Table 1 Effects of 10-wk intervention with EPA and α -lipoic acid on anthropometry, body composition, RMR, energy intake and energy balance 1

	Control	Control EPA	α-lipoic acid	EPA + α-lipoic acid	Tv	vo-way Al	NOVA ⁸
N	22	18	20	17	EPA	α- lipoic	EPA x α-lipoic
Age (years)	39 ± 8	38 ± 8	38 ± 7	39 ± 7	ns	ns	ns
Body weight (Kg)							
Before	84.6 ± 14.4	88.4 ± 10.9	83.5 ± 11.4	84.9 ± 13.6	ns	ns	ns
Change	-5.2 ± 2.7^2	-5.4 ± 1.9^2	-7.0 ± 3.1^2	-6.5 ± 3.6^2	ns	0.032	ns
Waist circumference (cm)							
Before	99.1 ± 14.5	101.4 ± 7.3	95.6 ± 8.9	97.5 ± 9.0	ns	ns	ns
Change	-5.3 ± 2.5^2	-6.6 ± 3.4^2	-6.2 ± 3.3^2	-6.3 ± 3.0^2	ns	ns	ns
Hip circumference (cm)							
Before	115.4 ± 9.6	117.7 ± 8.1	115.0 ± 9.1	114.8 ± 8.6	ns	ns	ns
Change	-4.3 ± 2.4^2	-3.6 ± 1.7^2	-5.5 ± 2.5^2	-5.3 ± 2.7^2	ns	0.010	ns
Adjusted change ⁵	-4.9 (0.3)	-4.0 (0.3)	-4.8 (0.3)	-5.0 (0.3)	ns	ns	ns
Waist to hip ratio							
Before	0.85 ± 0.08	0.86 ± 0.06	0.83 ± 0.07	0.85 ± 0.06	ns	ns	ns
Change	-0.014 ± 0.02^3	-0.033 ± 0.026^2	-0.015 ± 0.021^3	-0.018 ± 0.020^3	0.032	ns	ns
Adjusted change ⁵	-0.015 (0.004)	-0.033 (0.005)	-0.014 (0.004)	-0.017 (0.005)	0.028	ns	ns
Fat mass (Kg)							
Before	39.1 ± 9.3	41.2 ± 5.8	38.6 ± 8.7	39.3 ± 8.7	ns	ns	ns

Android fat (%)							
Before	57.1 ± 5.3	57.1 ± 5.1	56.1 ± 6.2	57.3 ± 6.1	ns	ns	ns
Change	-3.2 ± 2.7^2	-3.7 ± 2.4^2	-4.7 ± 3.1^2	-4.7 ± 3.5^2	ns	ns	ns
Gynoid fat (%)							
Before	57.0 ± 4.7	57.6 ± 3.8	58.0 ± 4.2	56.6 ± 4.0	ns	ns	ns
Change	-2.1 ± 1.8^2	-2.3 ± 1.4^2	-3.0 ± 1.9^2	-3.2 ± 2.3^2	ns	0.039	ns
Adjusted change ⁵	-2.3 (0.4)	-2.5 (0.4)	-2.7 (0.4)	-3.1 (0.4)	ns	ns	ns
Android/Gynoid ratio							
Before	1.00 ± 0.11	0.99 ± 0.09	0.97 ± 0.09	1.01 ± 0.09	ns	ns	ns
Change	-0.02 ± 0.04^4	-0.03 ± 0.04^3	-0.03 ± 0.04^3	-0.03 ± 0.05^4	ns	ns	ns
$RMR (KJ/d)^6$							
Before	6576 (139)	6866 (164)	6479 (150)	6501 (154)	ns	ns	ns
Change	$-399.2(37.6)^2$	-305.0 (44.5) ²	-448.8 (40.6) ²	-370.3 (41.8) ²	0.039	ns	ns
Adjusted change ⁵	-416.2 (34.6)	-327.5 (41.0)	-421.2 (37.8)	-358.7 (38.3)	0.049	ns	ns
Energy intake (KJ/d)							
Before	7650 ± 1178	9072 ± 1865	8485 ± 2617	8346 ± 1704	ns	ns	ns
Change	-2543.6 ± 1713.2^2	-3693.2 ± -1887.3^{2}	-2731.6 ± 2594.0^2	-3045.1 ± 2056.8^2	ns	ns	ns
Adjusted change ⁷	-3201.0 (260.3)	-3029.0 (282.8)	-2612.9 (269.8)	-3055.5 (287.0)	ns	ns	ns

 $^{^{1}}$ Means \pm SDs (all unadjusted such values). EPA, eicosapentaenoic acid; RMR, resting metabolic rate. For all secondary outcomes the *P*-values were adjusted by the Benjamini-Hochberg multiple-testing correction (16). Data from all subjects for whom baseline and follow-up measurements were available were included.

^{2,3,4}Significantly different from baseline (paired samples t test): ${}^{2}P < 0.001 {}^{3}P < 0.01 {}^{4}P < 0.05$.

^{5,6,7}Means (SEMs): ⁵adjusted for the changes in body weight; ⁶adjusted by the age and lean mass; ⁷adjusted by energy intake at baseline.

 $^{^{8}}$ Differences between groups at baseline and in changes (10 wk – before) were evaluated by 2-way ANOVA (P < 0.05; ns, non-significant). No significant differences between groups were found in secondary outcomes after the adjustment by Benjamini-Hochberg.

Table 2 Effects of 10-wk intervention with EPA and α-lipoic acid on glucose metabolism, β-hydroxybutyrate, leptin and ghrelin¹

	Control	EPA	α-lipoic acid	EPA + α-lipoic acid	T'wo_v		-way ANOVA ¹¹	
N	21	16	19	17	EPA	α-lipoic acid	EPA x α-lipoic	
Glucose (mmol/L)								
Before	5.0 ± 0.4	5.0 ± 0.3	5.0 ± 0.4	5.2 ± 0.5	ns	ns	ns	
Change	$-0.23 \pm 0.31^{3,a,b}$	-0.04 ± 0.28^{a}	-0.04 ± 0.32^{a}	$-0.25 \pm 0.26^{3,b}$	ns	ns	0.005*	
Adjusted change ^{8,9}	$-0.25 (0.06)^{a,b}$	-0.06 (0.07) ^a	-0.01 (0.07) ^a	-0.23 (0.07) ^b	ns	ns	0.004*	
Insulin (pmol/L)								
Before	52.6 ± 47.0	42.4 ± 29.4	43.4 ± 18.9	62.3 ± 53.4	ns	ns	ns	
Change	-17.5 ± 31.7^6	-3.4 ± 34.6	-12.7 ± 20.2^7	-22.6 ± 21.8^{5}	ns	ns	ns	
HOMA-IR								
Before	1.89 ± 1.78	1.55 ± 1.11	1.54 ± 0.68	2.36 ± 2.06	ns	ns	ns	
Change	-0.67 ± 1.24^6	-0.13 ± 1.28	-0.46 ± 0.70^6	-0.92 ± 0.85^5	ns	ns	0.047	
Adjusted change ⁸	-0.68 (0.23)	-0.14 (0.26)	-0.44 (0.24)	-0.91 (0.26)	ns	ns	0.047	
Adjusted change ⁸ , ⁹	-0.66 (0.15)	-0.34 (0.17)	-0.53 (0.15)	-0.63 (0.16)	ns	ns	ns	
β -hydroxybutyrate (mmol/L)								
Before	0.36 ± 0.25	0.27 ± 0.23	0.38 ± 0.22	0.32 ± 0.31	ns	ns	ns	
Change	-0.08 ± 0.25	0.16 ± 0.38	-0.02 ± 0.30	0.08 ± 0.38	0.033	ns	ns	
Adjusted change ⁸	-0.05 (0.07)	0.18 (0.08)	-0.06 (0.07)	0.06 (0.07)	0.018	ns	ns	
Leptin (ng/mL)								
Before	23.6 ± 7.6	21.7 ± 8.0	22.5 ± 10.0	20.4 ± 7.0	ns	ns	ns	
Change	-6.4 ± 6.4^2	-0.9 ± 5.2	-8.7 ± 8.3^2	-3.5 ± 5.4^4	0.0009*	ns	ns	
Adjusted change ⁸	-7.2 (1.2)	-1.8 (1.4)	-7.6 (1.3)	-2.9 (1.3)	0.0003*	ns	ns	
Ghrelin (ng/mL)								
Before	230.1 ± 103.3	251.2 ± 98.0	240.8 ± 136.3	170.1 ± 91.3	ns	ns	ns	
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Change	15.2 ± 117.5	11.4 ± 79.9	8.8 ± 76.7	56.7 ± 56.4^3	ns	ns	ns
Adjusted change ^{8,10}	18.3 (17.9)	21.6 (21.4)	13.0 (19.0)	38.2 (21.1)	ns	ns	ns

 $^{^{1}}$ Means \pm SDs (all unadjusted such values). EPA, eicosapentaenoic acid. For all secondary outcomes the *P*-values were adjusted by the Benjamini-Hochberg multiple-testing correction (16).

^{2,3,4}Significantly different from baseline in normally distributed samples (paired samples t test): ${}^{2}P < 0.001 {}^{3}P < 0.01 {}^{4}P < 0.05$.

 $^{^{5,6,7}}$ Significantly different from baseline in non-normally distributed variables (Wilcoxon's test): $^5P < 0.001$ $^6P < 0.01$ $^7P < 0.05$.

^{8, 9, 10}Means (SEMs): ⁸adjusted for the changes in body weight; ⁹adjusted changes for the insulin levels at baseline; ¹⁰adjusted by ghrelin levels at baseline.

¹¹Differences between groups at baseline and in changes (10 wk – before) were evaluated by 2-way ANOVA (P<0.05; ns, non-significant). *Statistically significant differences between groups after the adjustment by Benjamini-Hochberg. When a significant interaction between groups was found (P<0.05) it was performed an unpaired samples t test, means that do not share a common superscript letter in a horizontal line were significantly different (P<0.05).