

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**

2 **Abstract**

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

6 **Design and participants:** Healthy subjects in three age groups (23±1, 50±1 and
7 76±2 y old) were given a ketogenic meal and plasma β -hydroxybutyrate, glucose,
8 insulin, triacylglycerols, total cholesterol, non-esterified fatty acids and breath acetone
9 were measured over the subsequent 6 h. Each subject completed the protocol twice
10 in order to determine the oxidation of a tracer dose of both carbon-13 (^{13}C) glucose
11 and ^{13}C - β -hydroxybutyrate. The tracers were given separately in random order.
12 Apolipoprotein E genotype was also determined in all subjects.

13 **Results:** Plasma glucose decreased and β -hydroxybutyrate, acetone and insulin
14 increased similarly over 6 h in all three groups after the ketogenic meal. There was
15 no significant change in cholesterol, triacylglycerols or non-esterified fatty acids over
16 the 6 h. ^{13}C -glucose and ^{13}C - β -hydroxybutyrate oxidation peaked at 2-3 h post-dose
17 for all age groups. Cumulative ^{13}C -glucose oxidation over 24 h was significantly
18 higher in the elderly but only versus the middle-aged group. There was no difference
19 in cumulative ^{13}C - β -hydroxybutyrate oxidation between the three groups.

20 Apolipoprotein E ($\epsilon 4$) was associated with elevated fasting cholesterol but was
21 unrelated to the other plasma metabolites.

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

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

26

27 **Introduction**

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

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

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

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

56

57 **Materials and Methods**

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

73

74 *Tracer protocol and sample collection:* Subjects arrived at 7:30 a.m. after having
75 fasted overnight for 12 h. An intravenous forearm catheter was installed and baseline
76 blood samples taken. The catheter was kept patent by flushing hourly with non-
77 heparinized saline. The stable isotope tracer was then consumed (¹³C-glucose or
78 ¹³C-β-OHB), followed immediately by the ketogenic breakfast drink, which was
79 consumed within approximately 30 mins. After consuming the ketogenic breakfast,
80 blood samples were taken hourly over 6 h using a 5 ml latex-free syringe (Becton
81 Dickinson, Franklin Lakes, NJ) and transferred immediately to a 5 mL K₂-EDTA-

82 coated tube (Becton Dickinson, Franklin Lakes, NJ). Tubes were stored on ice at 4°C
83 until the conclusion of the study period at which point they were all centrifuged at
84 3500 rpm for 18 min at 4°C. The separated plasma was stored at -20°C until further
85 analyzed. During the 6 h study period, water was available *ad libitum* and subjects
86 were asked to remain in a resting position with short walks.

87 Each subject participated in two identical metabolic study days, one to test
88 ¹³C-glucose metabolism and the other to test ¹³C-β-OHB metabolism. The tracers
89 were U-¹³C₆ D-glucose or 2,4-¹³C₂ sodium D-3-hydroxybutyrate (50 mg each;
90 Cambridge Isotope Laboratories, Andover, MA) were consumed in 15 mL nanopure
91 water and in randomized order. The two study days were separated by at least one
92 but not more than three weeks. Breath samples for ¹³CO₂ and acetone analysis were
93 collected in triplicate at baseline and every 30 min afterwards using a breath
94 collection device (Easysampler, Quintron Instrument Company, Milwaukee, WI) and
95 10 mL evacuated glass tubes (Exetainer, Labco Ltd, Buckinghamshire, UK). The first
96 ~150 mL of exhaled air is dead space (13), so to collect a true alveolar breath
97 sample, the subjects exhaled for 3 sec before breath sample collection. For acetone
98 analysis, 1 mL of breath was transferred from one of the three Exetainer tubes to a
99 glass gas-tight syringe (Hamilton Company, Reno, NV).

100

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

107 protein plus carbohydrate of 4.5:1, which is sufficient to induce mild, short-term
 108 ketosis in young adults (2). The total carbohydrate content of the drink was limited to
 109 the carbohydrate already in the cream (3.2%). Total protein content was calculated to
 110 be 1/3 of the subject's daily protein requirement as determined by the Harris-Benedict
 111 equation and the Canada Food Guide (Health Canada, Ottawa, ON, CA). Total fat
 112 was then adjusted to be equivalent to 4.5 times the protein plus carbohydrate
 113 content. Subjects received an average of 1104 kCal, 90% of which was fat. In the
 114 breakfast drink, the amount of total fat (g), MCT (g), fat/body weight (g/kg), or fat/BMI
 115 (g/kg/m²) did not differ significantly across the three study groups.

116

117 *Isotope ratio mass spectrometry:* Enrichment of ¹³C in breath CO₂ following the
 118 ingestion of the ¹³C tracer was analyzed by isotope ratio mass spectrometry (Europa
 119 20-20, Sercon Ltd, Crewe, Cheshire, UK) as previously described (14). 5% CO₂/N₂
 120 was the reference gas and He was the carrier gas (Praxair Canada Inc. Mississauga,
 121 ON, Canada). Atom percent (AP) is the relative abundance of ¹³C in the sample
 122 calculated by the following equation:

123 (1)

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

124

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

129 (2)

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

130

131 In which atom percent excess (APE) is calculated using of the value obtained in
132 equation (1) for time t minus the value obtained at time 0. Taking into account the
133 chemical purity, the isotopic enrichment of the tracer, and the natural abundance of
134 ^{13}C , the quantity of ^{13}C excreted on breath (mmol) was calculated as shown in
135 equation (3):

$$136 \quad (3) \quad \text{mmol } ^{13}\text{C} = \frac{\text{mg tracer}}{\text{molecular weight}} \times \text{chemical purity} \times ([99\% \#^{13}\text{C}] + [1\% \text{ total } \# \text{C}])$$

137

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

143

144 *Gas chromatographic analysis of acetone:* Triplicate 0.3 ml samples of breath
145 collected into gastight syringes were injected directly on to a capillary gas
146 chromatograph equipped with a flame ionization detector (Agilent model 6890, Palo
147 Alto, CA) and 30 m DB-WAX column (0.25 mm i.d.; Agilent J&W Scientific Santa
148 Clara, CA). The temperature of the oven was set at 30°C and held for one minute
149 and then increased at a rate of 5°C/min to 60°C where it was held for 2 min. The
150 carrier gas was He and the flow rate was 7 mL/min. The injector temperature was
151 150°C and the detector temperature was 250°C. Acetone peak areas were calibrated
152 against an aqueous acetone standard. A 0.2 mL of the aqueous standard was then
153 injected into the gas chromatograph.

154

155 *Other analyses:* Plasma glucose, β -OHB, cholesterol, triacylglycerols (TG), and non-
156 esterified fatty acids (NEFA) were measured by colorimetric assay using an
157 automated clinical chemistry analyzer (Dimension XPand Plus, Dade Behring Inc.,
158 Newark, DE) and commercially available reagent kits from the same company,
159 except for β -OHB (RX Daytona kit; Randox Laboratories Ltd., Antrim, UK), and NEFA
160 (Wako Diagnostics, Richmond, VA). Insulin was analyzed by ELISA (Merckodia,
161 Upssala, Sweden) and a microplate reader (model 3550, BioRad, Hercules, CA).
162 ApoE genotype was analyzed at the McGill University Center for Studies in Aging
163 (19).

164 Fatty acid composition of the ketogenic breakfast, MCT, and cream was
165 analyzed by extraction of the total lipids into 2:1 chloroform/methanol with 0.02%
166 BHT, using triheptadecanoin as the internal standard (20). The total lipids were then
167 saponified with 1 M methanolic KOH followed by derivitization of the fatty acids to
168 fatty acid methyl esters using 14% BF_3 methanol. Fatty acid methyl esters were
169 analyzed using a gas chromatograph (Agilent model 6890) equipped with a 50 m
170 BPX-70 fused capillary column (0.25 mm i.d. x 0.25 μm film thickness; J&W Scientific,
171 Folsom, CA). Splitless injection and flame ionization detection were performed at
172 250°C. The oven temperature program was 50°C for 2 min, increasing to 170°C at a
173 rate of 20°C/min, held for 15 min, increased to 210°C at a rate of 5°C/min and held
174 there for 7 min. The inlet pressure of the carrier gas (He) was 233 kPa at 50°C. The
175 identity of individual fatty acids was determined by comparing retention times with
176 standard mixtures of fatty acids (NuChek 68A, 411, 455; NuChek Prep, Inc., Elysian,
177 MN) and a custom mixture of saturated fatty acid standards.

178

179 *Statistical analysis:* Results are given as mean \pm SEM. Comparisons during the
180 metabolic study period are shown from baseline (time 0 h; T₀) up to 6 h later (T₆), and
181 again 24 h later (T₂₄) for tracer oxidation. To determine if tracer oxidation differed over
182 time or between age groups, a repeated measures two-way ANOVA was performed
183 followed by a Bonferroni *post-hoc* test to determine where significant differences
184 existed. The Pearson test was used to test the significance of correlations between
185 plasma and breath metabolites. Ketogenic breakfast composition was analyzed by
186 one-way ANOVA. Statistical analysis of tracer oxidation data, differences in ketogenic
187 meals composition and fatty acid profile between groups, and correlations were
188 performed with Prism software (version 4.0, GraphPad Prism, San Diego, CA). An
189 independent variables ANOVA test for time and age was performed to determine if
190 any of the plasma metabolites differed between age groups or by ApoE ϵ 4 genotype.
191 Statistical analysis of plasma metabolites was performed with SPSS software
192 (version 12.0, SPSS Inc, Chicago, IL). Significance was set at $p \leq 0.05$.
193
194

195 **Results**

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

206

207 *^{13}C Tracer oxidation:* In all subjects and with both tracers, $^{13}\text{CO}_2$ excretion on breath
208 peaked at 2-4 h post-dose and returned close to baseline within 24 h of tracer
209 administration. In all three age groups, ^{13}C -glucose oxidation peaked at 6.4 to 7.4 %
210 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
211 significantly higher in the E compared to the M group. Cumulative ^{13}C glucose
212 oxidation 24 h after dosing was 72%, 62%, and 77% of dose for Y, M and E subjects,
213 respectively (**Figure 3**). From T_5 to T_{24} , cumulative oxidation of ^{13}C glucose was
214 significantly higher in the E versus M group ($P < 0.05$), but not compared to the Y
215 group. In all three groups, ^{13}C β -OHB oxidation peaked at ~ 7.5 % dose/h at T_2 .
216 Cumulative 24 h ^{13}C β -OHB oxidation was 65%, 74%, and 77% of the dose
217 administered in Y, M and E subjects, respectively, with no significant differences
218 between groups (**Figure 3**).

219

220 *Other measurements:* There was no significant effect of the ketogenic breakfast on
221 plasma TG, NEFA, or total cholesterol over the 6 h study period (**Figure 4**). However,
222 from T₃ to T₆, plasma TG and total cholesterol were significantly elevated in the E
223 group compared to the Y group.

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

229

230 **Discussion**

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

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

254 Statistically significant differences between age groups in cholesterol and TG
255 also emerged 3-6 h after taking the breakfast meal. Issa et al. have also reported
256 somewhat slower TG clearance after consuming a meal containing 40 g of fat (22).
257 Several studies have suggested that slower post-prandial clearance of an oral fat
258 load may contribute to aging-associated pathology such as coronary heart disease
259 (23, 24) and may be influenced by declining insulin sensitivity (25-27). Post-
260 prandially, the plasma cholesterol response of both the M and the E groups was
261 elevated compared to the Y group. This could be attributed to the presence of four
262 subjects in the M group who were ApoE ϵ 4 carriers, as this polymorphism is known to
263 elevate cholesterol levels (28). In fact, when the ϵ 4 carriers were removed,
264 cholesterol data for the M group fell between the Y and E groups (data not shown).

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

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

279 energy needs, which takes into account several parameters including gender, age,
280 and anthropometric parameters. Other methods to match meals across groups with
281 different anthropometry include normalizing to only one parameter such as fat in the
282 meal to body weight, BMI, or hip-to-waist ratio. Recent studies suggest a stronger
283 relation of parameters such as insulin resistance to body fat mass rather than to age
284 itself (31, 32). As such, determining % body fat distribution might have helped us
285 more accurately compare subjects. Regardless, neither the calculated values for
286 basal energy expenditure nor the total fat content (g), MCT content (g), fat
287 content/body weight (g/kg), or fat content/BMI (g/kg/m²) differed significantly between
288 the three age groups (P>0.05).

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

294

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301 Desgagné, Doris Dea, and Mary Ann Ryan for their excellent technical assistance.

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 composition¹

	(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 3Fatty acid composition (%) of the ketogenic breakfast and its fat components¹

	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.

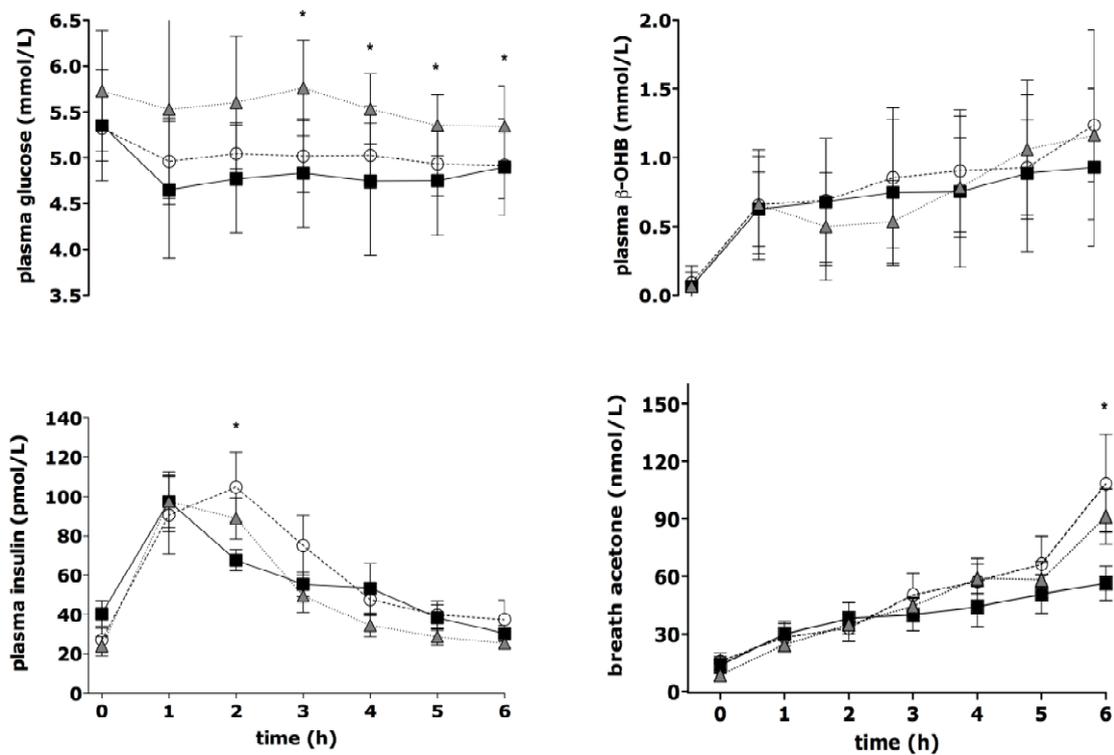


Figure 1.

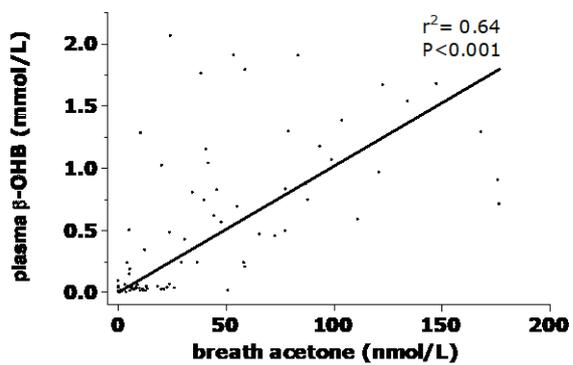


Figure 2.

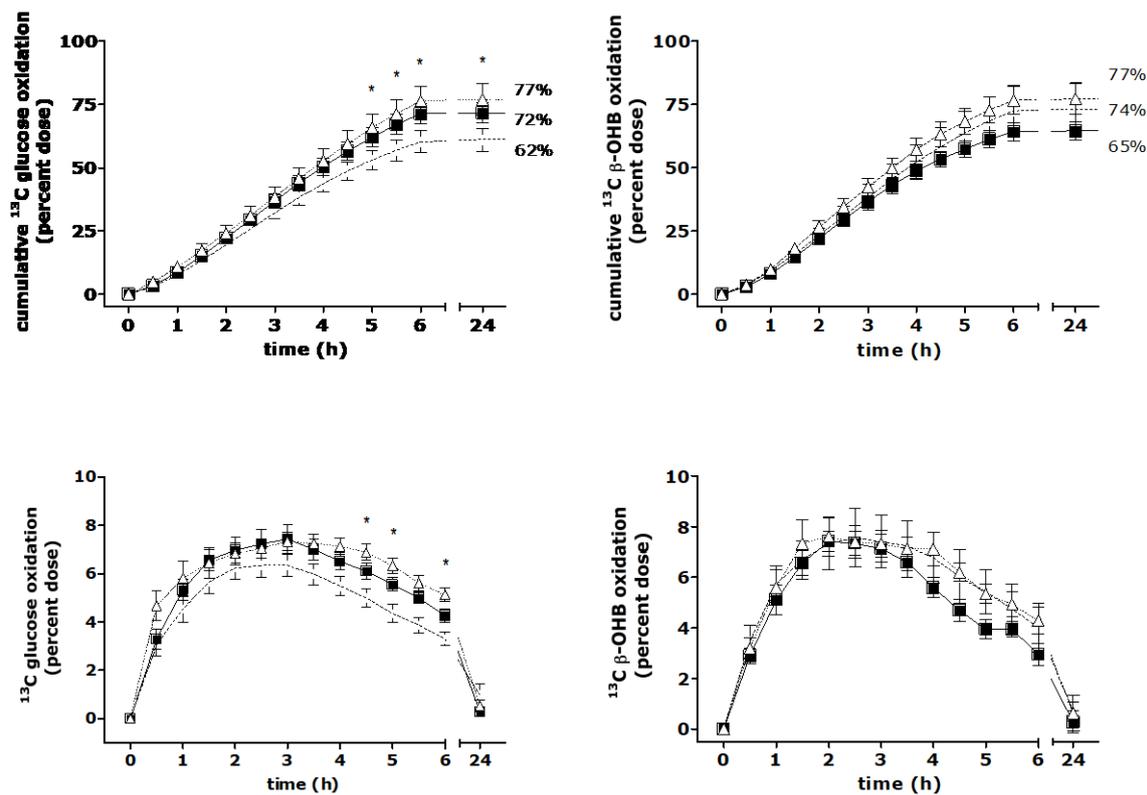


Figure 3.

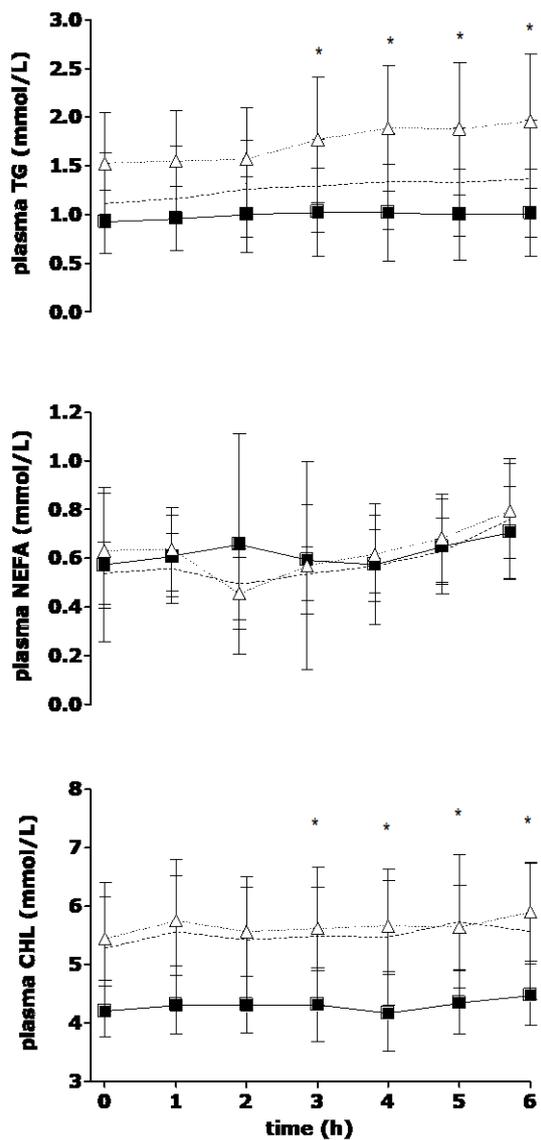


Figure 4.

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 \pm 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 \pm 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 \pm SEM; * P <0.05).

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