Metabolic Response to a Ketogenic Breakfast in the Healthy Elderly

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Running Head: **Metabolic response to a ketogenic breakfast in the healthy elderly**

Abstract

Objective: To determine whether the metabolism of glucose or ketones differs in the healthy elderly compared to young or middle-aged adults during mild, short-term ketosis induced by a ketogenic breakfast.

Design and participants: Healthy subjects in three age groups (23±1, 50±1 and 76±2 y old) were given a ketogenic meal and plasma β-hydroxybutyrate, glucose, insulin, triacylglycerols, total cholesterol, non-esterified fatty acids and breath acetone were measured over the subsequent 6 h. Each subject completed the protocol twice in order to determine the oxidation of a tracer dose of both carbon-13 (^{13}C) glucose and ^{13}C-β-hydroxybutyrate. The tracers were given separately in random order. Apolipoprotein E genotype was also determined in all subjects.

Results: Plasma glucose decreased and β-hydroxybutyrate, acetone and insulin increased similarly over 6 h in all three groups after the ketogenic meal. There was no significant change in cholesterol, triacylglycerols or non-esterified fatty acids over the 6 h. ^{13}C-glucose and ^{13}C-β-hydroxybutyrate oxidation peaked at 2-3 h post-dose for all age groups. Cumulative ^{13}C-glucose oxidation over 24 h was significantly higher in the elderly but only versus the middle-aged group. There was no difference in cumulative ^{13}C-β-hydroxybutyrate oxidation between the three groups. Apolipoprotein E (ε4) was associated with elevated fasting cholesterol but was unrelated to the other plasma metabolites.

Conclusion: Elderly people in relatively good health have a similar capacity to produce ketones and to oxidize ^{13}C-β-hydroxybutyrate as middle-aged or young adults, but oxidize ^{13}C-glucose a little more rapidly than healthy middle-aged adults.

Keywords: ketones, glucose, healthy elderly, ^{13}C stable isotope tracers.

Introduction

In humans, glucose is the brain's primary energy substrate and ketone bodies (ketones) are it's primary replacement fuel during fasting or low carbohydrate intake (1). Ketones refers collectively to three molecules: acetoacetate (AcAc), β-hydroxybutyrate (β-OHB), and acetone (2). During ketogenesis, AcAc is formed first and is the only ketone metabolized by the tricarboxylic acid cycle as an energy substrate. After being converted back to AcAc by β-OHB dehydrogenase, β-OHB can also serve as an energy substrate (3). Acetone is produced by decarboxylation of AcAc and is exhaled in the breath in proportion to plasma ketone concentrations (2).

Impaired availability of energy substrates to the brain may be implicated in the progression towards Alzheimer's disease (4, 5). Raising blood ketones with a ketogenic meal shows preliminary potential to alleviate some features of the cognitive deficit in Alzheimer's disease (6). Given this potentially important clinical application, but the relative scarcity of information about how energy substrates are utilized during healthy aging, i.e. during aging minimally confounded by symptomatic degenerative disease, our primary objective was to evaluate glucose and ketone utilization in the healthy elderly compared to young and middle-aged adults.

Insulin inhibits ketone production so to achieve short-term ketogenesis subjects were given a very low carbohydrate breakfast composed of medium chain triacylglycerol (MCT), heavy cream, protein powder and water. MCT efficiently induce mild to moderate ketosis in humans (7) because they are rapidly absorbed and pass directly via the hepatic portal venous circulation to the liver where they are β-oxidized with some of the resulting acetyl CoA being captured in ketones. MCT do not require a carnitine-dependent transport system to enter the inner mitochondrial space, and are thus more readily available for oxidation and at a lower energetic cost than long

chain triacylglycerol (LCT) (8). Although the present study was not designed or powered for analysis of the effect of genotype, apolipoprotein E genotype of our subjects was determined since it affects both post-prandial fat metabolism (9) and risk of Alzheimer's disease (10, 11).

Materials and Methods

Subjects: Subjects were recruited in three age groups: 18-25 y old (young: Y), 40-55 y old (middle-aged: M), and 70-85 y old (elderly: E). This distribution maintained a minimum 15 y gap between age groups and also avoided the increasing impact of frailty beyond 85 y old (12). All subjects were non-smokers and determined to be in relatively good health by a medical evaluation and blood screening done after a 12 h overnight fast. Fasting glucose and hemoglobin HbA_{1c} were used to rule out the presence of overt diabetes. A complete blood cell count was used for blood disorders; electrolyte profile, AST and ALT for renal and liver function; HDL and LDL cholesterol, triglycerides; albumin for nutritional status; C-reactive protein as a marker of inflammatory processes; and TSH for thyroid function. Anthropometric parameters such as height, weight, body mass index (BMI), and fasting plasma metabolites did not differ significantly between age groups (**Table 1)**. Approval for the study was obtained from the Research Ethics Committee of the Health and Social Services Center – Sherbrooke University Geriatrics Institute, which oversees all human research done at the Research Center on Aging.

Tracer protocol and sample collection: Subjects arrived at 7:30 a.m. after having fasted overnight for 12 h. An intravenous forearm catheter was installed and baseline blood samples taken. The catheter was kept patent by flushing hourly with non-heparinized saline. The stable isotope tracer was then consumed (^{13}C-glucose or ^{13}C-β-OHB), followed immediately by the ketogenic breakfast drink, which was consumed within approximately 30 mins. After consuming the ketogenic breakfast, blood samples were taken hourly over 6 h using a 5 ml latex-free syringe (Becton Dickinson, Franklin Lakes, NJ) and transferred immediately to a 5 mL K_2-EDTA-

coated tube (Becton Dickinson, Franklin Lakes, NJ). Tubes were stored on ice at 4˚C until the conclusion of the study period at which point they were all centrifuged at 3500 rpm for 18 min at 4˚C. The separated plasma was stored at -20˚C until further analyzed. During the 6 h study period, water was available *ad libitum* and subjects were asked to remain in a resting position with short walks.

Each subject participated in two identical metabolic study days, one to test ^{13}C-glucose metabolism and the other to test ^{13}C-β-OHB metabolism. The tracers were U-$^{13}C_6$ D-glucose or 2,4-$^{13}C_2$ sodium D-3-hydroxybutyrate (50 mg each; Cambridge Isotope Laboratories, Andover, MA) were consumed in 15 mL nanopure water and in randomized order. The two study days were separated by at least one but not more than three weeks. Breath samples for $^{13}CO_2$ and acetone analysis were collected in triplicate at baseline and every 30 min afterwards using a breath collection device (Easysampler, Quintron Instrument Company, Milwaukee, WI) and 10 mL evacuated glass tubes (Exetainer, Labco Ltd, Buckinghamshire, UK). The first ~150 mL of exhaled air is dead space (13), so to collect a true alveolar breath sample, the subjects exhaled for 3 sec before breath sample collection. For acetone analysis, 1 mL of breath was transferred from one of the three Exetainer tubes to a glass gas-tight syringe (Hamilton Company, Reno, NV).

Ketogenic breakfast drink: The ketogenic breakfast drink consisted of a blend of MCT (Mead Johnson, Ottawa, ONT, CA), 35% heavy cream (Québon Ultra Crème, Longueuil, QC, CA), raspberry-flavored milk protein powder (Davisco Foods International, Inc., Eden Prairie, MN, courtesy of Agropur Cooperative, Granby, QC, CA) and water (**Table 2).** The fatty acid composition of the ketogenic breakfast is shown in **Table 3**. This ketogenic breakfast was designed to give a ratio of total fat to

protein plus carbohydrate of 4.5:1, which is sufficient to induce mild, short-term ketosis in young adults (2). The total carbohydrate content of the drink was limited to the carbohydrate already in the cream (3.2%). Total protein content was calculated to be 1/3 of the subject's daily protein requirement as determined by the Harris-Benedict equation and the Canada Food Guide (Health Canada, Ottawa, ON, CA). Total fat was then adjusted to be equivalent to 4.5 times the protein plus carbohydrate content. Subjects received an average of 1104 kCal, 90% of which was fat. In the breakfast drink, the amount of total fat (g), MCT (g), fat/body weight (g/kg), or fat/BMI (g/kg/m^2) did not differ significantly across the three study groups.

Isotope ratio mass spectrometry: Enrichment of ^{13}C in breath CO_2 following the ingestion of the ^{13}C tracer was analyzed by isotope ratio mass spectrometry (Europa 20-20, Sercon Ltd, Crewe, Cheshire, UK) as previously described (14). 5% CO_2/N_2 was the reference gas and He was the carrier gas (Praxair Canada Inc. Mississauga, ON, Canada). Atom percent (AP) is the relative abundance of ^{13}C in the sample calculated by the following equation:

(1)

$$AP = \frac{100}{1/[(\delta/1000 + 1)\ {}^{13}C_{ref} + 1]}$$

^{13}C data in delta notation (δ) is the ratio of ^{13}C to ^{12}C calibrated against the reference gas and the international standard, Peedee Belemnite (15). The percent dose recovered (PDR) of the tracer administered to the subjects was calculated as in equation (2),

(2)

$$PDR = \frac{APE \times VCO_2}{\text{mmol } {}^{13}\text{C-tracer administered}} \times 100\%$$

In which atom percent excess (APE) is calculated using of the value obtained in equation (1) for time t minus the value obtained at time 0. Taking into account the chemical purity, the isotopic enrichment of the tracer, and the natural abundance of ^{13}C, the quantity of ^{13}C excreted on breath (mmol) was calculated as shown in equation (3):

(3) $$\text{mmol } {}^{13}C = \frac{\text{mg tracer}}{\text{molecular weight}} \times \text{chemical purity} \times ([99\% \#{}^{13}C] + [1\% \text{ total } \# C])$$

The chemical purity of both tracers was 98% and their isotopic purity was 99%. The CO_2 production constant of 300 mmol/h was used as determined by Schofield (16) and previously validated for healthy adults (17). V_{CO2} was then calculated by multiplying the CO_2 production constant (300 mmol/h) by body surface area, calculated according to Gehan and George (18).

Gas chromatographic analysis of acetone: Triplicate 0.3 ml samples of breath collected into gastight syringes were injected directly on to a capillary gas chromatograph equipped with a flame ionization detector (Agilent model 6890, Palo Alto, CA) and 30 m DB-WAX column (0.25 mm i.d.; Agilent J&W Scientific Santa Clara, CA). The temperature of the oven was set at 30°C and held for one minute and then increased at a rate of 5°C/min to 60°C where it was held for 2 min. The carrier gas was He and the flow rate was 7 mL/min. The injector temperature was 150°C and the detector temperature was 250°C. Acetone peak areas were calibrated against an aqueous acetone standard. A 0.2 mL of the aqueous standard was then injected into the gas chromatograph.

Other analyses: Plasma glucose, β-OHB, cholesterol, triacylglycerols (TG), and non-esterified fatty acids (NEFA) were measured by colorimetric assay using an automated clinical chemistry analyzer (Dimension XPand Plus, Dade Behring Inc., Newark, DE) and commercially available reagent kits from the same company, except for β-OHB (RX Daytona kit; Randox Laboratories Ltd., Antrim, UK), and NEFA (Wako Diagnostics, Richmond, VA). Insulin was analyzed by ELISA (Mercodia, Upssala, Sweden) and a microplate reader (model 3550, BioRad, Hercules, CA). ApoE genotype was analyzed at the McGill University Center for Studies in Aging (19).

Fatty acid composition of the ketogenic breakfast, MCT, and cream was analyzed by extraction of the total lipids into 2:1 chloroform/methanol with 0.02% BHT, using triheptadecanoin as the internal standard (20). The total lipids were then saponified with 1 M methanolic KOH followed by derivitization of the fatty acids to fatty acid methyl esters using 14% BF_3 methanol. Fatty acid methyl esters were analyzed using a gas chromatograph (Agilent model 6890) equipped with a 50 m BPX-70 fused capillary column (0.25 mm i.d. x 0.25 µm film thickness; J&W Scientific, Folsom, CA). Splitless injection and flame ionization detection were performed at 250°C. The oven temperature program was 50°C for 2 min, increasing to 170°C at a rate of 20°C/min, held for 15 min, increased to 210°C at a rate of 5°C/min and held there for 7 min. The inlet pressure of the carrier gas (He) was 233 kPa at 50°C. The identity of individual fatty acids was determined by comparing retention times with standard mixtures of fatty acids (NuChek 68A, 411, 455; NuChek Prep, Inc., Elysian, MN) and a custom mixture of saturated fatty acid standards.

Statistical analysis: Results are given as mean ± SEM. Comparisons during the metabolic study period are shown from baseline (time 0 h; T_0) up to 6 h later (T_6), and again 24 h later (T_{24}) for tracer oxidation. To determine if tracer oxidation differed over time or between age groups, a repeated measures two-way ANOVA was performed followed by a Bonferroni *post-hoc* test to determine where significant differences existed. The Pearson test was used to test the significance of correlations between plasma and breath metabolites. Ketogenic breakfast composition was analyzed by one-way ANOVA. Statistical analysis of tracer oxidation data, differences in ketogenic meals composition and fatty acid profile between groups, and correlations were performed with Prism software (version 4.0, GraphPad Prism, San Diego, CA). An independent variables ANOVA test for time and age was performed to determine if any of the plasma metabolites differed between age groups or by ApoE ε4 genotype. Statistical analysis of plasma metabolites was performed with SPSS software (version 12.0, SPSS Inc, Chicago, IL). Significance was set at $p \leq 0.05$.

Results

Plasma and breath metabolites: From baseline (T_0) to 6 h after taking the ketogenic breakfast drink and tracer (T_6), plasma glucose was mostly stable in all three groups but between T_3 and T_6, glucose was 12% higher in the E compared to the Y group ($p< 0.05$; **Figure 1**). In all three groups, plasma insulin peaked at 90-105 pmol/L at T_1 to T_2. Except at T_2 in the M group, the M and E groups had a similar post-prandial insulin response to the Y group. Between T_0 and T_6 and in all three groups, plasma β-OHB rose from ~0.1 to ~1.3 mmol/L and breath acetone rose from ~13 to ~87 nmol/L (**Figure 1**). Breath acetone was higher at T_6 in the M and E groups versus the Y group. For all subjects, there was a significant positive correlation between plasma β-OHB and breath acetone at T_0 and T_6 (**Figure 2**).

^{13}C Tracer oxidation: In all subjects and with both tracers, $^{13}CO_2$ excretion on breath peaked at 2-4 h post-dose and returned close to baseline within 24 h of tracer administration. In all three age groups, ^{13}C-glucose oxidation peaked at 6.4 to 7.4 % dose/h between $T_{2.5}$ and T_3 (**Figure 3**). At $T_{4.5}$, T_5 and T_6, ^{13}C glucose oxidation was significantly higher in the E compared to the M group. Cumulative ^{13}C glucose oxidation 24 h after dosing was 72%, 62%, and 77% of dose for Y, M and E subjects, respectively (**Figure 3**). From T_5 to T_{24}, cumulative oxidation of ^{13}C glucose was significantly higher in the E versus M group ($P<0.05$), but not compared to the Y group. In all three groups, ^{13}C β-OHB oxidation peaked at ~7.5 % dose/h at T_2. Cumulative 24 h ^{13}C β-OHB oxidation was 65%, 74%, and 77% of the dose administered in Y, M and E subjects, respectively, with no significant differences between groups (**Figure 3**).

Other measurements: There was no significant effect of the ketogenic breakfast on plasma TG, NEFA, or total cholesterol over the 6 h study period (**Figure 4**). However, from T_3 to T_6, plasma TG and total cholesterol were significantly elevated in the E group compared to the Y group.

Genotype distribution could only be determined for 27 of the 31 subjects (**Table 4).** For statistical comparisons, genotypes were grouped according to presence or not of the ApoE ε4 allele. As expected, ε4 carriers had significantly elevated plasma cholesterol, but had no significant differences in other metabolites (data not shown).

Discussion

Overall, we found that for 6 h after consuming a ketogenic breakfast drink, elderly, middle-aged and young adults in good health had a comparable changes in plasma β-OHB and breath acetone. To our knowledge, previously published studies of ketone levels in the elderly have not reported their production after a ketogenic meal. For instance, higher plasma β-OHB was reported for the elderly, but only after an 18 h fast (21). Our study confirms the previously reported short term ketogenic effect of a very low carbohydrate breakfast (2), and shows that the healthy elderly achieve a level of ketosis (plasma β-OHB and breath acetone) and 24 h oxidation of β-OHB that is equivalent to or slightly above what is observed in healthy young and middle-aged subjects. In the absence of differences in plasma β-OHB or β-OHB oxidation, whether the doubling of breath acetone at the end of the 6 h metabolic study day is physiologically meaningful remains to be determined.

Our elderly group had statistically significant but very modest differences in glucose metabolism compared to the middle-aged our young adults. Although fasting glucose was not statistically different between the three groups, plasma glucose (but not insulin) was statistically higher in the elderly towards the end of the metabolic study period. Cumulative glucose oxidation over 24 h was 24% higher in the elderly but only versus the middle-aged group; the glucose oxidation did not differ significantly between the elderly and young groups. Without further experimentation, these data are difficult to interpret because although higher plasma glucose could be due to various mechanisms related to emerging insulin resistance, one would not expect a concomitant rise in glucose oxidation (Figure 3) if, in fact, glucose metabolism was impaired.

Statistically significant differences between age groups in cholesterol and TG also emerged 3-6 h after taking the breakfast meal. Issa et al. have also reported somewhat slower TG clearance after consuming a meal containing 40 g of fat (22). Several studies have suggested that slower post-prandial clearance of an oral fat load may contribute to aging-associated pathology such as coronary heart disease (23, 24) and may be influenced by declining insulin sensitivity (25-27). Post-prandially, the plasma cholesterol response of both the M and the E groups was elevated compared to the Y group. This could be attributed to the presence of four subjects in the M group who were ApoE ε4 carriers, as this polymorphism is known to elevate cholesterol levels (28). In fact, when the ε4 carriers were removed, cholesterol data for the M group fell between the Y and E groups (data not shown).

Although baseline plasma TG was non-significantly higher in the elderly, none of the subjects showed a significant post-prandial TG response between T_0 - T_6. Given that the ketogenic breakfast contained approximately 50% LCT (**Table 3**), a post-prandial increase in plasma TG would have been anticipated. Seaton et al. found that in comparison with LCT, there was no significant change in plasma TG and even a slight decrease during the first hour after a single dose of 48 g of MCT (29). Hill et al. observed an increase in fasting TG but no change over 6 h after giving a single dose of MCT following a 6 day diet in which MCT represented 40% of daily energy requirements (30). MCT are clearly absorbed differently from LCT but, in our study, it is still not clear whether MCT or the low carbohydrate content of the meal could have suppressed the plasma TG response to the LCT in the cream.

By design, the ketogenic breakfast given to our subjects was not strictly isoenergetic across groups. Rather, using the Harris-Benedict equation, the energy content of the ketogenic breakfast was calculated in terms of percentage of basal

energy needs, which takes into account several parameters including gender, age, and anthropometric parameters. Other methods to match meals across groups with different anthropometry include normalizing to only one parameter such as fat in the meal to body weight, BMI, or hip-to-waist ratio. Recent studies suggest a stronger relation of parameters such as insulin resistance to body fat mass rather than to age itself (31, 32). As such, determining % body fat distribution might have helped us more accurately compare subjects. Regardless, neither the calculated values for basal energy expenditure nor the total fat content (g), MCT content (g), fat content/body weight (g/kg), or fat content/BMI (g/kg/m^2) differed significantly between the three age groups ($P>0.05$).

Our main objective was to assess the short-term ketone response to a ketogenic breakfast during healthy aging and we conclude that the ability to produce ketones appears to be fully functional during healthy aging. Hence, these results support emerging strategies aiming to use physiological levels of ketones to correct or bypass deteriorating brain glucose uptake in the elderly.

Acknowledgements

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Table 1

Anthropometric characteristics and fasting plasma constituents.

	Young (n = 11)	Middle-aged (n = 12)	Elderly (n = 9)
Anthropometry:			
Age (y)	23 ± 1	50 ± 1	76 ± 2
Height (m)	1.74 ± 0.03	1.65 ± 0.03	1.67 ± 0.08
Weight (kg)	77.4 ± 4.9	74.2 ± 4.6	72.3 ± 3.7
BMI (kg/m^2)	25.3 ± 1.1	27.2 ± 1.6	25.7 ± 1.3
Fasting plasma measures:			
β-Hydroxybutyrate (mmol/L)	0.07 ± 0.10	0.09 ± 0.13	0.07 ± 0.04
Glucose (mmol/L)	5.4 ± 0.6	5.3 ± 0.4	5.7 ± 0.7
Insulin (mUI/L)	6.8 ± 4.4	4.5 ± 3.9	4.0 ± 2.6
Triacylglycerol (mmol/L)	0.9 ± 0.3	1.1 ± 0.5	1.5 ± 0.5
Non-esterified fatty acids (mmol/L)	0.6 ± 0.3	0.5 ± 0.1	0.6 ± 0.2
Cholesterol (mmol/L)	4.2 ± 0.4	5.3 ± 1.1	5.3 ± 0.7

Mean ± SEM. No significant difference in any parameter except age ($P<0.0001$).

Table 2

Ketogenic breakfast meal composition[1]

	(g)	(%)
Components:		
protein powder	25 ± 1	10
cream	100 ± 0	41
medium chain triacylglycerol	71 ± 4	29
water	46 ± 2	20
Macronutrients:		
protein	25 ± 1	18
carbohydrate	3 ± 0	2
fat	110 ± 4	80

[1] Calculated to give a ratio of 4.5:1 parts fat to protein plus carbohydrates based on 1/3 of the subject's daily protein requirements according to basal energy expenditure. Meal components and macronutrients are given as mean ± SEM (n = 32). Meal content did not differ significantly between age groups.

Table 3

Fatty acid composition (%) of the ketogenic breakfast and its fat components[1]

	Breakfast n = 32	MCT n = 3	Cream n = 3
8:0	14.4 ± 1.5	39.8 ± 0.4	N/D
10:0	31.3 ± 0.8	58.6 ± 0.3	5.9 ± 0.1
12:0	4.0 ± 0.1	1.6 ± 0.1	8.9 ± 0.1
14:0	9.8 ± 0.4	N/D	21.9 ± 0.2
16:0	20.4 ± 0.7	N/D	31.9 ± 0.1
18:0	4.9 ± 0.3	N/D	6.5 ± 0.2
Total Saturates	**84.7 ± 1.3**	**100.0 ± 0**	**75.0 ± 0.2**
14:1n-5	1.3 ± 0.6	N/D	2.3 ± 0.0
16:1n-7	1.0 ± 0.1	N/D	2.4 ± 0.1
18:1n-9	11.0 ± 0.6	N/D	18.1 ± 0.2
Total Monounsaturates	**14.0 ± 0.6**	**N/D**	**22.8 ± 0.2**
18:2n-6	1.1 ± 0.2	N/D	2.3 ± 0.1
Total Polyunsaturates	**1.1 ± 0.2**	**N/D**	**2.3 ± 0.1**

[1] Meal composition, given as mean ± SEM. Meal energy content did not differ significantly between age groups. N/D = not detected.

Table 4.

Apolipoprotein E genotype of the subjects.

	2/2	3/2	3/3	4/3	4/4	4/2	total
Young	0	4	5	0	0	0	9
Middle-aged	1	3	3	3	0	1	11
Elderly	0	0	6	1	0	0	7
% Frequency	4	26	51	15	0	4	100

Apolipoprotein E genotype is shown as the combinations of Apolipoprotein E ε 2, 3, or 4 variant alleles.

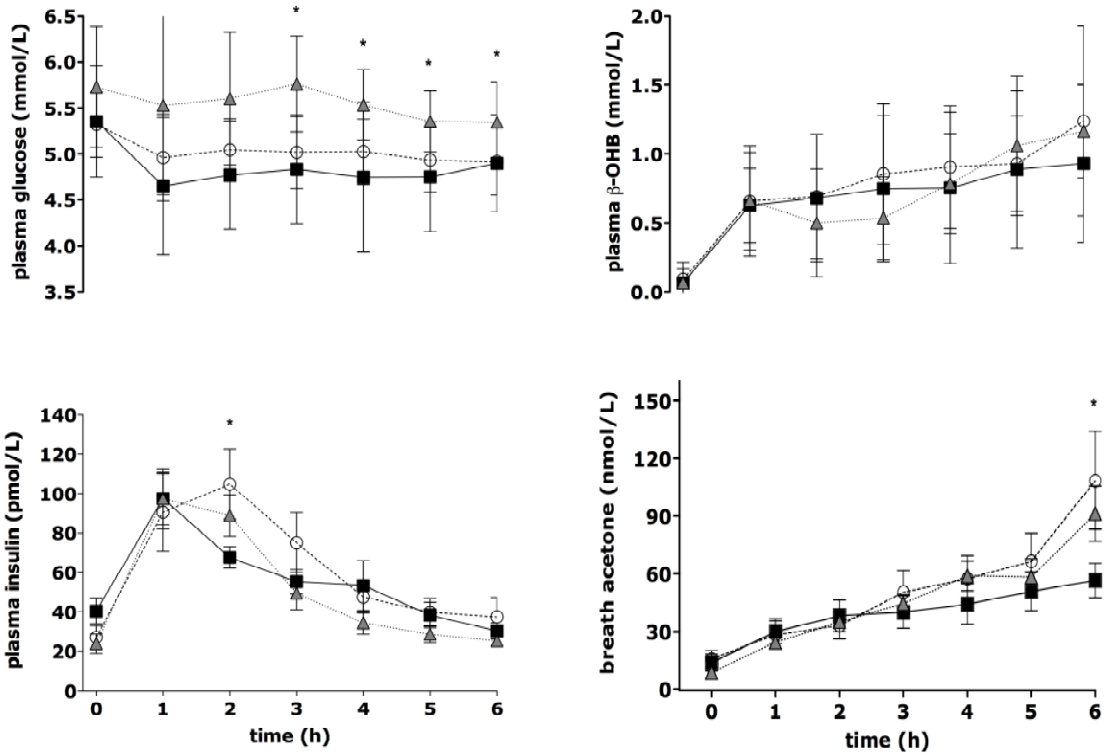
plasma glucose (mmol/L)
6.5
6.0
5.5
5.0
4.5
4.0
3.5
plasma β-OHB (mmol/L)
2.0
1.5
1.0
0.5
0.0
plasma insulin (pmol/L)
140
120
100
80
60
40
20
0
breath acetone (nmol/L)
150
120
90
60
30
0
0 1 2 3 4 5 6
time (h)
*

Figure 1.

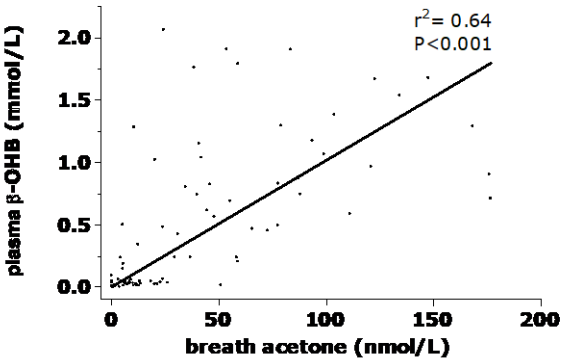
r^2= 0.64
P<0.001
plasma β-OHB (mmol/L)
2.0
1.5
1.0
0.5
0.0
0
50
100
150
200
breath acetone (nmol/L)

Figure 2.

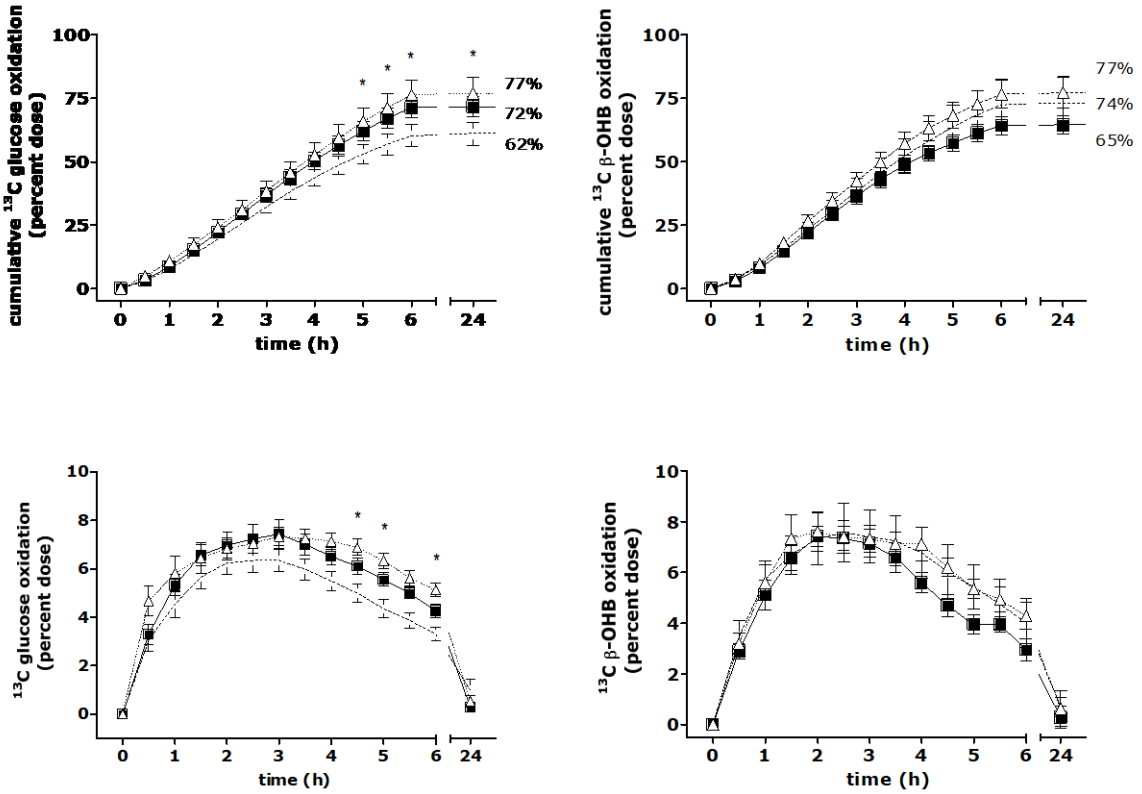
cumulative ^{13}C glucose oxidation (percent dose)
100
75
50
25
0
0 1 2 3 4 5 6 24
time (h)
77%
72%
62%
cumulative ^{13}C β-OHB oxidation (percent dose)
77%
74%
65%
^{13}C glucose oxidation (percent dose)
10
8
6
4
2
0
^{13}C β-OHB oxidation (percent dose)

Figure 3.

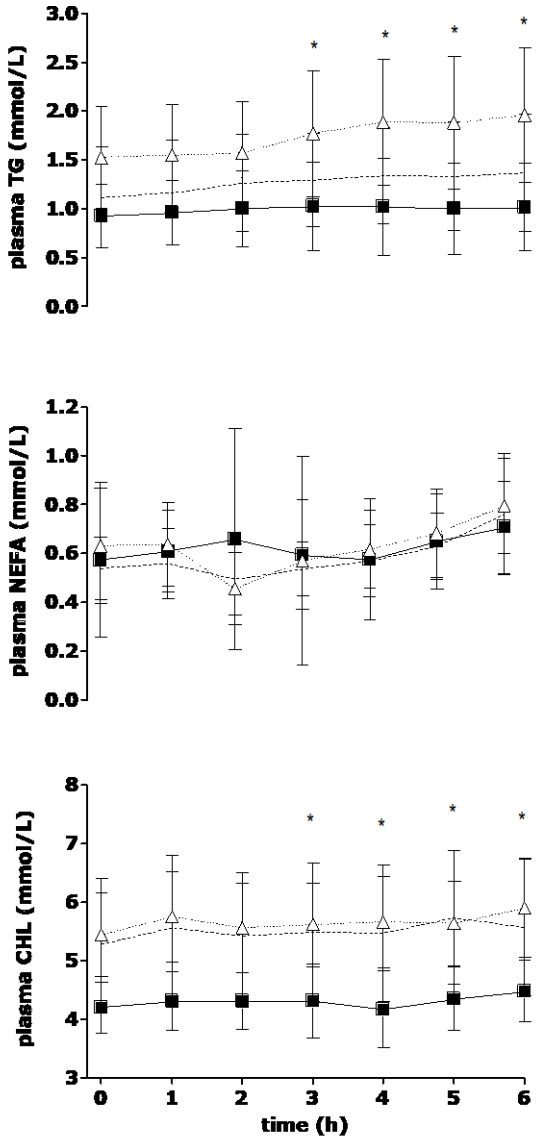
plasma TG (mmol/L)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
plasma NEFA (mmol/L)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
plasma CHL (mmol/L)
8
7
6
5
4
3
0
1
2
3
4
5
6
time (h)

Figure 4.

Figure Legends

Figure 1.

Plasma glucose (upper left), insulin (lower left), β-hydroxybutyrate (upper right), and breath acetone (lower right) over 6 h following consumption of a ketogenic breakfast at time 0 (mean ± SEM; *P<0.05). Symbols represent young (■), middle-aged (○) and elderly (▲) subjects.

Figure 2.

Correlation between breath acetone and plasma β-hydroxybutyrate before and 6 h after consuming a ketogenic breakfast.

Figure 3.

Oxidation of ^{13}C glucose (lower left - % dose/h; upper left – cumulative oxidation/24 h) and ^{13}C β-hydroxybutyrate (lower right - % dose/h; upper right – cumulative oxidation/24 h) following consumption of a ketogenic breakfast and the respective tracer at time 0 (mean ± SEM; *P<0.05). Symbols represent young (■), middle-aged (○) and elderly (▲) subjects.

Figure 4.

Plasma triacylglycerols (TG), non-esterified fatty acids (NEFA), and cholesterol (CHL) over 6 h following consumption of a ketogenic breakfast at time 0. Symbols represent young (■), middle-aged (○) and elderly (▲) subjects (mean ± SEM; *P<0.05).

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