BACKGROUND

• Obesity has become a pandemic of global proportion.
• Obesity-related morbidity and mortality are ever increasing.

Fat Mass and Obesity Associated Gene (FTO) resides on the 16th chromosome in humans (Figure 1).

- FTO is largely expressed within the brain at the hypothalamic nuclei, sites crucial for appetite regulation.
- The association between numerous single nucleotide polymorphisms (SNPs) of FTO and obesity has been well-documented in child, adolescent and adult populations.
- Emerging experimental studies suggest that the association between FTO and obesity might be the result of FTO influencing eating behaviour and satiety cues.
- FTO neurons are ‘activated’ in the hunger-mediating hypothalamic sites at the end of feeding, suggesting that FTO might regulate eating behaviour by influencing feeding termination mechanisms.

The aim of this systematic review is to investigate the following research question: “Is the association between the fat mass and obesity associated gene (FTO) and obesity in humans the result of FTO influencing eating behaviour?”

AIM

METHODS

Literature search strategy

- Exhaustive search for potentially relevant research papers performed between February 10 and 21, 2014 on PubMed; Ovid: Medline (1946-present); Embase (1974-2014); and Web of Science (combined Web of Science Core Collection (2003-present) and SciELO Citation Index (1997-present) (Figure 2).

- Search terms included the following, as well as variations (*) (Table 1).

- Panels 8

Table 1. Search terms as entered into databases.

Inclusion Criteria

- Studies performed on human subjects.
- Children/adolescents aged 4-17 years and adults aged 18-75; male and female; any ethnicities; any socio-economic classes.
- Papers written in English and accessible.
- Studies of evidence levels I-IV.
- FTO is the primary or one of multiple primary gene(s) investigated.
- At least one measure of adiposity utilized (BMI, waist circumference, etc.).
- Participants genotyped for at least one FTO SNP/variant.
- Data collected on participants’ food consumption habits and/or energy intake and/or relationship with food.

Exclusion Criteria

- Participants with significant medical conditions other than, or as well as, obesity (e.g. diabetes mellitus, polycystic ovary syndrome, cardiovascular disease and psychiatric illness).
- Participants involved in a pharmacological, lifestyle, medical or surgical intervention (e.g. diet or exercise regime, gastric bypass surgery).

RESULTS

- Study demographics: 14 European populations; 1 Asian; 1 American.
- The effects of five FTO SNPs were assessed across 16 studies: rs939609, rs1421085, rs17817449, rs1121980 and rs9939973.
- All five of the SNPs were significantly associated with increased adiposity in at least one study.
- Seven studies significantly linked rs939609 to multiple obesity-associated appetite behaviors in children, including: increased energy intake and fat intake, risky eating behavior (“loss-of-control eating”), decreased satiety responsiveness (Figure 3) and preference for energy-dense foods.
- Two studies significantly associated rs9939609 with adult eating behaviors, including: increased energy intake and preference for energy-dense, snack-type foods.
- The rs1421085, rs17817449, rs1121980 and rs9939973 variants were not linked to eating behavior in either children or adults across the 16 studies.

Figure 2. Search strategy.

AIM

The results from this systematic review provide significant evidence in support of the rs939609 FTO variant predisposing to obesity in children by affecting central components of ingestive behavior. It is not, however, possible to conclude which of the eating behaviors observed induces the greatest effect on body weight. Evidence for an influential role of rs939609 on energy and food intake in adults relative to adiposity is also demonstrated, but in substantially decreased proportion. These results provide insight into one potential mechanism of action underlying FTO’s contribution to common obesity. One practical application of these results could be to encourage risk-allele carriers of the rs939609 SNP to closely monitor their dietary intake habits as a method of obesity prevention.