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REVIEW ARTICLE

Obese fathers lead to an altered metabolism and obesity in their children in adulthood: review of experimental and human studies☆

Q1 Fernanda Ornellas, Priscila V. Carapeto, Carlos A. Mandarim-de-Lacerda*, Marcia B. Aguila

Universidade do Estado do Rio de Janeiro (UERJ), Centro Biomédico, Laboratório de Morfometria, Metabolismo e Doenças Cardiovasculares, Rio de Janeiro, RJ, Brazil

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KEYWORDS
Q2 Paternal obesity;
Programming;
Obese child;
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Epigenetics

Abstract
Objective: To discuss the recent literature on paternal obesity, focusing on the possible mechanisms of transmission of the phenotypes from the father to the children.
Sources: A non-systematic review in the PubMed database found few publications in which paternal obesity was implicated in the adverse transmission of characteristics to offspring. Specific articles on epigenetics were also evaluated. As the subject is recent and still controversial, all articles were considered regardless of year of publication.
Summary of findings: Studies in humans and animals have established that paternal obesity impairs their hormones, metabolism, and sperm function, which can be transmitted to their offspring. In humans, paternal obesity results in insulin resistance/type 2 diabetes and increased levels of cortisol in umbilical cord blood, which increases the risk factors for cardiovascular disease. Notably, there is an association between body fat in parents and the prevalence of obesity in their daughters. In animals, paternal obesity led to offspring alterations on glucose-insulin homeostasis, hepatic lipogenesis, hypothalamus/feeding behavior, kidney of the offspring; it also impairs the reproductive potential of male offspring with sperm oxidative stress and mitochondrial dysfunction. An explanation for these observations (human and animal) is epigenetics, considered the primary tool for the transmission of phenotypes from the father to offspring, such as DNA methylation, histone modifications, and non-coding RNA.

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* Corresponding author.
E-mails: mandarim@uerj.br, mandarim.ca@gmail.com (C.A. Mandarim-de-Lacerda).

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Conclusions: Paternal obesity can induce programmed phenotypes in offspring through epigenetics. Therefore, it can be considered a public health problem, affecting the children's future life.

PALAVRAS-CHAVE
Obesidade paterna;
Programação;
Criança obesa;
Programação de doenças crônicas;
Epigenética

Pais obesos levam a metabolismo alterado e obesidade em seus filhos na idade adulta: revisão de estudos experimentais e humanos

Resumo
Objetivo: Discutir a literatura recente sobre obesidade paterna, focalizando os possíveis mecanismos de transmissão dos fenótipos do pai para os filhos.
Fontes: Uma revisão não-sistemática no banco de dados PubMed encontrou poucas publicações com obesidade paterna implicada com a transmissão adversa das características à prole. Artigos específicos sobre epigenética também foram avaliados. Como o assunto é recente e ainda controverso, todos os trabalhos foram considerados independentemente do ano de publicação.
Resumo dos achados: Estudos em seres humanos e animais estabeleceram que a obesidade do pai prejudica seus hormônios, metabolismo e função espermática, que pode ser transmitida à prole. Em humanos, a obesidade paterna resulta em resistência à insulina/diabetes tipo 2 e aumento do nível de cortisol no sangue do cordão umbilical, que aumenta os fatores de risco para doença cardiovascular. Notavelmente, existe associação entre a gordura corporal nos pais e a prevalência de obesidade em suas filhas. Em animais, pais obesos condicionam, na prole, a homeostase glicose-insulina, lipogênese hepática, hipotálamo/comportamento alimentar, rim, prejudicam o potencial reprodutivo da prole masculina com estresse oxidativo espermático e disfunção mitocondrial. Uma explicação para estas observações (humanos e animais) é a epigenética, considerada a ferramenta básica para a transmissão de fenótipos do pai à prole, como a metilação do DNA, modificações nas histonas, e RNA não codificante.
Conclusões: A obesidade paterna pode induzir fenótipos programados na prole através da epigenética. Portanto, a obesidade paterna pode ser considerada um problema de saúde pública, afetando a vida futura das crianças.

Introduction

Obesity has been growing in a disorderly way, constituting a real epidemic described as ''globesity,'' which represents a serious public health problem nowadays.[1]

It is now known that the risk of developing obesity and metabolic syndrome (MS) in adulthood may be influenced by the initial period of life, especially through inadequate nutrition available to the fetus and newborn.[2,3] ''Programming'' is the process by which early life factors may influence the offspring's health in adulthood. Programming is considered an essential mechanism for the establishment of obesity and metabolic changes in the offspring.[4,5] Various models are used to understand the mechanisms associated with programming, in which the hormonal and metabolic environment during the prenatal or postnatal period is altered through changes in maternal nutritional status.[6–8]

Most epidemiological and experimental studies have focused on the maternal influence on offspring's health. However, recent experiments with rodents have demonstrated that the paternal involvement affects glucose homeostasis and the lifetime of pancreatic islets in female offspring.[9] Clinical and animal testing have challenged conventional ideas about metabolic programming, suggesting that something else might act in this process via paternal programming. Recent studies now indicate that paternal metabolic health at conception can also impact children's health, and that obese fathers are more likely to generate an obese child.[10]

This review reports the recent findings and proposed mechanisms involved in paternal programming of the offspring.

Human studies

Studies in humans analyzed the relationship between paternal lifestyle-related factors, environmental exposure factors, and offspring's health outcome in early and later life, suggesting that paternal effects may play a significant role in the pathogenesis of offspring chronic diseases in later life (e.g., insulin resistance and type 2 diabetes). More than 60% of all adults are classified as overweight or obese in most Westernized societies; as the prevalence of obesity increases, it is responsible for an ever-larger proportion of the overall burden of disease.[9,11]