BMI at age 8 years is influenced by the type 2 diabetes susceptibility genes HHEX-IDE and CDKAL1.

Abstract:
To determine whether HHEX-IDE and CDKAL1 genes, which are associated with birth weight and susceptibility to type 2 diabetes, continue to influence growth during childhood. BMI, weight, and height at age 8 years expressed as age- and sex-corrected standard deviation scores (SDS) against national reference data and single-nucleotide polymorphism genotyping of HHEX-IDE and CDKAL1 loci were analyzed in 646 prospectively followed children in the German BABYDIAB cohort. All children were singleton full-term births; 386 had mothers with type 1 diabetes, and 260 had fathers with type 1 diabetes and a nondiabetic mother. Type 2 diabetes risk alleles at the HHEX-IDE locus were associated with reduced BMI-SDS at age 8 years (0.17 SDS per allele; P = 0.004). After stratification for birth weight, both HHEX-IDE and CDKAL1 risk alleles were associated with reduced BMI-SDS (0.45 SDS, P = 0.0002; 0.52 SDS, P = 0.0001) and weight-SDS (0.22 SDS, P = 0.04; 0.56 SDS, P = 0.0002) in children born large for gestational age (>90th percentile) but not children born small or appropriate for gestational age. Within children born large for gestational age, BMI and weight decreased with each additional type 2 diabetes risk allele (approximately -2 kg per allele; >8 kg overall). Findings were consistent in children of mothers with type 1 diabetes (P< 0.0001) and children of nondiabetic mothers (P = 0.008). The type 2 diabetes susceptibility alleles at
HHEX-IDE and CDKAL1 loci are associated with low BMI at age 8 years in children who were born large for gestational age.