride and cholesterol concentrations of the fractions were estimated on an Olympus AU640 Analyser (Olympus Diagnostics, Southall, UK) using enzymatic methods.

13C enrichments of lipid fractions and breath samples were determined by elemental-analyzer combustion continuous flow isotope ratio mass spectrometry using an automated nitrogen carbon analysis unit for solids and liquids (ANCA-SL) linked to a 20/20 mass spectrometer (PDZ Europa, Crewe, UK). For 13C enrichment analysis of plasma samples, samples were preweighed into smooth tin capsules and freeze dried, and capsules were prepared for stable isotope analysis. The reference material used in the analysis was IAEA-NBS22 (oil) with an accepted delta 13C value of −29.7%. All results of 13C enrichment of lipoprotein fractions and expired air are expressed as atom percent excess (APE).

**Blood Glucose, Plasma Insulin, and Metabolites**

Blood glucose was measured with a HemoCue photometer analyzer (HemoCue, Angelholm, Sweden). Plasma NEFA was measured on a Roche Cobas centrifugal analyzer with a Wako kit (Wako Chemicals, Neuss, Germany). Plasma insulin was measured using a Dako insulin enzyme-linked immunosorbent assay kit (DAKO, Ely, UK). Metabolites (glycerol, lactate, ketone bodies) were measured using a COBAS biocentrifugal analyzer with fluorometric attachment (Roche Diagnostics, Welwyn Garden City, UK).

**Statistical Analysis**

All data are expressed as means ± SE in the text. Statistical analyses were performed using MINITAB software (Release 13.1; Minitab, State College, PA). Comparisons were carried out using Student’s t-test (two tailed), and relationships were tested using the linear correlation analysis. A P value of <0.05 was considered to indicate statistical significance. A prior power calculation on the primary outcome measure of tissue triglyceride accumulation was not possible in view of the novel nature of the MRS methodology.

**RESULTS**

*Turnover of Intrahepatic and Intramuscular Triglyceride*

**Hepatic triglyceride.** In the control group, postprandial increment in 13C-fatty acid content in hepatic triglyceride was rapid, rising significantly from baseline of 48.0 ± 11.6 mmol/l by 4 h (+4.6 ± 1.4 mmol/l, P = 0.012), reaching a peak increment of +7.3 ± 1.5 mmol/l by 6 h (P = 0.002). After this, there was sharp decrease in 13C enrichment back to baseline levels by 8 h (P < 0.001), and this persisted at 24 h (Fig. 2A).

At peak uptake, ~9% of the meal triglyceride was stored in the liver. In the diabetic group, the postprandial increment in hepatic 13C-fatty acid enrichment was more striking, rising significantly from baseline of 120.6 ± 29 mmol/l by 2 h (+6.7 ± 2.5 mmol/l, P = 0.026), reaching a peak increment of +10.8 ± 3.4 mmol/l by 4 h (P = 0.009). After this, there was a sharp decrease in 13C enrichment toward baseline levels by 6 h (Fig. 2A). At peak uptake, ~13% of ingested meal triglyceride was stored in the liver. The rate of rise in hepatic 13C-fatty acid enrichment was significantly faster in the diabetic group compared with the control group. There was a greater increase in 13C enrichment by 2 h in the diabetic group compared with the control group (+6.7 ± 2.5 vs. +0.9 ± 0.9 mmol/l, P = 0.05). In addition, the peak increment was seen earlier in the diabetic group (4 vs. 6 h, respectively; Fig. 2A).

The mean postprandial incremental area under the curve (AUC) of hepatic 13C enrichment between the first and second meals (0 and 4 h) was significantly higher in the diabetic group compared with the control group (+6.1 ± 1.4 vs. 1.7 ± 0.3 mmol/h, P = 0.019). The mean 24-h incremental AUC of hepatic 13C enrichment for the diabetic group was similar to that of the control group because of the sharper decline in 13C labeling in the diabetic group after the second meal (2.3 ± 2.6 vs. 2.1 ± 1.8 mmol/h, P = 0.94).

**Muscle triglyceride.** In the control group, the postprandial increment in 13C-fatty acid content in skeletal muscle triglyceride was small, peaking at 5 h (0.2 ± 0.6 mmol/l, P = 0.71). After this, 13C enrichment remained close to baseline levels of 32.5 ± 4.6 mmol/l (Fig. 2B). Considering the average total muscle mass in humans, at peak uptake, ~4% of meal triglyc-
Plasma Lipid Fractions and Incorporation of $^{13}$C-Fatty Acids into Plasma Lipoproteins and $^{13}$C Oxidation

**Plasma triglyceride.** Fasting plasma triglyceride was slightly higher in the diabetic group (1.73 ± 0.25 vs. 1.34 ± 0.13, $P = 0.18$). Plasma triglyceride levels rose steadily during the course of the study in both control and diabetic groups, reaching levels significantly greater from baseline, peaking at 8 h (2.22 ± 0.30 mmol/l, $P = 0.007$ and 2.54 ± 0.42 mmol/l, $P = 0.005$, respectively; Fig. 3A).

**Plasma lipoproteins.** Mean plasma chylomicron-triglyceride (CM-TG) and triglyceride-rich lipoprotein-triglyceride (TRL-TG) (representing very-low-density lipoproteins and chylomicron remnants) rose steadily in both groups, reaching significantly greater levels than baseline at 8 h (Fig. 3, B and C, respectively). Plasma TG, CM-TG, and TRL-TG levels returned to baseline levels by 24 h in both groups. There was negligible change in the cholesterol-rich lipoprotein-triglyceride (CRL-TG; representing low-, intermediate-, and high-density lipoproteins) concentrations during the course of the study in both groups (Fig. 3D). There was no significant difference in plasma triglyceride or lipoprotein-triglyceride levels between the two groups at any time point during the study.

$^{13}$C enrichment of lipoproteins. The postprandial appearance of $^{13}$C-fatty acids was highest in the CM-TG fraction in both control and diabetic groups, reaching a peak at 6 h ($P = 0.031$ and $P = 0.004$, respectively; Fig. 4A). Although the $^{13}$C enrichment decreased in both groups by 8 h, meal-derived fatty acids were still present in small amounts in the CM-TG fraction at 24 h in both control and diabetic groups ($P = 0.004$ and $P = 0.019$, respectively; Fig. 4A). The incorporation of label into TRL-TG was also rapid in both groups, reaching a peak in the control group at 8 h ($P = 0.002$) and reaching an earlier peak in the diabetic group at 6 h ($P = 0.01$). Meal-derived fatty acids were still present in the CRL-TG fraction at 24 h ($P = 0.001$ and $P < 0.001$, respectively; Fig. 4B). $^{13}$C labeling in the CRL-TG was small but reached significant peak levels in both groups at 24 h (Fig. 4C). There was no difference in $^{13}$C enrichment of CM-TG, TRL-TG, or CRL-TG fractions between the two groups at any time point during the study. $^{13}$CO$_2$ content in expired air was similar in both groups, peaking at 8 h in both groups and remaining slightly elevated at 24 h (Fig. 4D).

**Plasma NEFA and $^{13}$C enrichment of NEFA fraction.** Mean fasting NEFA levels were similar in both groups (0.50 ± 0.08 vs. 0.52 ± 0.06 mmol/l in control and diabetic subjects, respectively). Plasma NEFA fell in both groups to a nadir after 2 h and remained suppressed following the second meal and rose back to fasting levels by 24 h (Fig. 5A). $^{13}$C appearance in the plasma NEFA pool was minimal in both groups during the daytime but increased significantly in both groups during the overnight fast, reaching a maximum at 24 h ($P = 0.02$, both groups compared with baseline; Fig. 5B).

Other Metabolic Changes

**Blood glucose and plasma insulin.** Mean fasting blood glucose was significantly higher in the diabetic group (6.3 ± 0.2 vs. 5.1 ± 0.1 mmol/l, $P < 0.005$) and remained higher throughout the study (Fig. 6A). Mean fasting plasma insulin was also significantly higher in the diabetic group (86.4 ± 21

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**Relationship Between Tissue Triglyceride Levels and Insulin Resistance**

Baseline fasting levels of liver triglyceride correlated with insulin resistance as assessed by homeostasis model assessment (HOMA-IR) and fasting plasma insulin concentrations ($r = 0.71$, $P < 0.005$; $r = 0.69$, $P < 0.005$, respectively) in the whole group. The relationship between baseline muscle triglyceride and insulin resistance (HOMA-IR and fasting plasma insulin) was significant, although weaker ($r = 0.44$, $P = 0.05$; $r = 0.45$, $P < 0.05$, respectively).
vs. 35.8 ± 6.3 pmol/l, $P < 0.05$) and remained elevated throughout the study (Fig. 6B).

**Plasma lactate.** Fasting plasma lactate levels were similar in the control and diabetic groups (0.78 ± 0.08 vs. 0.82 ± 0.09 mmol/l). There was a significant increase from basal after the first meal (1.22 ± 0.17 vs. 1.34 ± 0.1 mmol/l, $P < 0.001$ and $P = 0.05$, respectively). Plasma lactate levels subsequently fell, but there was a further significant rise after the second meal ($1.56 ± 0.16$ vs. $1.40 ± 0.11$ mmol/l at 6 h, $P < 0.01$ both groups compared with 4 h; Fig. 7A). There was no significant difference between the two groups at any time point during the study.

![Graph A](image1)

![Graph B](image2)

![Graph C](image3)

![Graph D](image4)

**Fig. 3.** Postprandial changes in plasma TG (A), chylomicron (CM)-TG (B), TG-rich lipoprotein-triglyceride (TRL-TG; C), and cholesterol-rich lipoprotein-TG (CRL-TG; D) fractions in control and diabetic subjects.

![Graph A](image5)

![Graph B](image6)

![Graph C](image7)

![Graph D](image8)

**Fig. 4.** Postprandial $^{13}$C appearance in CM-TG (A), TRL-TG (B), and CRL-TG (C) fractions and increase in $^{13}$C atom percent excess (APE) in expired air (D) in control and diabetic subjects.
Plasma β-hydroxybutyrate. Mean fasting β-hydroxybutyrate levels were similar in both groups (72.5 ± 19 vs. 62.1 ± 6.9 μmol/l). There was a significant fall from basal after the first meal (3.1 ± 2.4 vs. 16.6 ± 2.2 μmol/l, P < 0.02, both groups). Plasma β-hydroxybutyrate levels were incompletely suppressed in the diabetic group and were significantly higher than in the control group throughout the postprandial period (P < 0.02) and remained higher after the overnight fast (P = 0.032; Fig. 7B).

Plasma glycerol. Mean fasting glycerol levels in the two groups were similar (55.3 ± 11 vs. 41.6 ± 5.6 μmol/l). There was a significant fall from basal after the first meal (16.5 ± 4.8 vs. 21.1 ± 3.6 μmol/l, P < 0.01, both groups), remaining suppressed throughout the day, and rising back to baseline levels after the overnight fast in both groups (Fig. 7C). There was no significant difference between the two groups at any time point during the study.

DISCUSSION

The active role of both liver and muscle in handling the postprandial tide of triglyceride has been demonstrated in humans for the first time. The noninvasive observations were possible under physiological conditions by use of novel 13C MRS methodology, a technique that holds great promise for the further investigation of conditions characterized by insulin resistance. We observed rapid incorporation of dietary fatty acids into liver triglyceride in the type 2 diabetic subjects, peak uptake being earlier (4 vs. 6 h) and almost 50% higher compared with control subjects. In skeletal muscle, peak uptake of fatty acids was sixfold greater in the diabetic group compared with the control group with retention of meal-derived fatty acids at 24 h. In contrast, there was minimal retention of meal-derived fatty acids at 24 h in muscle of the control subjects.

There have been no previous in vivo human studies on dietary fatty acid handling by liver, to our knowledge. Here, we show that there is rapid incorporation of dietary fatty acids into the hepatic triglyceride pool in both normal and diabetic subjects. After rapid uptake, the fatty acids appear to be rapidly displaced by subsequent unlabeled meals in both groups. This was associated with an increase in 13C appearance in the TRL-TG fraction in both groups, consistent with a precursor-product relationship. The rapid flux of fatty acids in and out of the liver suggests that the liver protects the body from excessive plasma triglyceride fluxes in the immediate postprandial period. These observations are in agreement with studies in rats by Bessesen et al. (2) and Li et al. (19), who also showed rapid postprandial uptake of dietary fatty acids into liver triglyceride using 14C-labeled oral fatty acids.

Hepatic triglyceride is a major determinant of insulin sensitivity, independent of body weight (29). Hepatic insulin sensitivity is improved dramatically by decreasing hepatic triglyceride content, as shown by thiazolidinedione treatment (20), transplantation of adipose tissue in fatless mice (9), and leptin treatment (32). Therefore, the presence of excess fatty acids in the intrahepatic pool during the postprandial period could underlie the slower rate of postprandial suppression of hepatic glucose output (30, 36) and the lower postprandial rates of hepatic glycogen storage observed in type 2 diabetes (17).

Calculations from arteriovenous difference studies have shown that the proportion of the triacylglycerol storage occur-
More strikingly, we found a sixfold increase in peak intramuscular triglyceride in control and diabetic groups, respectively. Storage in skeletal muscle (peak storage of \( \text{IMCL} \)) reflects a substantial increment in whole body triglyceride averaged 20 kg in healthy humans (39); hence, our observation of peak uptake in the liver. However, skeletal muscle mass by skeletal muscle in our study was small compared with the second meal, may relate to mobilization of enterocyte chylomicrons to simulate the day-to-day physiological situation and avoids assumptions inherent in studies using intravenous tracer infusions. Meal-derived fatty acids were observed to be incorporated rapidly into CM-TG and TRL-TG fractions in both groups. The peak of labeled CM-TG at 6 h, 1 h after the second meal, may relate to mobilization of enterocyte chylomicron stores following successive meals (26). The subsequent decrease is likely a consequence of the displacement of isotopic label with unlabeled triglyceride arising from subsequent meals together with tissue uptake. The TRL-TG, however, remained labeled throughout the 24-h period, indicating continuing export of labeled fatty acids from hepatic stores. The observed low level of labeling of the meal-derived NEFA pool.

The principle has been established that induction of increased fatty acid uptake, for instance by tissue-specific overexpression of lipoprotein lipase in skeletal muscle and liver, is followed secondarily by tissue-specific insulin resistance (16). The mechanisms behind the increased postprandial uptake of fatty acids into liver and skeletal muscle in diabetes must therefore be considered. It has been proposed that hyperglycemia attenuates fatty acid oxidation across the splanchnic region and results in increased hepatic accumulation of hepatic triglyceride (35). In the current study, increased hepatic triglyceride storage in diabetes was accompanied by similar rates of whole body lipid oxidation in both groups. There are no human data on rates of hepatic fatty acid oxidation in diabetes. The mechanism of the increased hepatic fatty acid uptake in diabetes is not immediately clear, and this warrants further investigation. However, basic information on skeletal muscle fatty acid transport in humans is in keeping with our observations. Bonen et al. (5), using giant sarcolemmal vesicles to study long-chain fatty acid (LCFA) transport, showed that skeletal muscle in obese and type 2 diabetes subjects has increased LCFA uptake compared with lean humans. The increased uptake was associated with increased skeletal muscle expression of fatty acid translocase/CD36 (5). This may partly explain the overall diabetes-associated increase in skeletal muscle fatty acid uptake as observed in our study. Other studies have reported decreased mitochondrial skeletal muscle oxidative capacity in insulin-resistant offspring of type 2 diabetes (25) and in type 2 diabetes (13). As these were direct studies of skeletal muscle, it is possible that there is a combined storage and oxidative defect in type 2 diabetes even though we observed no abnormality in whole body lipid oxidation of meal triglyceride.

Previously, intravenous fatty acid tracers (4, 12, 15) and chylomicron infusions (22) have been used to study lipid metabolism in humans. The behavior of intravenous lipid infusions is different from that of native chylomicrons. The use of intravenous fatty acid tracers to estimate fatty acid metabolism induces errors due to a lack of labeling of lipoprotein pools and a need for calculated correction factors (34). The oral fatty acid tracer used in this study achieves labeling of native chylomicrons to simulate the day-to-day physiological situation and avoids assumptions inherent in studies using intravenous tracer infusions. Meal-derived fatty acids were observed to be incorporated rapidly into CM-TG and TRL-TG fractions in both groups. The peak of labeled CM-TG at 6 h, 1 h after the second meal, may relate to mobilization of enterocyte chylomicron stores following successive meals (26). The subsequent decrease is likely a consequence of the displacement of isotopic label with unlabeled triglyceride arising from subsequent meals together with tissue uptake. The TRL-TG, however, remained labeled throughout the 24-h period, indicating continuing export of labeled fatty acids from hepatic stores. The observed low level of labeling of the meal-derived NEFA pool.
during the daytime period implies minimal net efflux of meal-derived fatty acids from tissue triglyceride stores while plasma insulin concentration is suprabasal. Conversely, NEFA labeling increased during the overnight fast in the presence of basal insulin levels, indicating lipolysis of stored meal-derived triglyceride. These results are in keeping with already published data on the fate of dietary fatty acid in postprandial lipoproteins (3, 11).

The hypothesis that the increased fatty acid uptake by liver and skeletal muscle may underlie the excess tissue triglyceride accretion seen in type 2 diabetes of the spectrum and precise measurement.

The novel 13C MRS protocol reported here make use of the effects of the carbon-carbon couplings. Homonuclear carbon multiplets are usually lost in the noise when 13C spectra of liver or muscle are recorded at natural abundance. The presence of labeled fatty acids in the liver or muscle triglyceride introduces new peaks due to 13C-13C coupling, since the intensity of the “satellite” signals are much higher than the normal 1.1% of the main singlet signal. The carbon-carbon couplings provide increased amplitude and increased width where there is overcrowding of signals (20–40 ppm) and result in high resolution of the spectrum and precise measurement.

In summary, our results suggest that the increased postprandial fatty acid uptake by liver and skeletal muscle may underlie the excess tissue triglyceride accretion seen in type 2 diabetes and may be a primary cause of insulin resistance for glucose metabolism.

The hypothesis that the increased fatty acid uptake may underlie the mitochondrial defect in ATP production can now be tested by examination of the earliest stages of glucose tolerance. Regulation of fatty acid uptake into liver and skeletal muscle may be a potential target in treatment and prevention of type 2 diabetes.

GRANTS

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REFERENCES


