Intake of total dietary sugar and fibre is associated with insulin resistance among Danish 8–10- and 14–16-year-old girls but not boys. European Youth Heart Studies I and II

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Abstract

Objective: To examine the dietary intake of total sugar, added sugar, non-added sugar and starch as well as dietary fibre and glycaemic index (GI) and their respective associations with insulin resistance.

Design: Mixed linear models were used to study both cross-sectional and prospective associations between carbohydrate components and insulin resistance separately in girls and boys. Diet was assessed by a single 24 h recall interview and insulin resistance was calculated using the homoeostasis model assessment (HOMA).

Setting: The Danish part of the European Youth Heart Studies (EYHS) I and II.

Subjects: Girls and boys at 8–10 and 14–16 years from EYHS I (n 651) and 8–10-year-olds from baseline followed up 6 years later in EYHS II (n 233).

Results: Among girls, a difference in dietary total sugar of 43 g/MJ was associated with a 1SD difference of HOMA and a difference in dietary fibre of 28 g/MJ was associated with a 1SD difference of HOMA, independent of age, maturity and other confounders (both P < 0.03). No baseline associations were found among boys and no prospective associations were found in either sex.

Conclusions: Dietary intake of total sugar may play an adverse role and fibre may play a beneficial role in concurrent insulin resistance among girls but not boys. Sex differences may be due to differences in maturity, physical activity, food patterns and selective reporting behaviours.

The prevalence of overweight and type 2 diabetes in children has continued to increase since the early 1990s(1,2). Controlling obesity and insulin resistance through diet and physical activity is essential in limiting metabolic disturbances and type 2 diabetes(3). The short absorption time that follows the consumption of some dietary carbohydrates may impair blood glucose control, which may result in increased release of non-esterified fatty acids, hyperinsulinaemia(4) and peripheral insulin resistance(5). A diet with a content high in fibre, low in refined sugars with a low-dietary glycaemic index (GI) is required for preventing glucose intolerance, insulin resistance and type 2 diabetes in adults(6). There is a lack of studies on carbohydrate nutrition and insulin resistance among healthy children. Our aim was to study the hypothesis that high intake of total sugar, added sugar and starch, and a high dietary GI as well as low intake of non-added sugar and dietary fibre in children are associated with insulin resistance concurrently and 6 years later.

Design

Data are based on the Danish part of the European Youth Heart Studies (EYHS) I and II, a prospective multicentre survey of lifestyle and cardiovascular risk factors in childhood and youth. The studies were carried out from September 1997 to June 1998 and again from September 2003 to June 2004(7) and included schoolchildren from twenty-five primary schools in Odense, Denmark. Schools

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were stratified according to the location and socio-economic status of the geographical area. From each stratum, a two-stage cluster sampling was applied with the schools as the primary unit and the children as the secondary unit. Schools were selected using probability proportional to school size and children were allocated code numbers and randomly selected using random number tables. International standardised procedures were followed and investigators were either health professionals or trained personnel. Parents gave written consent for their child to participate, and children had the option to withdraw from the study at any time. The study followed the principles stipulated in the Helsinki Declaration and was approved by the scientific ethics committee of the local counties of Vejle and Funen, Denmark (VF 20030067).

Participants
Of 1019 children of predominantly Danish ethnicity, 341 girls and 310 boys from the third (58%) and ninth (42%) grades were included in the cross-sectional analyses at baseline. The study population was reduced progressively due to missing data on the following variables as percentage of the eligible population of 1019 children: homoestasis model assessment (HOMA; 9%), diet (6%), sexual maturity levels (1%), body anthropometrics (1%), cardiorespiratory fitness (6%), parents’ education (13%) and physical activity (1%). Follow-up data on serum glucose and insulin existed for 138 girls and 103 boys. The overall participation rates were 75% at baseline and 65% at follow-up. The children included in the study were more mature and more active than those excluded at baseline, but not at follow-up, after Bonferroni correction (data not shown).

Insulin resistance
Blood samples were obtained from an antecubital vein after children had fasted overnight. Samples were frozen at −80°C until further analysis. Serum glucose concentrations were quantified using a hexokinase method and serum insulin concentrations using an enzyme immunoassay method at WHO-certified laboratories at baseline (Bristol, England) and at follow-up (Cambridge, England)(7). Insulin resistance was evaluated using the HOMA: insulin (μU/ml) × glucose (mmol/l)/22.5(10) and standardised to the mean of each sex (Z-scores). That is, the means of HOMA Z-scores are defined as zero with a standard deviation of one in each of the study populations of girls and boys.

Dietary intake
The individual food intake was assessed using one 24 h recall interview supplemented with a qualitative food record from the same day. Standard measures were visualised with glasses, plates and spoonfuls. The interviews were conducted Monday–Friday and lasted 20–30 min. Third graders were assisted by a parent. Foods were converted into nutrients using the software program Dankost 3000 (Danish Catering Center, Copenhagen, Denmark), referring to national food composition lists(9). The six dietary carbohydrate components were measured as: (i) total sugar comprising all mono- and disaccharides; (ii) added sugar comprising liquid and solid sugars that are not naturally present in foods; (iii) non-added sugar comprising sugars that are naturally present in foods; (iv) dietary fibre comprising soluble and insoluble fibres; (v) starch comprising amylose and amylopectin; and (vi) dietary GI calculated by summing up the GI of each carbohydrate food item (GIi) weighted by the specific contribution of each food item (i) to the total amount of available carbohydrates (CHO), except dietary fibres: dietary GI = Σ (GIi × CHO/CHO)GI(10). GI values were calculated using international tables with white bread equal to 100 GI units(10). Further details are presented elsewhere(11).

Confounding factors
Children and parents or guardians completed electronic questionnaires with information on sex, date of birth and physical activity level of the child, and educational status of both parents. Physical activity level was categorised as no exercise, occasional exercise or regular exercise. Sexual maturity was assessed using five development stages of breasts or genitals and pubic hair. Children were grouped as prepubertal with Tanner stage 1, pubertal with Tanner stages 2, 3 and 4, and postpubertal with Tanner stage 5(12). Height without shoes was measured to the nearest 0.5 cm and weight with light clothing to the nearest 0.1 kg.

Statistical analysis
Statistical analyses were carried out in the SAS for Windows statistical software package version 9.1 (SAS Institute Inc., Cary, NC, USA). Linear regressions of each carbohydrate component in association with insulin resistance were analysed in cross-sectional and prospective models, stratified by sex. The random effect of primary school was included in the models to counterbalance the effect of schools deriving from the cluster-sampling design. Models were additionally adjusted for the fixed effects of age, BMI, sexual maturity (at both years in prospective analyses), self-reported physical activity and mother’s education and other significant carbohydrate components. Statistical significance was determined by a two-sided probability level of ≤5% for the results and ≤10% for selecting confounders.

Results
Baseline characteristics of anthropometrics, lifestyle and clinical parameters among girls and boys included in cross-sectional and prospective analyses are described in Table 1. Compared with girls, boys were older, more active, had higher serum glucose and consumed more...
total energy, less carbohydrates as a proportion of total energy and less dietary fibre in g/MJ. However, the only sex difference remaining after Bonferroni corrections was the fibre intake. Among girls, HOMA Z-score was directly associated with total dietary sugar intake and inversely associated with dietary fibre after adjustment for age, sexual maturity, BMI, physical activity, mother’s education and school location (Fig. 1). The magnitude of the relationships was that 1 SD difference of HOMA was associated with a difference in dietary total sugar of 43 g/MJ and a difference in dietary fibre of −8 g/MJ. After Bonferroni correction, results became non-significant. Interactions were found between total dietary sugar intake and sex (*P = 0.001) as the only carbohydrate component. Among girls, interactions were found between physical activity and dietary intake of total sugar (P = 0.001) and fibre (P = 0.054) such that the associations between diet and HOMA Z-scores were stronger for girls with a lower rather than a higher activity level. No interactions were identified for grade, sexual maturity or overweight.

Between baseline and follow-up, HOMA increased from 1.8 (SD 1.0) to 2.2 (SD 1.0) units among girls and from 1.7 (SD 0.9) to 2.1 (SD 1.0) HOMA units among boys (P < 0.05). None of the carbohydrate components was associated with HOMA Z-scores 6 years later among girls or boys after adjustment for the same confounders as mentioned above and baseline HOMA Z-scores and sexual maturity at follow-up (Table 2). In order to study the impact of changes in BMI, physical activity and dietary intake, associations were additionally adjusted for BMI in 2001, physical activity in 2003–2004, and carbohydrate components in 2003–2004 in 117 girls and 82 boys (data not shown). No associations were found, except for a strengthened negative estimate for dietary added sugar among girls compared with the analyses without follow-up lifestyle data presented in Table 2. This result did not remain significant after Bonferroni correction.

### Discussion

Our study suggests a link between the dietary intake of total sugar and fibre and insulin resistance among girls in a sizeable sample of healthy Danish school children at 8–10 and 14–16 years old. To obtain a decrease in insulin resistance of one standard deviation from either an increased fibre intake or a decreased total sugar intake, a dietary change of 3.5 times the mean intake is required. Dietary changes will normally affect more than one carbohydrate component at one time and findings may still be clinically significant for children with a low fibre intake and a high intake of total sugar. In line with our findings, high intake of total dietary sugar was associated with increased insulin secretion and increased insulin resistance in a high-risk population of overweight Latino adolescents with a family history of type 2 diabetes (13). Previous findings among overweight, adolescent girls found no specific effect of dietary fibre intake on insulin secretion after 12 weeks’ lifestyle intervention, independent of added sugar intake (14). Danish girls with an overall fibre-rich diet tended to under-report their total dietary intake to a larger extent than girls with a lower dietary fibre intake (data not shown). The results on dietary fibre may therefore be partly explained by dietary-reporting behaviour. No associations were found between dietary GI and insulin resistance. Consistent with our findings, a study using repeated 24 h interviews found...
no association between dietary GI and insulin resistance in overweight children with a family history of CVD(13). In the latter study, GI values were assessed using similar international tables to those used in the present study. Another study has found that unadjusted fasting insulin concentrations were directly associated with dietary GI among 8-year-old children(15). However, the study was based on unadjusted analyses and may be confounded by sex, puberty, physical activity or body fatness. We found no association between dietary starch and insulin resistance, and no previous studies have investigated the effect of dietary starch on insulin resistance in children. The cross-sectional results among girls extend prior findings of total dietary sugar to a sample of both normal and overweight children. Sex differences in lifestyle parameters, food compositions and physical activity are likely to explain why we find significant associations among girls and not among boys. Given that girls were less active than boys, girls may have a reduced metabolic flexibility compared with boys, and thus increased susceptibility to the diet.

During the 6 study years, girls progressed from either prepuberty to puberty or puberty to postpuberty, whereas boys progressed from prepuberty to puberty. It has been shown that insulin secretion increases with the onset of puberty, returning to prepubertal levels in postpuberty(16). Although analyses in the present study were adjusted for the maturity stage at baseline and follow-up, it is likely that the non-linear development of insulin resistance has biased the prospective results. Changes in lifestyle from baseline to follow-up did not seem to influence the prospective results. Statistical power was sufficient in the prospective analyses, and the non-significant results may be caused by a smaller variation in the change in insulin resistance between studies than baseline insulin resistance.

Some methodological issues may have influenced the validity of the results of the present study. Both diet and physical activity assessments were based on self-reported data, which may have resulted in selective reporting behaviour. More 24 h recall interviews for each person could have added to the accuracy of the dietary data, as a single diet recall represents only a snapshot of a child's habitual dietary intake, and therefore, random errors due to day-to-day variations are likely to have blurred true associations. However, another study on diet, obesity and insulin resistance among children showed similarity among the dietary and clinical data of children with a single 24 h recall interview compared with those with repeated interviews(15). The advantages of the 24 h recall interview are that the time taken by the child to complete the interview is relatively less and that reading and writing skills are not required. The disadvantages are that the child could have difficulty remembering what and how much they consumed during the last 24 h. The GI assessment may be limited due to a number of reasons. First, the GI assessment was based on food composition tables, comprising primarily Australian and American foods(10). Second, the studies referenced in the tables have been conducted primarily in healthy adults and small sample sizes(17,18) and may not replicate to other groups than healthy adults. Third, the 24 h interview method was not constructed to distinguish between preparation or processing of foods, e.g. raw, peeled and heated foods, which could have affected the physiological role of starch and other carbohydrate components influencing the GI(19). Although objectively measured physical activity using accelerometers has been assessed in EYHS, we chose to use self-reported activity measures because approximately one-third of the children did not wear the accelerometers and the self-reported measure was more strongly associated with insulin resistance than was the accelerometer measure. Technically, significant

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**Fig. 1** Insulin resistance measured as HOMA Z-scores of 8–10- and 14–16-year-old girls (– – ○ – ; n 341) and boys (– – ● – – ; n 310) from the Danish part of the European Youth Heart Study I as a function of (a) quintiles of total dietary sugar intake adjusted for primary school, age, sexual maturity, BMI, mother’s education, physical activity, and dietary fibre intake and (b) quintiles of total dietary fibre intake adjusted for primary school, age, sexual maturity, BMI, mother’s education, physical activity, and total dietary sugar intake. Error bars indicate the SEM.
findings could be a result of statistical artefacts due to multiple testing, as 5% statistical uncertainty is accepted. The diet was not assessed on Fridays and Saturdays, and the actual proportion of dietary added sugar intake may therefore be higher than the measured daily intake in the present study. This might not have affected the findings, as the ranking of individuals is probably the same.

In conclusion, the results suggest that high dietary intake of total sugar and low intake of dietary fibre may be associated with insulin resistance among 8–10-year-old Danish girls but not boys. The cross-sectional finding confirms current recommendations for consuming dietary fibre and minimising added sugar intake. However, the study should be replicated using a more precise diet method. No prospective associations were found between dietary carbohydrate components and insulin resistance. Future research should focus on large-scale, quantitative studies with frequent follow-up intervals during the progression of puberty and more precise diet assessments.

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