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Body fat and dairy product intake in lactase persistent and non-persistent children and adolescents

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Abstract

Background: Lactase non-persistent (LNP) individuals may be lactose intolerant and therefore on a more restricted diet concerning milk and milk products compared to lactase persistent (LP) individuals. This may have an impact on body fat mass.
Objective: This study examines if LP and LNP children and adolescents, defined by genotyping for the LCT-13910 C>T polymorphism, differ from each other with regard to milk and milk product intake, and measures of body fat mass.
Design: Children ($n = 298$, mean age 9.6 years) and adolescents ($n = 386$, mean age 15.6 years), belonging to the Swedish part of the European Youth Heart Study, were genotyped for the LCT-13910 C>T polymorphism. Dietary intakes of reduced and full-fat dairy varieties were determined.
Results: LNP (CC genotype) subjects consumed less milk, soured milk and yoghurt compared to LP (CT/TT genotype) subjects ($p < 0.001$). Subsequent partitioning for age group attenuated this observation ($p = 0.002$ for children and $p = 0.023$ in adolescents). Six subjects were reported by parents to be 'lactose intolerant', none of whom were LNP. LNP children and adolescents consumed significantly less reduced fat milk and milk products than LP children and adolescents ($p = 0.009$ for children and $p = 0.001$ for adolescents).
Conclusions: We conclude that LP is linked to an overall higher milk and dairy intake, but is not linked to higher body fat mass in children and adolescents.

Keywords: *milk consumption*; *lactose intolerance*; *LCT-13910 C>T polymorphism*; *obesity*; *nutrigenetics*

Lactase non-persistence (LNP) is an inherited condition defined as the inability to digest lactose due to a reduced production of lactase after weaning (1). A single nucleotide polymorphism (SNP) located 14 kb upstream of the lactase gene (LCT-13910 C>T) has been shown to be associated with lactase persistence (LP). The T allele appears to be dominant over the C allele that represents LNP (2–4). LP (CT/TT genotype) is thus a dominant trait controlled by the lactase gene (LCT). LNP (CC genotype) is also known as adult-type hypolactasia (AtH) or primary hypolactasia (5). Homozygosity for the C allele contributes to the restricted consumption of fresh milk and some dairy products to approximately 12 g of lactose or two cups of milk daily (6). The perception of symptoms related to

lactose maldigestion can nevertheless vary between single subjects with LNP and even LP.

The underlying hypothesis of this study is that LP and LNP might influence the consumption of milk and milk products in children and adolescents, which in turn could be associated with differences in body fat mass between LP and LNP.

Some studies suggest that dairy products may help prevent weight gain and promote weight loss in children and adolescents (7–10). Other studies, in contrast, have not found an effect of milk and milk product intake on body fat mass (11–14), or shown increased weight gain in children and adolescents (15). Also, a recent review suggests that the 'dogma' of promoting the intake of reduced fat diary should be readdressed by interventional

studies. The authors conclude that reduced fat varieties of dairy products could constitute a significant contributory factor to hyperphagia and obesity observed in children and adolescents (16). Thus, the role of cow's milk consumption in relation to childhood and adolescent obesity is debated and remains controversial.

The main purpose of this study is to examine if children and adolescents with and without the LCT-13910 C >T polymorphism differed in their intakes of milk and milk products, and thereby in measures of body fat mass. Full- and low-fat varieties of milk and milk products were studied.

Subjects and methods

Population
Blood samples were obtained from 686 subjects (300 children and 386 adolescents) belonging to the Swedish part of the European Youth Heart Study (EYHS). EYHS is a cross-sectional school-based study of risk factors for future cardiovascular disease among children (9–10 years old) and adolescents (15–16 years old). The mean ages in the Swedish sample for children and adolescents were 9.6 years and 15.6 years, respectively. Sampling procedures and participation rates have been described previously (17).

Anthropometric variables
Height, weight, hip and waist circumferences were measured by internationally accepted standardized procedures (18). Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Body fat percentage was calculated by using Slaughter's equation based on skinfold thickness measurements (19). These measurements have been shown to correlate highly with dual-energy X-ray absorptiometry-measured body fat percentages in children of similar age groups (20). These measurements were taken using a Harpenden caliper at the biceps, triceps, subscapular, suprailiac and triceps surae sites on the left side of the body. All measurements were taken twice and then the mean thickness was calculated. If the first two measurements differed by more than 2 mm, a third measurement was taken and the two closest measurements were averaged.

Dietary variables
The consumption of milk and milk products was assessed by an interviewer-mediated 24-hour recall. In the nine-year olds, a qualitative food record completed the day before the interview with the help of parents served as a checklist for the data obtained during the recall. A food atlas was used to estimate portion sizes. Dietary data were processed by StorMats (version 4.02, Rudans Lättdata, Sweden) and analysed using the Swedish National Food database (version 99.1). The milk products of interest

were milk, soured milk (a traditional milk product, 'filmjölk', in Swedish), yoghurt and cheese, both reduced- and full-fat versions. As part of a broad-ranging questionnaire, parents of the participants were asked if their child had a chronic illness or adhered to a special diet.

Genetic analysis
For the genetic analysis genomic DNA was isolated from whole blood samples EDTA from the individuals with the QIAamp DNA Blood Mini Kit spin procedure. The DNA fragment spanning the -13910-C/T polymorphic site was amplified using a biotinylated forward-primer (5′-GGGCTGGCAATACAGATAAGATA-3′) and an unbiotinylated reverse-primer (5′-AGCAGGGCTCAAA GAACAATCTA-3′). The applied sequencing primer was: 5′-CTTTGAGGCCAGGG-3′. Sequencing was performed using a PSQ96 SNP reagent Kit and a PSQ 96MA system (Pyrosequencing AB) PSQ96MA 2.0.1 software. The procedure has been previously described in detail (21, 22).

Statistical analysis
Statistical analyses were performed with the Statistical Package for Social Sciences software (SPSS, version 13.0 for Windows; SPSS Inc, Chicago, IL). The data are presented as means and SD in Tables 1 and 3. Quantitative effects on the selected anthropometric and food intake variables were tested in two- and three-way ANOVA/ANCOVA models with age group (children or adolescents), sex (girls or boys) and LCT-13910 C >T genotype CT/TT vs. CC (LNP vs. LP) as fixed factors. Adjustments for daily energy intake were performed using the residual method when body fat percentage was dependent variable in ANCOVA models.

Ethics
Parents and 15-year olds gave specific written informed consent to participation in the present genetic study. The study was approved by the Research Ethics Committees of Örebro County Council and Huddinge University Hospital.

Results
The baseline characteristics of both girls and boys are shown in Table 1. Analysis of the LCT-13910 C >T genotype showed that the CT and TT genotypes, associated with LP, were found in 261 (87.0%) children and 329 (85.2%) adolescent subjects. The genotype LCT-13910 CC that is associated with LNP was found in 37 children (13.0%) and 57 adolescents (14.8%).

Table 2 shows an analysis of the overall effect of the LCT-13910 C >T polymorphism on the studied variables using the levels TT/CT vs. CC in a three-way ANCOVA/ANOVA model. Taken together, milk, soured milk and yoghurt intakes, specifically intakes of reduced fat

Table 1. Anthropometric characteristics, total energy intake (kJ/day) and dietary intake (g/day) at baseline ($N = 686$)

	Children		Adolescents	
	Girls ($n = 138$)	Boys ($n = 162$)	Girls ($n = 196$)	Boys ($n = 190$)
Age (years)	9.6 ± 0.4	9.6 ± 0.3	15.6 ± 0.4	15.6 ± 0.4
Height (cm)	138 ± 6.3	139 ± 5.7	165 ± 6.4	176 ± 7.7
Weight (kg)	33.5 ± 6.0	33.2 ± 5.6	56.9 ± 7.8	64.1 ± 10.7
BMI (kg/m^2)	17.3 ± 2.1	17.1 ± 2.2	20.9 ± 2.4	20.6 ± 2.6
Waist circumference (cm)	60.1 ± 5.4	60.5 ± 5.4	69.2 ± 5.7	73.5 ± 7.0
Body fat (%)	18.5 ± 5.3	15.8 ± 5.8	22.6 ± 4.1	13.0 ± 5.6
Energy intake (kJ/day)	$8,481 \pm 1,920$	$8,891 \pm 2,368$	$8,753 \pm 2,665$	$12,372 \pm 3,686$
Milk, soured milk and yoghurt intake (g/day)	562 ± 315	683 ± 340	501 ± 380	801 ± 521
Full-fat milk, soured milk and yoghurt intake (g/day)	218 ± 286	253 ± 292	134 ± 233	246 ± 381
Reduced fat milk, soured milk and yoghurt intake (g/day)	352 ± 295	423 ± 392	367 ± 343	579 ± 477
Milk intake (g/day)	489 ± 291	566 ± 367	410 ± 345	696 ± 477
Full-fat milk (g/day)	149 ± 230	162 ± 249	67 ± 185	151 ± 325
Reduced fat milk (g/day)	339 ± 292	404 ± 368	342 ± 334	544 ± 466
Soured milk intake (g/day)	48 ± 118	78 ± 169	52 ± 126	80 ± 192
Full-fat soured milk (g/day)	42 ± 112	62 ± 157	41 ± 119	58 ± 172
Reduced fat soured milk (g/day)	6.5 ± 44	16 ± 71	11 ± 50	22 ± 106
Yoghurt intake (g/day)	33 ± 101	32 ± 101	39 ± 109	51 ± 138
Full-fat yoghurt (g/day)	27 ± 95	29 ± 97	25 ± 82	37 ± 120
Reduced fat yoghurt (g/day)	5.9 ± 40	3.1 ± 29	14 ± 77	13 ± 70
Cheese intake (g/day)	18 ± 33	23 ± 38	30 ± 39	47 ± 63
Cream intake (g/day)	4.4 ± 16	2.2 ± 9	5.6 ± 22	6.1 ± 30
Ice cream intake (g/day)	21 ± 39	19 ± 44	13 ± 35	21 ± 52
LCT-genotype [n (%)]				
CC	19 (13.8)	18 (11.1)	28 (14.3)	29 (15.3)
CT	55 (40.0)	65 (40.1)	77 (39.3)	76 (40.0)
TT	63 (46.2)	78 (48.8)	91 (46.4)	85 (44.7)

versions, were significantly lower in individuals with LNP ($p < 0.001$). Analysed separately, milk intake (g/d) and specifically reduced fat milk (g/d) was lower ($p = 0.001$ and $p < 0.001$, respectively) in LNP children and adolescents. Body fat percentage (adjusted and unadjusted for energy intake) as well as daily energy intake were not related to the LCT-13910 C>T genotype.

Table 2 presents the distribution of milk and milk product intake-related variables, which were significantly related to the genotype in Table 2, stratified for age group and sex, and according to LCT-13910 C>T genotypes.

As shown in Table 3, after subsequent partitioning of milk and milk product intake-related variables, the LCT-13910 CC genotype was associated with statistically significantly lower intake of total milk, soured milk and yoghurt ($p = 0.002$ for children and $p = 0.023$ for adolescents). Milk intake was significantly lower in LNP children ($p = 0.005$) and in LNP adolescents ($p = 0.043$) compared to LP children and adolescents. Analysed by fat content, the CC genotype was associated with

significantly lower intake of total reduced fat milk, soured milk and yoghurt, in both children and adolescents ($p = 0.009$ and $p = 0.019$, respectively). Reduced fat milk intake was also significantly lower in LNP children and adolescents ($p = 0.010$ and $p = 0.001$, respectively).

No statistically significant interactions of the LCT-13910 C>T polymorphism with age and sex for the selected variables were found in either the two-way ANCOVA/ANOVA or three-way ANCOVA/ANOVA models.

In response to a question about the presence of chronic conditions in, or adherence to special diets by, their children, parents reported lactose intolerance in just six cases (two children and four adolescents). None of these cases demonstrated genetically determined LNP.

Discussion

We conducted the current study to investigate the possible differences in dairy product intake and in body fat mass among LP and LNP children and adolescents.

Table 2. Effects of genotype, sex and age group, on total energy intake (kJ/day), dietary intake (g/day) and body fat (%)

Effect	Genotype	Sex	Age group
P value[a]	(P)	(P)	(P)
Body fat[b]	0.906	<0.001	0.075
Energy	0.407	<0.001	<0.001
Milk, soured milk and yoghurt	<0.001	0.223	0.258
Full-fat milk, soured milk and yoghurt	0.588	0.754	0.061
Reduced fat milk, soured milk and yoghurt	<0.001	0.140	0.739
Milk	0.001	0.224	0.313
Full-fat milk	0.246	0.581	0.091
Reduced fat milk	<0.001	0.116	0.867
Soured milk	0.320	0.438	0.941
Full-fat soured milk	0.495	0.759	0.586
Reduced fat soured milk	0.427	0.291	0.225
Yoghurt	0.502	0.392	0.486
Full-fat yoghurt	0.749	0.989	0.597
Reduced fat yoghurt	0.461	0.101	0.661
Cheese	0.255	0.467	0.294
Cream	0.901	0.780	0.889
Ice cream	0.680	0.919	0.469

[a]Three-way ANOVA, LCT-13910 C >T (CC vs. CT/TT), sex and age group as factors.
[b]Three-way ANCOVA, LCT-13910 C >T (CC vs. CT/TT), sex and age group as factors; adjusted for daily energy intake (kJ/d).

There was a statistically significant difference between milk and milk product consumption in LP and LNP subjects. LNP was associated with a lower consumption of milk, soured milk and yoghurt. Interestingly, LP children and adolescents consumed statistically significantly more reduced fat milk than LNP subjects.

Concerning the key question of our study, whether LP and LNP influence the consumption of milk and milk products, which in turn could be associated with differences in body fat mass, we found no differences between LP and LNP as regards body fat mass.

A recent study, performed on the National Health and Nutrition Survey (NHANES) 1999–2004, showed that a dietary pattern characterised by greater milk intake was associated with increased BMI among preschool children (23). Sweden has traditionally one of the highest consumption rates of milk in the world (24) and we hypothesise that the potential physiologic effects of single food components, such as milk and milk products, may differ between countries due to their particular food and farming culture, agricultural inheritance and geographical as well as climatic singularities.

The higher consumption of reduced fat milk, compared to full-fat milk, in all age and genotype groups might reflect a secular trend. Krachler et al. (25) reported in 2005 a switch from 3% of fat milk to 1.5% of fat milk among northern Swedes that occurred between 1986 and 1999.

About 83% of the LNP individuals consumed some amount of milk. On average, they consumed 421 g (95% CI 399, 502) milk per day. This is compatible with many

Table 3. Effects of genotype on milk intake related variables significant in Table 2 (stratified by age group)

Genotype	Age	Sex	Milk, soured milk and yoghurt	Reduced fat milk, soured milk and yoghurt	Milk intake (g/day)	Reduced fat milk (g/day)
CC	Children	Girls	471±299	269±235	412±276	203±292
		Boys	427±192	355±316	352±183	269±235
	Adolescents	Girls	381±328	202±265	313±294	190±260
		Boys	380±636	387±436	573±576	365±428
CT	Children	Girls	577±330	355±316	477±304	339±315
		Boys	689±435	442±421	597±412	427±402
	Adolescents	Girls	891±516	390±629	424±734	368±390
		Boys	891±557	629±510	734±502	581±497
TT	Children	Girls	598±306	390±291	524±287	381±290
		Boys	717±380	438±397	582±344	412±361
	Adolescents	Girls	525±343	428±306	428±306	368±290
		Boys	817±434	703±411	703±411	572±440
Effect LCT[a]	Children		0.002[b]	0.009[b]	0.005[b]	0.010[b]
(P)	Adolescents		0.023[b]	0.019[b]	0.043[b]	0.001[b]

[a]LCT-13910 C >T polymorphism.
[b]Two-way ANOVA: LCT-13910 C >T (CC vs. CT/TT) and sex as factor.

studies showing that LNP subjects can tolerate a certain amount of lactose intake per day (6, 26–28).

Concerning the high prevalence of LNP (14%) compared to the traditional prevalence data of LNP in Sweden (2%), we have found a trend towards an increasing prevalence of LNP in Sweden. This increase seems to have taken place in the course of the second half of the twentieth century due to higher immigration rates to Sweden after the Second World War (29).

The strengths to be considered in this study are that we use the concept of Mendelian randomisation (MR), by subdividing genotypes in LP and LNP, to readdress the question of whether nutrigenetically defined factors, like milk and milk product intake, affect body fat mass in children and adolescents. MR studies modifiable causes of disease in genetic epidemiology. A functional genetic variant, in our study LCT-13910 C >T polymorphism, acts as proxy for modifiable lifetime exposure patterns, i.e. milk consumption. The LCT-13910 C >T polymorphism is known to influence the exposure pattern, milk consumption (2, 5, 6, 30–32). In addition, we analysed both, full fat and reduced fat varieties as regards the key question of this work.

Limitations of this study include the drawbacks inherent to 24-hour dietary recall, which may not fully reflect long-term food intake behaviour (33). Yet the genetically determined condition of LP or LNP, which we studied in this work, is not subject to changes during life. The results should be interpreted bearing in mind the limitations inherent in any cross-sectional study. Furthermore, results of genetic epidemiological studies obtained in one defined population should not be applied without reserve to other populations or ethnic groups.

The age of onset of LNP shows a wide regional and ethnical variation (4). In persons of European descent, the onset of genetically determined LNP is rarely seen before five years of age (34–36); Finnish children who develop LNP have done so by the age of 10 (4). Thus, it could be assumed that the majority of children and almost all adolescents with LCT-13910 CC genotype had developed manifest LNP at the time of inclusion in this study. However, the correlation between LNP and self-reported 'lactose intolerance' has been previously suggested to be poor (37–39), which we confirm in this study: six cases parents reported 'lactose intolerance' in their children, in two children and four adolescents, and none of them were LNP according to genotyping data.

In conclusion, LP is linked to an overall higher milk and dairy intake, but is not linked to higher measures of body fat mass in children and adolescents.

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