Do FTO gene mutations raise the risk of overweight and obesity?

Steve Minsky

American College of Healthcare Sciences

Abstract

Screenings for genetic mutations, also known as single nucleotide polymorphisms, are becoming popular tools for prevention of lifestyle-related disease; however, data on how the negative expression of genes affect, or lead to, disease is still relatively new and undefined.

The purpose of this study was to assess whether fat mass and obesity-associated gene mutations raise the risk of overweight and obesity. Of the 55 published studies evaluated, seven were chosen. The studies covered a variety of different age groups, including children, pregnant women, and adults; genetic screenings were performed on subjects from all over the world, including Nigeria, Romania, and United Arab Emirates. The evidence reinforced the idea that fat mass and obesity-associated gene mutations raised the risk of overweight and obesity. Data elucidated several biochemical methods that were negatively manipulated by fat mass and obesity-associated gene mutations, including impaired brown fat thermogenesis and mitochondrial function. Several studies purported that negative genetic expression enhanced visual food cues, thus leading to increased appetite. The evidence emphasized one preventive tool that can be implemented at every corner the world to mitigate negative genetic expression: exercise. For public health professionals to have the ability to use genetic screenings to prevent or treat overweight and obesity would be valuable because genetic screenings are not only economical, but non-invasive.

Keywords: fat mass and obesity-associated gene, FTO, overweight and obesity, rs1421085, rs17817449, rs9939609, single nucleotide polymorphisms, SNPs.

Introduction

Also known as alpha-ketoglutarate-dependent dioxygenase protein (AlkB), fat mass and obesity-associated protein (FTO) is an enzyme that is encoded by the FTO gene, located on chromosome 16. This gene is related to non-heme iron and 2-oxoglutarate-dependent oxygenase superfamily (Genetics Home Reference, paragraph 1). Evidence demonstrate a part in nervous and cardiovascular systems, as well as a strong connection to body mass index, obesity risk, appetite, satiety, and type 2 diabetes (Mittal, Srivastava, & Srivastava, 2016).

Evidence suggests an increase in susceptibility to obesity, owing to increased desire to eat and diminished satiety after meals in FTO mutations carriers. Carriers may be more likely to lose weight through diet and lifestyle modifications than non-carriers, but are more susceptible to weight regain after discontinuation of a weight management program (van der Klaauw & Farooqi, 2015).

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Results

Martins, Trujillo, Faria, Struchiner, and Kac (2016) assessed the link between FTO mutations, specifically the rs9939609 gene, and alterations in maternal body weight during pregnancy. The authors examined data from a cohort of women at first trimester, second trimester, third trimester, and postpartum who were weighed prepregnancy, during pregnancy,

and postpartum. The results divulged that not only did women with the AA genotype of the FTO (rs9939609 locus) gene have significantly higher prepregnancy weight than those with AT/TT genotypes, but were heavier at first and second trimesters, and approximately 9 kilograms heavier throughout their pregnancies.

In a study to examine if the FTO genotype increases the risk of obesity, Melhorn et al. (2018) searched impaired central nervous system functions having to do with satiety perception. Using a functional MRI, the authors screened AA FTO genotype (rs9939609 locus) subjects and AT or TT FTO genotype subjects for appetite, appetite-regulating hormones, caloric intake at a buffet meal, and brain response to visual food cues before and after a meal. The authors concluded that subjects with AA alleles of the FTO gene, when presented with visual cues of calorically dense foods, did not achieve satiety compared to those with AT and TT alleles, and that visual cue brain activation in those with AA FTO alleles consume more calories compared with those with AT and TT alleles.

To ascertain whether the FTO gene is the strongest link to obesity, Claussnitzer et al. (2015) pored over five categories of genetic function in mice and humans. Using CRISPR-Cas9 genome editing, the authors found that the rs1421085 FTO allele impairs mitochondrial thermogenesis in adipocyte precursor cells, thus turning beige adipocytes into white adipocytes at a higher rate. The authors concluded that the FTO gene can be manipulated to act with pro-obesity or anti-obesity effects.

Oyeyemi, Ologunde, Olaoye, and Alamukii (2017) investigated the interaction between the FTO rs9939609 genotype and obesity, physical activity, time spent sitting, and energy intake. The authors canvased randomly selected, unrelated young adults with and without obesity and

screened their FTO gene. The results showed that obese adults were much more likely to have the AA FTO allele, especially when physical activity was low, but the authors were able to show that physical activity, reduced energy intake, and less time spent sitting had a positive effect with regard to body mass index.

In a study evaluating the link between FTO genetic mutations and obesity in children, Parthasarthy et al. (2017) investigated obese versus normal weight children. The authors found that 57% of obese children had the AA allele compared with 35% in normal weight children; and obese children with the AA allele had the least physical activity; and obese children with the AT allele had the highest intake of calories. The authors purport that diet and lifestyle modifications can have a significant impact on muting negative expression of the FTO gene.

In a trial examining the Emirati population, Kahn, Chehadeh, Abdulrahman, Osman, and Al Safar, (2018) assessed the association between obesity and the FTO and VDR gene mutations. Researchers performed a case control study evaluating genetic data from obese, overweight, and normal weight subjects from the United Arab Emirates. The authors state that while they did not find an association between vitamin D receptor gene (VDR) mutations and obesity, they did find a significant association between the AA allele of the FTO genotype and increased body mass index (BMI).

Duicu, Mărginean, Voidăzan, Tripon, and Bănescu (2016) aimed to connect FTO gene variants rs9939609 and rs17817449 with fasting glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, adiponectin and leptin, all biomarkers that can be linked to obesity. The case control study examined a group of obese and nonobese Romanian children who were screened for their FTO gene. According to the authors, children with the rs9939609 AA

allele has a 2.02 higher risk for obesity than the heterozygous or wild type alleles. Children with the GG allele of rs17817449 had higher values of weight, body mass index, waist and hip circumference, total cholesterol, triglycerides, adiponectin, and fasting glucose.

Discussion

The evidence supports that FTO gene mutations raise the risk of overweight and obesity. Out of 55 research articles assessed, 29 did not pass muster because of faulty design or they analyzed multiple health issues, with overweight and obesity only being one of them. Of the remaining 26 research articles, the best seven were chosen for their strong design and lack of repetition. The evidence is particularly supportive of this thesis statement because studies were performed in a variety of different age groups, and FTO genetic screenings were analyzed in populations from all over the world (Duicu et al., 2016). Hence, the evidence suggests that negative FTO genetic expression is in issue in human beings everywhere. In addition, it is fascinating how the evidence suggests two biochemical methods in which the FTO gene raises the risk of overweight and obesity. One study found that mutations of the FTO gene accelerate the turning of beige adipocyte cells into white (Claussnitzer et al., 2015); the other study showed those with FTO mutations are less sated because of stronger visual response to food cues (Melhorn et al., 2018).

There are few apparent limitations to the findings. There are a plethora of research articles to choose from with regard to the FTO gene, many with strong designs. That said, none of the researchers in the studies I chose used the same genetic testing lab to screen for FTO mutations. Because there are many genetic labs that are not registered internationally or by their

own countries, it is possible that there could be a lack of predictability with results, thus affecting the accuracy of mutations found in research participants.

The evidence has implications for public health and the health care of patients. For one, aside from family history, there are very few screening measures that can be applied on a massive scale to prevent overweight and obesity. Genetic testing does not require anything invasive. It can be as simple as a cheek swab or saliva specimen. Thus, FTO genetic screening can be performed on babies as soon as they are born, giving parents the impetus to work harder to give their child the proper nutrition and physical exercise necessary to stave off negative FTO genetic expression, if found to be homozygous. Second, for individuals who are already overweight or obese, FTO genetic screening could be a powerful tool for health professionals to use to explain why the patient is at increased risk for overweight and obesity, and explain what the patient can do to mitigate potential negative expression of the gene, which is very responsive to exercise (Oyeyemi et al., 2017).

Conclusion

The evidence supports that FTO gene mutations raise the risk of overweight and obesity. By examining populations on every continent, and at all stages of life, researchers replicated results showing that homozygous FTO mutations increase the risk of overweight and obesity. Researchers conclude that several metabolic systems and pathways are affected by FTO mutations, including the central nervous system, hunger hormones, visual perception, and mitochondrial thermogenesis. Evidence suggests that physical activity is a powerful mitigator of negative FTO expression, which could act as the first line of defense for overweight and obesity prevention.

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