Physical Activity Attenuates Increased Obesity Risk Associated with the High-Risk Genotype of the FTO Gene in a UK Adult Population

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Introduction

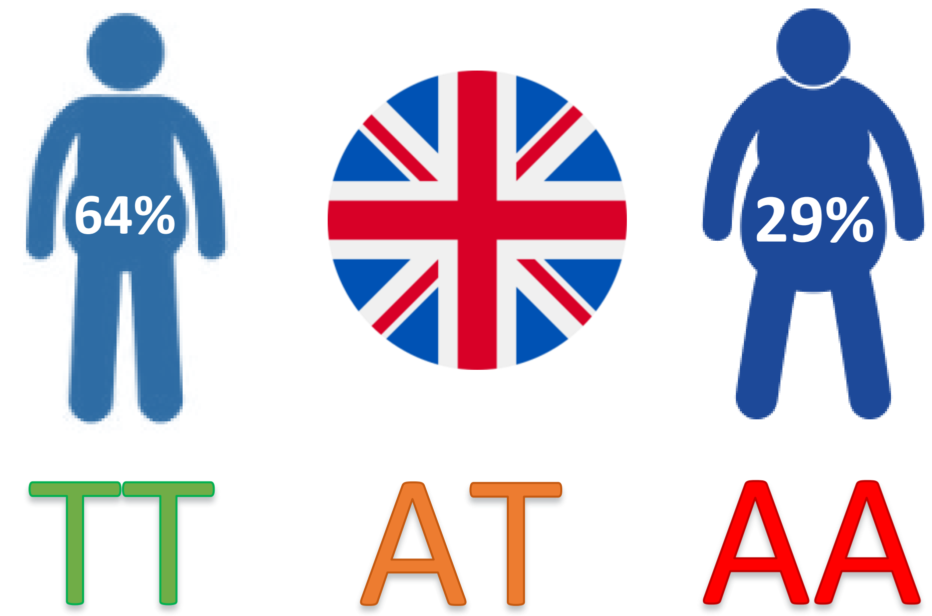
Obesity is a worldwide epidemic that has nearly tripled[11] since 1975. Genome-wide association studies[6,10] have identified the Fat-Mass and Obesity-Associated (FTO) gene as an obesity-susceptible gene with many single nucleotide polymorphisms (SNP) associated with an increased risk of Obesity, including the SNP rs9939609.

FTO, BMI and PAL

A Meta-analysis of 177,330 adults found a significant association between the minor allele (A-allele) and higher BMI of all participants[12]. Previous studies[8] suggest that increased physical activity level (PAL) can attenuate the obesity risks associated with the 'A' allele of FTO SNP rs9939609 by 30%.

FTO and Food Preference

The high-risk allele of FTO rs9939609 has been associated with twice the chance of having loss of control of eating episodes, higher preference towards fatty foods, higher satiety level[7] and a higher threshold for the appetite suppressing hormone ghrelin[4].



Aim – This study aims to investigate potential associations between the FTO SNP rs9939609 and BMI, PAL, body fat percentage (BF%) and food preference through genotypic and phenotypic analysis

Table 1. A table showing study population characteristics

Measure	Mean	Std Dev (±)
Age (yrs)	29	13
BMI (kg/m²)	25	4.3
BF%	27.7	7.5
Genotype	**Number**	**% Population**
TT	17	46
AT	14	38
AA	6	16

Table 2. A table showing the simple effect PAL, Genotype and PAL*Genotype has on BMI and BF%

Effect		Significance Value
PAL	BMI	0.006*
	BF%	0.635
Genotype	BMI	0.068
	BF%	0.281
PAL*Genotype	BMI	0.194
	BF%	0.267

Table 3. A Table showing the Effect PAL and Genotype combined has on the BMI and BF% of Participants

	PAL	$Genotype_1$	$Genotype_2$	Sig.
BMI	Low	TT	AT	0.645
			AA	0.013*
		AA	AT	0.007*
BF%	High	TT	AT	0.509
			AA	0.033*
		AA	AT	0.062

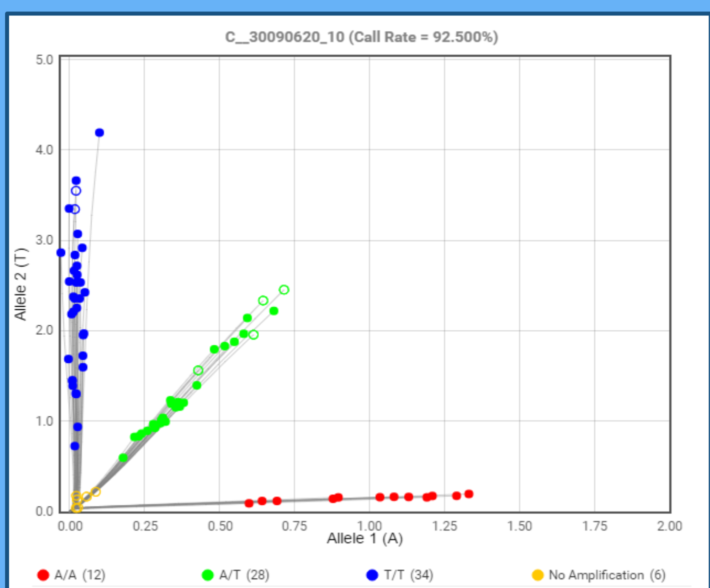


Figure 1. A Figure Showing the Allelic Discrimination Analysis of Participants for the SNP rs9939609 of the FTO Gene

Methods

Study Population: 37 UK Adults

Measures: BMI, BF% (bioelectrical impedance), Food preference (FFQ), PAL, Saliva Sample

Genotyping: DNA extraction (PSP SalivaGene kit), Quantification (Nanodrop System), Genotyping (StepOne Biosystems)

Analysis: FETA for FFQ analysis, Two-way MANOVA for genotype, BMI, BF% and PAL analysis, Chi-Squared for food preference analysis

Results

Genotype x PAL showed a significant difference in the BMI of TT participants compared to AA participants (p=0.013) with low PAL, and between AT participants and AA participants (p=0.007) with low PAL. A significant difference was found in the BF% of TT participants compared to that of AA participants (p=0.033) with high PAL. No significant associated was found between genotype and food preference (p>0.05).

Figure 1 shows the Allelic Discrimination Chart for all participants. This study's allelic discrimination respects the Hardy-Weinberg Equilibrium (p=0.81).

Discussion

FTO, BMI and PAL

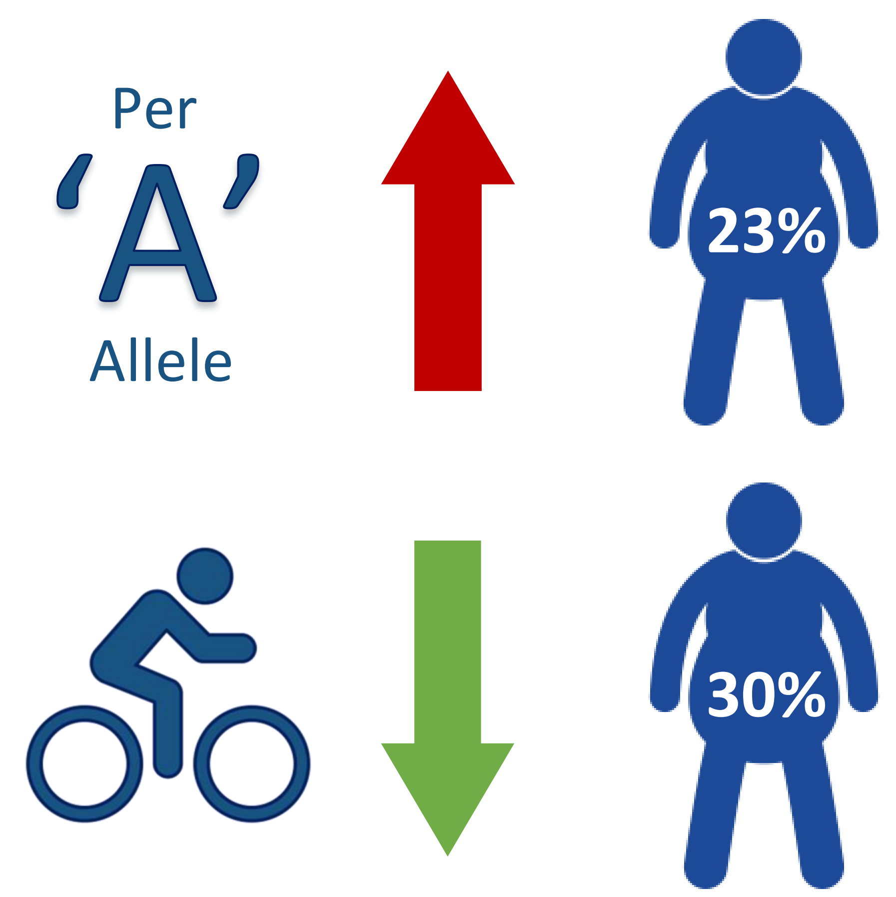
This study suggests that genotype alone does not influence adiposity, however when combined with a low PAL a significant effect can be seen. The BMI of TT participants with a low PAL was significantly lower than AA participants with low PAL. As PAL increased to medium or high, no significant differences in BMI were found between genotypes. This suggests that PAL attenuates the influence rs9939609 has on obesity risk, which supports previous studies that found similar results[3]. Kilpeläinen et al. 2011[8] determined that each additional A allele increased the risk of obesity by 23%, but that PAL reduced the risk of obesity by 30%.

FTO and BF%

A significant difference in the BF% of TT participants compared to AA participants (p=0.033) with High PAL was also found. Similar results were not found in low and medium PAL. This supports previous research suggesting BF% in highly active subjects is higher in AA subjects compared to that of TT subjects.[1, 9]

FTO and Food Preference

No significant association was found between food preference and genotype. This refutes previous theories that genotype increases total energy intake, fat and saturated fat intake and a preference for energy dense foods. This may be due to the use of a FFQ alone, compared to previous studies that used a combination of FFQ, Food diary and 24-hour recall.[2,7]



Conclusion - To conclude the influence the FTO SNP rs9939609 has on obesity can be attenuated by increased PAL. However, further research into the mechanisms behind the FTO gene, and potential obesity related epistasis, would aid the development of genetic-based personalised obesity interventions.

References: 1 Bravard, (2013) 'The expression of FTO in human adipose tissue is influenced by fat depot, adiposity, and insulin sensitivity', *Obesity*; 2 Brunkwall, (2013) ' Genetic variation in the fat mass and obesity-associated gene (FTO) in association with food preferences in healthy adults ', *Food & Nutrition Research*; 3 Celis-Morales, (2016) 'Physical activity attenuates the effect of the FTO genotype on obesity traits in European adults: The Food4Me study.', *Obesity (Silver Spring, Md.)*; 4 Dorling, (2019) 'A randomized crossover trial… FTO rs9939609 polymorphism.', *The American journal of clinical nutrition*; England, 5 H. S. (2018) *Health Survey for England 2017 Adult and child overweight and obesity.*; 6 Frayling, (2007) 'A common variant… adult obesity.', *Science (New York, N.Y.)*; 7 Karra, (2013) 'A link between FTO, ghrelin, and impaired brain food-cue responsivity', *Journal of Clinical Investigation*; 8 Kilpeläinen, (2011) 'Physical activity attenuates the influence of FTO variants on obesity risk: A meta-analysis of 218,166 adults and 19,268 children', *PLoS Medicine*; 9 Payne, (2014) 'Effect of FTO gene and physical activity interaction on trunk fat percentage among the newfoundland population', *Genetics and Epigenetics*; 10 Scuteri, (2007) 'Genome-wide association scan shows genetic variants in the FTO gene are associated with obesity-related traits.', *PLoS genetics*; 11 WHO (2018) *Obesity and overweight*. Available at: https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight; 12 Qi