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ORIGINAL ARTICLE

Associations Between Estimated Desaturase Activity and Insulin Resistance in Korean Boys

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Abstract
Objectives: Obesity in childhood increases the risk of obesity in adulthood, and is predictive of the development of metabolic disorders. The fatty acid compositions of various tissues, including blood, are associated with obesity and obesity-associated disorders. Thus, tracking plasma phospholipid (PL) features and metabolic parameters in young individuals may strengthen the utility of fatty acid composition as an early biomarker of future metabolic disorders.
Methods: Anthropometric and blood biochemical data were obtained from 131 Korean males aged 10.5 ± 0.4 years, and followed up at 2 years. We analyzed the plasma PL fatty acids according to obesity. Obese children were defined as those with a body mass index (BMI) greater than the 85th percentile for age and gender, based on Korean child growth standards.
Results: Activities of lipid desaturases, stearyl-CoAD (SCD-16,16:1n-7/16:0), delta-6D (D6D, 20:3n-6/18:2n-6), and delta-5D (D5D, 20:4n-6/20:3n-6), were estimated. Obese individuals had significantly higher proportions of palmitoleic acid (16:1n-7) and dihomo-gamma linolenic acid (DGLA, 20:3n-6) at both baseline and follow-up than did lean individuals. The activities of SCD-16 and D6D were higher in obese than lean boys. The baseline SCD-16 activity level was positively associated with the baseline waist circumference (WC) and the metabolic risk score. The baseline D6D level was positively associated with WC and also with the

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homeostasis model of assessment of insulin resistance (HOMA-IR), a surrogate marker of insulin resistance (IR), and metabolic risk score at both baseline and follow-up.
Conclusion: In young Korean males, higher D6D activity predicts the future development of IR and associated metabolic disorders including dyslipidemia.

1. Introduction

Obesity has become increasingly prevalent among children and adolescents in many countries. Childhood obesity increases the risk of developing health problems including insulin resistance (IR) and metabolic syndrome [1,2], and also adult obesity and cardiovascular disease [3,4]. Therefore, early detection of childhood obesity and metabolic disorders is required to efficiently prevent development of problems in adulthood. Studies on child populations may clarify the mechanisms underlying the development of obesity and metabolic disorders, because problems in children are not confounded by the consequences of advanced metabolic disorders.

The levels of specific serum fatty acids and fatty acid desaturases have been suggested to serve as useful biomarkers predicting the development of IR and metabolic disorders [5−11]. Higher levels of saturated fatty acids, palmitoleic acid, linoleic acid, and dihomo-gamma linolenic acid (DGLA), have been reported to be associated with obesity and metabolic syndrome. In addition, both animal and human studies have suggested that fatty acid desaturases play roles in various metabolic disturbances, including dyslipidemia and IR [12]. The data have been derived principally from cross-sectional studies, which cannot predict the future development of obesity and metabolic disorders. Longitudinal studies can yield integrated information on the development of metabolic disorders over time, and can identify the optimal points of intervention [13]. Therefore, in the present study, we explored the longitudinal relations of plasma phospholipid (PL) fatty acid composition and desaturase activities to IR and metabolic risk factors in Korean boys.

2. Materials and methods

2.1. Study participants and anthropometric parameters

This study is part of the Korean Children and Adolescent Cohort Study, which follows a student cohort from the time of entry into elementary school (at 7 years of age) to graduation (at age 19 years) in Seoul and Kyunggi provinces, Korea. The overall objective of the cohort study is to identify early risk factors for obesity and associated metabolic disease. The study was approved by the Institutional Review Board of the Korea Center for Disease Control and Prevention and the Ethics Committee of Seoul-Paik Hospital, Inje University, Seoul, Korea. Informed parental consent was obtained for each individual prior to enrolment. Body weight and body fat percentage were measured using a body composition analyzer (BC418; Tanita, Tokyo, Japan) and height was measured using an automatic stadiometer (DS-102; Jenix, Seoul, Korea). Obese children were defined as those with a body mass index (BMI) greater than the 85th percentile for age and gender, based on Korean child growth standards [14]. A total of 131 boys aged 9−11 years in 2008−2009 were included. After 2 years, health data were obtained once more.

2.2. Biochemical analysis

Each blood sample was collected from an antecubital vein into a vacutainer tube between 9:00 AM and 11:00 AM after a 12-hour overnight fast. Within 30 minutes, plasma and serum were separated and stored at −80°C prior to further analysis. The levels of triglyceride (TG), total cholesterol, high-density lipoprotein-cholesterol (HDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and glucose were measured using an autoanalyzer (model 7600II; Hitachi, Tokyo, Japan). The fasting serum insulin level was measured using a Roche E170 instrument (Roche Diagnostics, Mannheim, Germany). The IR index was calculated using the homeostasis model assessment of insulin resistance (HOMA-IR) [15]. A metabolic risk score was constructed by summing the *z*-score of five metabolic risk factors, which are BMI, systolic blood pressure (SBP), TG, HDL-C, and HOMA-IR [16].

2.3. Fatty acid analysis

Plasma lipids were extracted using a modification of the method of Folch et al [17]. The PL fraction was isolated by thin-layer chromatography and the fatty acids were converted into methyl esters using the method of Lepage and Roy [18]. The composition of the methylated fatty acid mix was determined by gas chromatography (HP 7890A; Hewlett-Packard, Palo Alto, CA, USA). Individual fatty acids were identified by comparing retention times to those of standards and quantified based on the peak area relative to the total methylated fatty acid peak area (set at 100%). Desaturase levels were estimated by calculating the product:precursor ratios of individual fatty acids (using the proportions calculated above) as follows: delta-6D (D6D) = [20:3n-6/18:2n-6]; delta-6D (D5D) = [20:4n-6/20:3n-6]; stearyl-CoAD-16 (SCD-

16) = [16:1n-7/16:0]; and stearyl-CoAD-18 (SCD-18) = [18:1n-9/18:0] [18].

2.4. Statistical analysis

Statistical analyses were performed with the aid of SAS software (version 9.1; SAS Institute, Cary, NC, USA). All data are expressed as mean ± standard deviation (SD). The normality of data distribution was checked. Variables with skewed distributions were log-transformed prior to analysis. The significance of observed between-group differences was assessed using the unpaired Student *t* test and the significance of among-group differences was analyzed using one-way analysis of variance (ANOVA). If a statistically significant effect was noted, Duncan's post-hoc test was applied to identify a between-group difference with a significance level of $p < 0.05$. Pearson correlation coefficients were calculated to measure the extent of correlation between pairs of variables.

3. Results

3.1. Participant characteristics

Anthropometric and biological characteristics of all individuals at baseline are shown in Table 1. At commencement of the study, 75 of 131 boys were obese, and all had a significantly greater body weight, BMI, BMI *z*-score, and waist circumference than did the others. HOMA-IR values and levels of serum ALT, TG, and insulin were significantly higher and HDL-C was significantly lower in obese individuals (Table 1). Two years later, the children were examined once more. Of the 56 individuals who were not obese at baseline, categorized as "lean", 40 boys had BMI values below the 60th percentile at follow-up. Of the 75 initially obese boys, 57 remained obese at follow-up. At this time, 14 boys who were not obese at baseline and 20 boys who were obese at that time had BMI values in the 60−85% percentile, and were categorized as "intermediate" in terms of obesity.

The baseline and follow-up data of lean and obese individuals were compared. Not surprisingly, the mean values of height, weight, BMI, and waist circumference of both groups increased significantly over the 2 years, as did blood glucose and insulin levels, and HOMA-IR values. The mean values of BMI *z*-score, AST, and ALT levels were lower in lean boys at follow-up than at baseline, but this was not true of obese individuals. The mean SBP, diastolic blood pressure (DBP), and lipid levels (total cholesterol, HDL-C, and TG) did not differ between baseline and follow-up in either group.

At follow-up, obese boys had a significantly greater BMI *z*-score, and waist circumference than lean or

Table 1. Anthropometric and biochemical characteristics of the study participants.[a]

	Baseline			Follow-up			
	Lean (n = 56)	Obese (n = 75)	p_0[a]	Lean (n = 40)	Intermediate (n = 34)	Obese (n = 57)	p_1[a]
Age (y)	10.5 ± 0.6***	10.4 ± 0.6†††	0.161	12.5 ± 0.7	12.2 ± 0.6	12.3 ± 0.7	0.274
Height (cm)	142.7 ± 5.3***	144.6 ± 6.6†††	0.073	156.9 ± 7.3	156.5 ± 7.9	157.0 ± 8.1	0.923
Body weight (kg)	37.1 ± 3.5***	50.0 ± 8.3†††	<0.0001	46.5 ± 5.1	53.3 ± 6.8	65.1 ± 12.1	<0.0001
BMI (kg/m^2)	18.2 ± 0.5***	23.8 ± 2.3†††	<0.0001	18.8 ± 0.8	21.7 ± 1.0	26.2 ± 3.0	<0.0001
BMI *z*-score	−0.02 ± 0.14***	1.49 ± 0.40†††	<0.0001	−0.21 ± 0.26	0.68 ± 0.24	1.60 ± 0.46	<0.0001
Waist circumference (cm)	62.4 ± 3.7***	77.6 ± 6.2†††	<0.0001	66.4 ± 5.1	74.9 ± 5.8	85.5 ± 8.1	<0.0001
SBP (mmHg)	108.0 ± 8.6	111.5 ± 13.1	0.064	107.8 ± 10.5	109.7 ± 11.7	115.1 ± 10.4	0.001
DBP (mmHg)	71.1 ± 7.5	71.2 ± 8.8	0.930	68.2 ± 10.3	69.1 ± 9.0	70.9 ± 8.3	0.152
AST (U/L)	23.3 ± 2.8**	26.3 ± 9.1	0.008	21.7 ± 3.1	23.0 ± 4.0	28.3 ± 14.8	0.001
ALT (U/L)[b]	13.8 ± 3.9*	26.7 ± 23.2	<0.0001	12.1 ± 3.6	16.0 ± 8.6	34.5 ± 37.1	<0.0001
Total cholesterol (mg/dL)	167.1 ± 24.5	173.8 ± 27.9	0.159	161.0 ± 18.6	161.4 ± 33.4	173.3 ± 31.2	0.030
HDL-C (mg/dL)	60.1 ± 12.0	52.0 ± 10.8	<0.0001	61.0 ± 10.9	55.9 ± 12.3	49.4 ± 9.4	<0.0001
TG (mg/dL)[a,b]	61.5 ± 34.1	104.5 ± 63.8	<0.0001	57.1 ± 28.0	89.8 ± 41.5	117.4 ± 60.5	<0.0001
Glucose (mg/dL)	86.3 ± 6.4**	85.8 ± 8.0††	0.714	90.8 ± 8.0	90.8 ± 6.4	90.7 ± 9.1	0.951
Insulin (μIU/mL)[a,b]	6.1 ± 4.2***	12.0 ± 11.0†††	<0.0001	8.8 ± 3.5	11.9 ± 8.2	21.6 ± 19.9	<0.0001
HOMA-IR[a,b]	1.3 ± 0.9***	2.5 ± 2.4†††	<0.0001	2.0 ± 0.8	2.72 ± 2.1	5.0 ± 4.9	<0.0001
Metabolic risk score	−1.59 ± 1.25***	1.19 ± 2.23†††	<0.0001	−1.87 ± 1.37	−0.58 ± 1.57	1.64 ± 2.51	<0.0001
MetS (%)	—	17.3	—	—	2.9	22.8	—

[a]*Tested by unpaired Student t test (p0, *, †) or one-way analysis of variance (ANOVA; p1 = p value for linear trends);* [b]*Data are log transformed prior to analysis.* All values are presented as mean ± standard deviation (SD). * Baseline vs. follow-up in control; *p < 0.05; **p < 0.01; ***p < 0.001. † Baseline vs. follow-up in obese; †p < 0.05; †† p < 0.01; †††p < 0.001. ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein-cholesterol; HOMA-IR = homeostasis model of assessment of insulin resistance; IU = international unit; SBP = systolic blood pressure; TG = triglyceride; U = unit.

intermediate individuals. In addition, obese individuals had significantly higher concentrations of ALT, TG, and insulin and a higher mean HOMA-IR value than the other groups.

3.2. Plasma PL fatty acid composition and desaturase levels

Table 2 shows the relative proportions of 25 individual fatty acids of plasma PLs. At baseline, over 63% of total fatty acids were saturated (SFAs), and no significant difference in the level of total SFA, palmitate, or stearate was evident between obese and lean individuals. Monounsaturated fatty acids (MUFAs) constituted 11% of total fatty acids in either group. However, the palmitoleic acid (16:1n-7) level was higher in obese individuals. Although no difference in total n-6 polyunsaturated fatty acid (PUFA) or 20:4n-6 level was observed, the DGLA (20:3n-6) level was higher in obese individuals as were the SCD-16 and D6D indices.

Baseline and follow-up data on lean and obese individuals were separately compared. The levels of only four fatty acids (22:0, 20:1, 22:5n-3, and 20:4n-6) differed between baseline and follow-up. The mean 22:5n-3 level increased in both groups at follow-up and the mean 20:4 level fell in lean boys at follow-up. Obese individuals had a higher palmitoleic acid and DGLA level than lean boys at follow-up. Also, trends toward increases in the SCD-16 and D6D indices were evident in boys of heavier weight.

Table 2. Plasma PL fatty acid composition and estimated desaturase activity of the study participants.[a,b]

	Baseline			Follow-up			
	Control (n = 56)	Obese (n = 75)	p_0	Control (n = 33)	Intermediate (n = 25)	Obese (n = 46)	p_1
Total SFA	63.5 ± 5.8	63.4 ± 7.5††	0.776	63.5 ± 9.7	60.6 ± 10.3	61.8 ± 9.2	0.515
c12:0	0.14 ± 0.08	0.13 ± 0.06	0.443	0.12 ± 0.06	0.14 ± 0.06	0.11 ± 0.05	0.666
c14:0	0.54 ± 0.14	0.51 ± 0.11	0.385	0.54 ± 0.22	0.52 ± 0.08	0.50 ± 0.14	0.435
c16:0	38.9 ± 3.7	38.1 ± 4.8	0.213	39.2 ± 6.4	36.9 ± 6.5	37.3 ± 6.2	0.217
c18:0	21.2 ± 2.3	21.7 ± 2.8	0.341	20.7 ± 3.3	20.2 ± 3.6	20.9 ± 2.9	0.620
c20:0	0.51 ± 0.16	0.53 ± 0.15	0.321	0.55 ± 0.10	0.52 ± 0.12	0.55 ± 0.11	0.941
c22:0	1.17 ± 0.49*	1.28 ± 0.45	0.163	1.26 ± 0.24	1.23 ± 0.23	1.33 ± 0.31	0.238
c24:0	1.05 ± 0.41	1.10 ± 0.38	0.371	1.12 ± 0.27	1.05 ± 0.24	1.07 ± 0.27	0.413
Total MUFA	11.0 ± 1.6	11.0 ± 1.6†	0.889	11.3 ± 1.0	11.1 ± 1.2	11.1 ± 1.1	0.545
c16:1n-7	0.43 ± 0.18	0.51 ± 0.20	0.018	0.36 ± 0.15	0.44 ± 0.18	0.44 ± 0.15	0.027
c18:1n-9	6.89 ± 1.46	6.79 ± 1.55	0.589	6.23 ± 1.68	6.68 ± 2.06	6.62 ± 1.48	0.278
c18:1n-7	1.25 ± 0.23	1.16 ± 0.21	0.039	1.20 ± 0.28	1.12 ± 0.20	1.13 ± 0.26	0.283
c20:1n-9	0.32 ± 0.26*	0.32 ± 0.32	0.446	0.62 ± 0.62	0.50 ± 0.59	0.43 ± 0.45	0.197
c22:1n-9	0.71 ± 0.42	0.69 ± 0.49	0.306	1.31 ± 1.08	0.89 ± 0.99	0.92 ± 0.84	0.271
c24:1n-9	1.40 ± 0.57	1.50 ± 0.57	0.248	1.52 ± 0.46	1.47 ± 0.38	1.57 ± 0.43	0.522
Total n-6 FA	21.7 ± 4.3***	21.8 ± 5.7†††	0.752	21.2 ± 8.0	24.1 ± 8.1	22.7 ± 7.5	0.428
c18:2n-6	14.2 ± 2.9	13.7 ± 3.2	0.285	14.0 ± 4.9	15.4 ± 4.8	14.4 ± 4.1	0.690
c18:3n-6	0.40 ± 0.13	0.39 ± 0.14	0.497	0.45 ± 0.18	0.37 ± 0.11	0.39 ± 0.11	0.153
c20:2n-6	0.29 ± 0.18	0.28 ± 0.12	0.993	0.29 ± 0.13	0.30 ± 0.14	0.29 ± 0.12	0.864
c20:3n-6	2.08 ± 0.48	2.38 ± 0.61	0.008	2.00 ± 0.53	2.28 ± 0.71	2.39 ± 0.55	0.007
c20:4n-6	4.44 ± 1.74*	4.74 ± 2.30	0.891	3.96 ± 3.11	5.22 ± 3.21	4.84 ± 3.24	0.255
c22:4n-6	0.18 ± 0.09	0.21 ± 0.09	0.108	0.24 ± 0.27	0.24 ± 0.11	0.21 ± 0.12	0.894
Total n-3 FA	3.72 ± 1.27	3.82 ± 1.19†††	0.632	3.72 ± 1.30	3.80 ± 1.15	3.80 ± 1.23	0.367
c18:3n-3	0.11 ± 0.07	0.13 ± 0.07	0.109	0.13 ± 0.09	0.14 ± 0.08	0.14 ± 0.11	0.955
c20:3n-3	1.15 ± 0.70	0.96 ± 0.63	0.319	1.26 ± 0.66	0.92 ± 0.64	1.17 ± 0.70	0.569
c20:5n-3	0.37 ± 0.33	0.42 ± 0.30	0.340	0.42 ± 0.45	0.53 ± 0.37	0.45 ± 0.35	0.663
c22:5n-3	0.58 ± 0.34*	0.59 ± 0.30†††	0.709	0.76 ± 0.37	0.72 ± 0.28	0.77 ± 0.29	0.532
c22:6n-3	1.51 ± 1.03	1.71 ± 1.14	0.453	1.54 ± 1.46	1.95 ± 1.42	1.89 ± 1.70	0.591
Desaturase activity							
D6D	0.15 ± 0.04	0.18 ± 0.04	<0.0001	0.15 ± 0.04	0.16 ± 0.04	0.18 ± 0.05	0.029
D5D	2.15 ± 0.78	1.95 ± 0.80	0.075	1.85 ± 1.38	2.10 ± 1.13	1.94 ± 1.26	0.590
SCD-16	0.011 ± 0.005	0.013 ± 0.006	0.016	0.009 ± 0.004	0.012 ± 0.006	0.012 ± 0.004	0.031
SCD-18	0.334 ± 0.100	0.323 ± 0.099	0.462	0.319 ± 0.126	0.354 ± 0.154	0.328 ± 0.103	0.572

[a]*Data are log transformed prior to analysis;* [b]*Tested by unpaired Student t test (p_0, *, †) or one-way analysis of variance (ANOVA; p_1 = p value for linear trends).* All values are presented as mean ± standard deviation (SD). * Baseline vs. follow-up in control; *p < 0.05; **p < 0.01; ***p < 0.001. † Baseline vs. follow-up in obese; †p < 0.05; ††p < 0.01; †††p < 0.001. D5D = delta-5D; D6D = delta-6D; FA = fatty acid; MUFA = monounsaturated fatty acid; PL = phospholipid; SCD = stearyl-CoAD; SFA = saturated fatty acid.

3.3. Correlation between fatty acid and desaturase levels and the risks of adiposity and IR

The baseline level of palmitoleic acid (as a percentage of all fatty acids) was closely associated with WC and metabolic risk score ($r = 0.217$, $p < 0.05$; $r = 0.221$, $p < 0.05$, respectively). DGLA level was also highly associated with WC, HDL-C, TG, and metabolic risk score ($r = 0.205$, $p < 0.05$; $r = -0.176$, $p < 0.05$; $r = 0.371$, $p < 0.001$; $r = 0.260$, $p < 0.01$, respectively). The SCD-16 level was closely associated with WC and metabolic risk score ($r = 0.209$, $p < 0.05$; $r = 0.200$, $p < 0.05$, respectively) but not with the HOMA-IR value (Table 3). The D6D level was highly associated with most of the metabolic risk factors such as WC, TG, and HDL-C. The D6D level was thus positively associated with the HOMA-IR value and the metabolic risk score ($r = 0.267$, $p < 0.01$; $r = 0.394$, $p < 0.001$). The baseline D6D level showed significant positive association with the follow-up WC, HOMA-IR, and metabolic risk score ($r = 0.480$, $r = 0.364$, and $r = 0.436$, respectively). The baseline D5D level exhibited a negative association with them (Table 3).

A stepwise multiple regression analysis with the baseline levels of age, BMI *z*-score, WC, TG, HDL-C, and four estimated desaturase indices was performed to investigate potential factors associated with the follow-up HOMA-IR. Significant associations with the follow-up HOMA-IR were found for baseline WC and D6D (Table 4). Similarly, strong associations with the follow-up metabolic risk score were found for baseline WC and D6D level. Based on the regression analysis, the baseline D6D level could be a major predictive marker for future metabolic risks.

4. Discussion

We investigated the relationships between individual plasma PL fatty acids and desaturase activities and

Table 3. Correlation coefficient between estimated desaturase activity and risks for metabolic syndrome.[a]

	D6D	D5D	SCD-16	SCD-18
Baseline				
BMI (kg/m^2)	0.414***	−0.203*	0.193*	−0.093
BMI *z*-score	0.410***	−0.209*	0.199*	−0.097
Waist circumference (cm)	0.414***	−0.254**	0.209*	−0.137
SBP (mmHg)	0.151	−0.137	0.153	0.068
DBP (mmHg)	0.181*	−0.160	−0.031	−0.039
AST	0.279**	−0.124	0.153	−0.013
ALT	0.370***	−0.164	0.155	−0.070
Total cholesterol (mg/dL)	0.214*	−0.030	0.073	0.110
HDL-C (mg/dL)	−0.292***	0.082	−0.090	0.055
TG (mg/dL)	0.482***	−0.144	0.166	0.015
Glucose (mg/dL)	−0.138	0.219*	0.119	0.126
Insulin (μIU/mL)	0.290**	−0.195*	0.036	−0.072
HOMA-IR	0.267**	−0.161	0.050	−0.054
Metabolic risk score	0.394***	−0.258**	0.200*	−0.006
Follow-up				
BMI (kg/m^2)	0.445***	−0.279**	0.155	−0.100
BMI *z*-score	0.456***	−0.297***	0.156	−0.103
Waist circumference (cm)	0.480***	−0.300***	0.153	−0.087
SBP (mmHg)	0.340***	−0.305***	−0.017	−0.181*
DBP (mmHg)	0.203*	−0.155	−0.092	−0.061
AST	0.131	−0.145	0.012	−0.092
ALT	0.306***	−0.258**	0.089	−0.116
Total cholesterol (mg/dL)	0.197*	−0.092	0.091	0.123
HDL-C (mg/dL)	−0.289***	0.147	0.000	0.135
TG (mg/dL)	0.356***	−0.233**	0.090	−0.105
Glucose (mg/dL)	0.004	−0.219*	−0.228**	−0.208*
Insulin (μIU/mL)	0.377***	−0.261**	0.046	−0.066
HOMA-IR	0.364***	−0.278**	0.014	−0.089
Metabolic risk score	0.436***	−0.340***	0.112	−0.107

[a]*Tested by age-adjusted partial correlation analysis; data are log transformed prior to analysis.* *p < 0.05; **p < 0.01; ***p < 0.001. ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; D5D = delta-5D; D6D = delta-6D; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein-cholesterol; HOMA-IR = homeostasis model of assessment of insulin resistance; IU = international unit; SBP = systolic blood pressure; SCD = stearyl-CoAD; TG = triglyceride.

Table 4. Stepwise multiple regression analysis for predicting follow-up HOMA-IR levels and metabolic risk score.[a,b]

Variable	Adjusted β Coefficient	*p*	r^2
Follow up HOMA-IR[c]			
Waist circumference	0.026	< 0.0001	0.206
D6D	0.619	0.007	0.250
Follow up metabolic risk score[d]			
Waist circumference	0.135	<0.0001	0.356
D6D	2.338	0.002	0.402

[a]Data are log transformed prior to analysis; [b]For multiple stepwise regression analysis, only the two independent variables incorporated into the model are listed, and the r^2 values displayed are cumulative; [c]Independent variables include: baseline age, BMI z-score, waist circumference, TG, HDL-C, and desaturase; [d]Independent variables include: baseline age, waist circumference, and desaturase. BMI = body mass index; HDL-C = high-density lipoprotein-cholesterol; HOMA-IR = homeostasis model of assessment of insulin resistance; TG = triglyceride.

metabolic risk factors in Korean children. Furthermore, we explored the longitudinal relations of estimates of desaturase activity to body fatness, IR, and metabolic risk score. Obese boys had significantly higher proportions of palmitoleic acid and DGLA at baseline than did lean children, in agreement with data on Japanese children [9]. Increased DGLA levels are positively associated with the development of metabolic disorders in both adults and children [19–21]. A previous cross-sectional study found that obese children have higher proportions of DGLA in plasma lipids than do those of normal weight [21]. Our data are in agreement with these earlier reports. The present study, a longitudinal study, also shows that obese boys had persistently high proportions of DGLA and palmitoleic acid at follow-up. Assessment of plasma DGLA level and/or palmitoleic acid level would give useful information on obesity status in children. Additionally, the present study shows that the baseline plasma DGLA content was positively associated with both present and future adiposity index values and metabolic risk score in Korean children.

Plasma fatty acid composition could be regulated by many factors such as dietary, hormonal, and environmental factors [12,22]. To assess the effect of dietary fatty acids on the serum PL fatty acid composition of the study participant, a reliable database for fatty acid composition of Korean food is needed, but was not available at this time. Linoleic acid (18:2n-6) is directly converted into 18:3n-6 by D6D and rapidly elongated to 20:3n-6 (DGLA) [22]. DGLA is converted into arachidonic acid by D5D [22]. The DGLA level, regulated by D6D activity, is increased by insulin [12]. Hyperinsulinemia induced by obesity might change the expression level of D6D. We observed D6D had a positive association with HOMA-IR, a surrogate marker of IR for epidemiology study. The observed increases in DGLA concentration and D6D activity, accompanied by a fall in D5D expression, in obese individuals suggest that impaired fatty acid metabolism, possibly caused by the development of IR, may trigger the accumulation of DGLA. Although DGLA plays multiple roles in protecting against inflammation and cell proliferation [22], increases in DGLA and D6D levels in association with IR could nonetheless aggravate metabolic disorders. A recent cross-sectional study with Korean adults suggested D6D as a major factor for determining plasma level of C-reactive protein, a surrogate marker for inflammation [23].

Not only was the baseline D6D activity significantly higher in obese than in lean children at baseline, but it was also positively associated with adiposity indices at follow-up. Baseline D6D activity also exhibited positive associations with the follow-up values of surrogate markers of IR and metabolic disorders, including the TG level, HOMA-IR value, and metabolic risk score. Accumulating evidence suggests that D6D plays a crucial role in the development of obesity and metabolic syndrome. High levels of D6D activity have been estimated in adults with obesity, diabetes, and metabolic syndrome [18,24,25]. Warensjo et al [25] found that a higher estimated D6D activity increased the risk of metabolic syndrome over 20 years in middle-aged men. To the best of our knowledge, only one prior study [26] explored the associations between longitudinal changes in fatty acid composition and body fatness in children. In that study, increased D6D activity was significantly associated with an elevated waist-to-hip ratio in both boys and girls. The authors suggested that D6D activity was positively associated with an increased HOMA-IR value only in girls [26]. However, their small sample size may have limited the observations that could be made. In the present study, the D6D levels did not vary greatly over the 2 years, whereas the HOMA-IR level increased. Thus, no positive association between changes in D6D and changes in the HOMA-IR value were noted. However, baseline D6D activity was positively associated with both baseline and follow-up HOMA-IR values, and also follow-up metabolic risk score. Results from the present multiple regression analysis suggested that WC and D6D were the major determinants of HOMA-IR and metabolic risk score, a suggested tool for an early-life determination of metabolic risk. Thus early detection of elevated D6D activity in Korean boys may predict the future development of IR and associated metabolic disorders including dyslipidemia. Adequate regulation of D6D level at an early age may help prevent the development of metabolic disorders.

Conflicts of interest

All authors declare no conflicts of interest.

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