Genetics, rapid childhood growth and the development of obesity

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A 38-year longitudinal study of New Zealanders suggests that individuals with higher genetic risk scores were more likely to be chronically obese in adulthood, according to a report published in the June issue of *Archives of Pediatrics & Adolescent Medicine*, a JAMA Network publication.

Obesity is capable of being inherited and genome-wide association studies (GWASs) have started to uncover the molecular roots of heritability by identifying multiple single-nucleotide polymorphisms (SNPs) associated with higher adult body mass index (BMI), the authors write in their study background.

"In this study, we asked how SNPs with replicated GWAS evidence for association with adult BMI relate to growth across the first four decades of life and to adult obesity in a birth cohort followed up prospectively from birth through 38 years of age," Daniel W. Belsky, Ph.D., of Duke University, Durham, N.C., and colleagues write in the study background.

Study participants were members of the Dunedin Multidisciplinary Health and Development Study, an investigation of health and behavior in a complete birth cohort. The 1,037 study members (52 percent were male) were born between April 1972 and March 1973 in Dunedin, New Zealand. Assessments were performed every few years starting at birth until 38 years.

Children with higher genetic risk scores (GRSs) had higher BMIs at

every age assessed from age 3 through 38 years. Children at high genetic risk were 1.61 to 2.41 times more likely to be obese in their second, third and fourth decades of life and were 1.90 times more likely to be chronically obese across more than three assessments compared with children at low genetic risk, according to study results.

Adiposity rebound, when children begin to gain body fat after losing it during early childhood, occurred earlier in development and at higher BMI for children at higher genetic risk, the results indicate.

Higher genetic risk also predicted faster growth and increased obesity risk in children with normal-weight and overweight parents, the study results note. The authors comment that the GRS contributed "independent and additive information" to the prediction of children's growth and their risk for obesity in adulthood beyond the family history information.

"Thus, the results present compelling evidence that SNPs identified in GWASs of adult BMI and other obesity-related phenotypes predispose to more rapid growth in childhood, leading to increased risk for obesity in adulthood, and provide information not forthcoming from a simple analysis of family history," the authors conclude.

In an editorial, Jose R. Fernandez, Ph.D., of the University of Alabama at Birmingham, writes: "This study provides clear evidence regarding the role of biological risk attributed to the development of obesity and suggests that genetic risk for obesity affects fat accumulation through accelerated growth in early childhood."

Fernandez continues: "Further insights and implications of the study, however, cause concern as much as they fascinate. Given that the associations identified were independent of parental body mass index, the findings from Belsky et al may imply a degree of genetic

determinism that challenges overall public health recommendations worldwide in a simple question: What about the role of the environment across the life span?"

"Attempting to translate the findings from Belsky and colleagues to clinical practice would be naïve at this point when more research is clearly needed to fully understand the genetic basis of many complex traits. ... Until we know more, and perhaps after we know more, preventive behaviors should be each individual's priority so that we all achieve the best health possible regardless of genetic profiles. Without taking this approach, we might risk the mistake of allowing genetic predisposition to become genetic determinism," Fernandez concludes.

More information: *Arch Pediatr Adolesc Med.* 2012;166[6]:515-521. *Arch Pediatr Adolesc Med.* 2012;166[6]:576-577.

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