Pediatric RESEARCH

EDITORIAL

Genetic background of obesity

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Childhood obesity is an extremely important public health problem and is associated with several diseases in the adult: hypertension, cardiovascular diseases, diabetes mellitus II, skeleton problems, and psychological disorders. According to OECD, children suffer mostly on that disorder because of less chances for education and less life satisfaction.[1] So far, the etiology of obesity is not very well understood; the explanation in textbooks of pediatrics is given in the following way: humans have the capacity to store energy in adipose tissue, allowing improved survival in times of famine; therefore, obesity results from an imbalance of caloric intake and energy expenditure.[2] If one looks to historical publications, one of the first clinical descriptions has been done by A. Froehlich, who reported on a boy with extreme obesity, growth retardation, vision problems, and polydipsia, which was caused by a tumor of the hypophysis.[3] The Austrian Paediatrician and assistant of Prof. Cl.v. Pirquet, E. Nobel, differentiated between exogenous (anomaly of the appetite regulator caused by overnutrition and laziness) with normal metabolism and endogenous obesity (caused by disorders of fat metabolism).[4] Richard Priesel, chairman of Pediatrics in Innsbruck, described two other forms, the Gigantism with progressed bone age and the endocrine thyreogenic obesity caused by hypothyreodism.[5]

In the 1960s and 1970s of the past century, research has been focused on the fat cell, speculating that the fat cell number is fixed at the early life and can be set at some higher level, which leads to adult obesity.[6,7] Since the concept of a fixed fat cell number has been criticized as being fatalistic, the association between fat cells and the central nervous system to alter feeding behavior and metabolism has been claimed. Later on, the influence of hormones as a function of cell size and cell number has been hypothesized.[7–9] It was in 1973 as Brook and J. LLoyd found that the degree of hyperinsulinemia could not be predicted by the fat cell size. At the end of the past century, results of research in adults showed that metabolic dearrangements, such as disturbed glucose metabolism, lipoprotein disorders, and hypertension, are strongly associated with changes in the whole body, such as atherogenesis, fatty liver, silent inflammation, and development of overt diabetes mellitus.[10,11] Furthermore, it has been shown that not everybody who is obese goes in that direction. This research led to the definition of the so-called "metabolic syndrome," for which a couple of different definitions have been developed.[12] One result of these studies is the differentiation of the "metabolic healthy" and the metabolic "unhealthy individual." The discriminators usually are fasting glucose, triglycerides, HDL-C and blood pressure. There are studies in adults showing that the lower expression of inflammatory genes and higher expression of mitochondrial genes in the adipose tissue can differ between these two forms.[13] On the other hand, Das et al.[14] found that the transcriptome profile in the subcutaneous tissue is different in genes involved in cardiovascular disease-related processes and immune/inflammatory responses.

In this regard, many researchers were unsure, which mechanisms—genetic or environmental—could play a pivotal role.

The paper by Plaza-Florido studies for the first time in two groups of obese children, one the metabolic healthy and the other the metabolic unhealthy subjects from the whole-blood transcriptome; surprisingly, they were able to show that the two groups revealed a distinct pattern of gene expression, which was linked to metabolism, mitochondrial, and immune function. They were able to identify 32 genes that were differentially expressed in children with healthy compared to unhealthy obesity. They found the most upregulated gene is *TRIMI1* and the most downregulated expression of the *ADAMTSL2* gene. The first is involved in the degradation of AIM2 inflammasome, which leads to the maturation of proinflammatory cytokines. In fact, the healthy obese children had a favorable inflammatory profile compared with the unhealthy obese children.

Furthermore, the authors were able to show that inflammatory markers tumor necrosis factor-α and interleukin-6 were significantly higher in children with unhealthy compared to those with healthy obesity. In addition, this study has shown that genes that are involved in the fatty acid synthesis and cholesterol metabolism (*CYP3A5* and *IRF2BP*) were higher expressed in whole blood.

These findings are without any doubt a very important mosaic stone in the understanding of the possible metabolic effects of obesity; it adds also some explanation why some children with the typical signs of the metabolic syndrome develop degenerative diseases and some not.

ADDITIONAL INFORMATION

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