Differences in the Metabolic Response to a High-Carbohydrate (HC) Meal Intake between Lean and Overweight/Obese (OW/OB) men - A metabolomics study

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Abstract

The OW/OB individuals exhibited more pronounced changes in the metabolic response to HC meal intake compared to normo-carbohyderate (NC) meal consumption. After the HC meal significantly different AUC for metabolites from several classes was observed. Among others, an increase of lysophosphatidylcholines (LPC) (from +35 to +185%, variable importance in the projection (VIP) range 1.1-1.9), lysophosphatidylethanolamines (LPE) (from +133 to +255%, VIP 1.4-2.2), long-chain fatty acids (LCFA) (from +54 to +133%, VIP 1.2-1.7), or leukotrienes (from +84 to 216%, VIP 1.4-1.9) and decrease of sphinganine (SM) (from -60 to -40%, VIP 1.3-1.6) in OW/OB compared to lean individuals was observed.

Background

Since last decade, the dietary recommendations of macronutrient intake have been changing enormously for the obese/overweight and type 2 diabetic patients (T2DM).

Initially, a low-calorie-diet (LC) comprising mainly of fats with a limited restriction on carbohydrates was considered ideal which was, later, changed to the promotion of high-carbohydrate (HC) and low-in-fat-diet consumption after recognizing the role of diabetes in developing the cardiovascular disease (1, 2). However, the consumption of HC-diets with low fat contents also failed to limit the incidences of metabolic syndrome (4, 5). A lot of data published in literature found no considerable difference in postprandial glucose and lipid metabolism in cases of either taking HC or LC-diets (3-5). These conflicting results in literature, prompted us to evaluate the postprandial metabolic response after HC/NC meals intake in normal-weight and overweight/obese men.

Objective

The short-term and immediate postprandial metabolic response to HC meal intake was evaluated and compared between lean and overweight/obese (OW/OB) healthy men.

Material and Methods

Two groups of non-diabetic male participants (i.e. OW/OB and lean, age: 23-38 years, BMI: from 23.8 to 30.8), each consisting of 12 subjects, underwent a randomized, controlled, and cross-over one-time HC-meal-challenge trial. On the two different visits (with 2-3 weeks of break between them) the participants received standardized HC meal (89% of energy from carbohydrate, 11% protein, and 0% fat) or normal-carbohydrate (NC) meal (45% carbohydrate, 30% protein, 25% fat). Fasting (0 min) and postprandial blood samples were collected at predefined time points (i.e. 30, 60, 120, 180 min) and untargeted plasma metabolomics was performed using LC-QTOF-MS. For each metabolic feature, based on its intensity change in time, the area under the curve (AUC) was calculated. Obtained AUC values were forwarded for multivariate statistical analysis.

This trial was registered at www.clinicaltrials.gov as NCT03792685

Results

Figure 1: PCA models based on postprandial plasma metabolite AUCs obtained after HC-meal intake showing a good separation between obese/overweight and lean men.

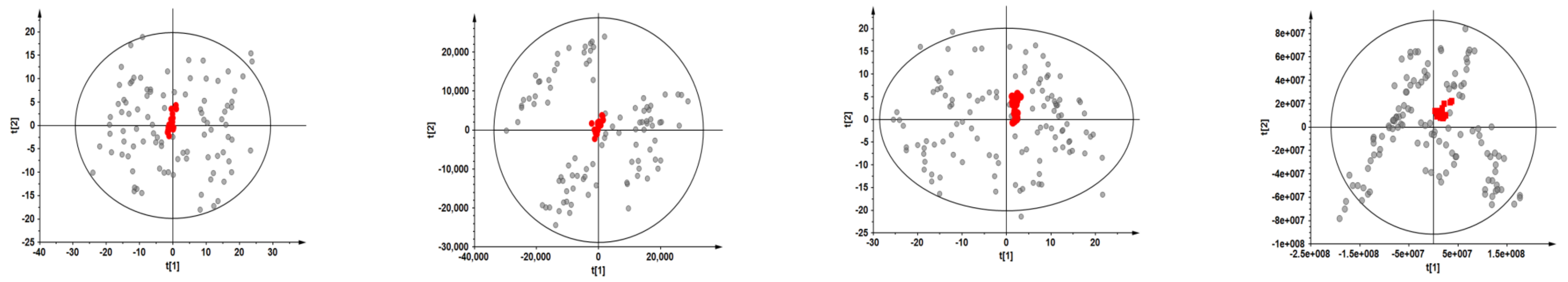

Figure 2: PLS-DA models based on postprandial plasma metabolite AUCs obtained after HC-meal intake showing a good separation between obese/overweight and lean men.

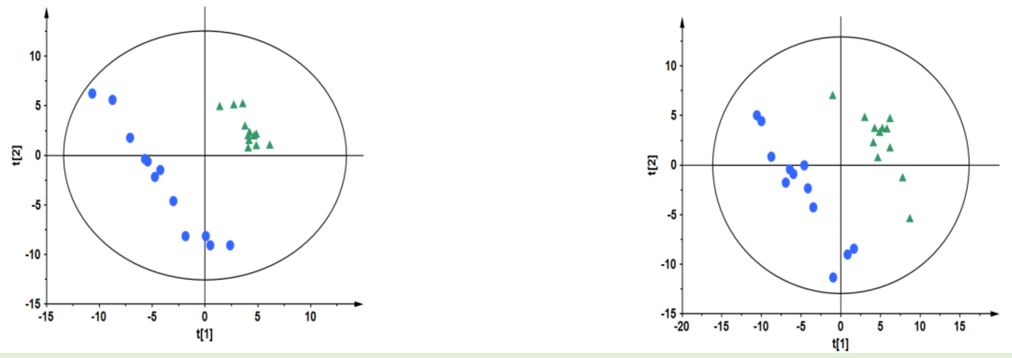

Table 1: Baseline characteristic of the non-diabetic obese/overweight population compared to lean (L) population.

Parameters	OB/OW	L	*p*-value
Age (years)	38±5.4	23.8±1.6	0.4
BMI (Kg/m2)	30.8±5.4	23.8±1.6	0.0009
Body Fat contents (%)	28.0±6.3	17.0±5.3	0.0001
Fat free mass (%)	69.8±12.2	66.3±6.6	0.4
Weight height ratio	0.99.8±0.06	0.91±0.06	0.003
Fasting glucose concentration (mg/dl)	87.9±5.8	84.2±8.1	0.2
Fasting Insulin concentration (IU/mL)	12.7±9.3	6.5±1.7	0.06
HOMA-IR	2.8±2.1	1.3±0.3	0.05
HOMA-β	186.3±121.1	157.5±150.4	0.6
HbA1c	15.3±0.3	5.2±0.3	0.3

Note: For quantitative variables with normal distribution, the parametric t-test was used; for the other variables, the non-parametric Mann–Whitney test was applied. The data are represented as the mean ± STD, and *p*-values< 0.05 were considered significant. * HOMA-IR= Homeostatic Model Assessment of Insulin Resistance; HOMA-β = Homeostatic Model Assessment of β-cell function; HbA1c= glycated hemoglobin; WHR= waist-hip ratio

Note:. Positive/negative value of per cent of change means higher/lower AUC of postprandial change of metabolite level in obese in comparison to lean individuals, S – identity of these metabolites was confirmed by analysis of the standard. The percentage differences in area under curves (AUCs) of postprandial metabolite concentrations in the obese/overweight men compared with the Lean (L) men are presented, unless otherwise indicated. The *P*(corr)—predictive loading value and VIP value were calculated based on respective PLS-DA models. Variables with VIP >1.0 and absolute *P*(corr) >0.4 were considered significant. DG, diglyceride; HC, high carbohydrate; HDoHe, hydroxydocosahexaenoic acid; HETE, hydroxyeicosatetraenoic acid; NC, normo-carbohydrate; LPC, lysophosphatidylcholine; LPE, lysophosphoethanolamine; LTB5, leukotrienes B5; PLS-DA, partial least squares discriminant analysis; RT, retention time; SM, sphingomyelin; VIP, variable importance into projection.

Table 2: Significant metabolites which postprandial change discriminate obese and lean individuals dependently of the meal type

Mass	RT (min)	Metabolites	High carbohydrate diet				Normal carbohydrate diet				Remarks
			Change (%)	VIP	*p*-corr	p-value	Change (%)	VIP	*p*-corr	p-value	
370.1814	3.9	Epiandosterone sulfate	114.22	1.3039	-0.514	0.1	-8.0926	0.445	0.0419	0.9	OK
304.2397	7.1	Arachidonic acid	89.3829	1.2136	-0.5557	0.1	5.9219	0.635	-0.1622	0.9	OK
344.2347	5.7	HDOHE	230.9431	2.039	-0.7173	0.02	-22.207	0.491	0.0774	0.6	OK
320.2348	5.8	HETE	129.0137	1.7674	-0.6441	0.08	-11.1626	0.465	-0.0092	0.9	OK
300.2659	7.4	Hydroxy stearic acid	53.8667	1.4469	-0.5061	0.07	-17.2622	0.338	0.0774	0.9	Frag
213.0097	0.7	Indoxylsulfuric acid	155.3375	2.249	-0.6696	0.07	-25.1716	0.328	0.1112	0.6	OK
90.03185	0.3	Lactic acid	73.0377	1.7011	-0.5579	0.05	10.4388	0.167	-0.0385	0.6	OK
467.3369	5.9	LPC 15:0	124.7424	1.6698	-0.6545	0.1	-18.5582	1.163	0.328	0.4	OK
507.333	5.8	LPC 17:1	34.9017	1.062	-0.5479	0.1	-29.2796	1.177	0.3667	0.2	OK
509.348	6.3	LPC 18:0	90.9997	1.6398	-0.5086	0.1	-14.8049	0.314	0.0691	0.8	OK
509.3481	6.2	LPC 18:0	94.4603	1.7454	-0.5447	0.1	-14.1671	0.3	0.0597	0.8	OK
551.3587	6	LPC 18:2	92.4192	1.4912	-0.6856	0.05	-22.2853	1.227	0.2816	0.4	OK
453.2856	5.6	LPE 16:0	254.733	1.6652	-0.6539	0.1	22.7943	0.331	0.0995	0.6	OK
481.317	6.3	LPE 18:0	164.2111	1.3974	-0.6323	0.1	100.2655	1.479	-0.2972	0.1	OK
439.3049	5.8	LPE O-16:0	211.3618	1.7429	-0.6604	0.04	2.3997	0.994	0.3101	0.9	OK
437.2904	5.8	LPE P-16:0	195.3989	1.7312	-0.6984	0.04	-29.7604	0.921	0.3264	0.2	OK
334.214	4.7	LTB5	83.9859	1.4035	-0.5714	0.1	-7.3469	0.398	0.0464	0.9	OK
334.2141	4.5	LTB5	216.514	1.9246	-0.6779	0.07	-9.8857	0.335	0.0229	0.8	OK
743.5467	10.2	PE 36:2	59.07282	1.2908	-0.5767	0.2	51.4131	0.979	-0.2149	0.2	OK
686.5363	8.5	SM 33:2	36.8755	1.0984	-0.5048	0.3	-24.0824	0.6	0.1741	0.5	OK
284.2712	6.3	Stearic acid	125.2366	1.7462	-0.7585	0.03	22.2998	1.064	-0.1803	0.5	OK
330.2402	3.8	Trihydroxyoctadecenoic acid	133.0237	1.4716	-0.6404	0.06	6.2266	0.388	-0.026	0.9	Frag
168.0282	0.2	Uric acid	144.523	1.4009	-0.6278	0.1	-15.5219	0.304	-0.0718	0.6	OK
273.2662	4.1	Hexadecasphinganine	-60.2866	1.5247	0.55948	0.02	-8.2612	0.174	0.0667	0.8	Frag
287.2456	5	Lauroyldiethanolamide	-70.8197	2.436	0.78004	0.002	-3.6148	0.254	0.0843	0.9	Frag
467.3007	5.1	LPC 14:0	185.2085	1.8755	-0.6471	0.03	1.6837	0.345	-0.1421	0.9	ok
495.3317	5.6	LPC 16:0	161.3187	1.6212	-0.7003	0.02	-23.1161	0.181	-0.0415	0.6	ok
523.3631	6.3	LPC 18:0	92.2312	1.3218	-0.6183	0.06	14.276	0.751	-0.2775	0.6	ok
507.3684	6	LPC 18:1	180.6202	1.443	-0.5378	0.09	-22.2036	0.665	0.2166	0.5	ok
517.3162	5.2	LPC 18:3	60.05464	1.4165	-0.6009	0.2	120.1516	0.456	-0.0988	0.2	ok
549.3789	6.3	LPC 20:1	274.3281	1.8653	-0.5479	0.03	-36.4529	0.335	0.0231	0.6	ok
547.3632	6	LPC 20:2	37.03726	1.0398	-0.5139	0.2	53.2641	0.877	-0.3437	0.3	ok
503.3008	5.7	LPE 20:3	-71.0096	2.1767	0.5299	0.06	15.201	0.428	0.1244	0.8	ok
477.3213	5.7	LPE P-19:1	132.7315	1.522	-0.6711	0.03	-22.9944	0.194	-0.0237	0.5	ok
271.2509	4.5	Sphinganine	-39.6883	1.3409	0.52921	0.02	11.5367	0.544	0.0982	0.2	ok
287.282	4.2	Sphinganine	-49.0484	1.648	0.50405	0.02	46.6706	0.841	-0.2708	0.8	ok
279.2558	5.5	Linoleamide	681.7416	3.60911	-0.77010	0.03	38.4297	0.7851	-0.4016	ESI+	OK
297.30246	7.8	Palmitoylethanolamide	69.2	1.67965	-0.501752	0.06	35.8	0.6701	-0.0106	ESI+	Frag
295.25055	5.7	Sphingosine	550.0194	2.5319	-0.54635	0.2	56.6863	0.6979	-0.2706	ESI+	OK
327.31308	7.3	Stearoylethanolamide	42.3067	1.23199	-0.50195	0.06	-47.8736	1.8172	0.4021	ESI+	Frag

Conclusion

Obvious postprandial metabolic differences were noted between lean and OW/OB individuals receiving HC meal. Metabolic pathways differentially affected by the HC meal belong to phospholipids and glucose metabolism, sphingomyelin signaling, as well as purines/pyrimidines and aldosterone catabolism.

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