No evidence for association of the FTO rs9939609 obesity risk allele with Binge Eating Disorder (BED) susceptibility

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Introduction

The common single nucleotide polymorphism (SNP) rs9939609 in the fat mass and obesity-associated gene (*FTO*) is the most frequently described variant associated with risk of obesity (Loos and Yeo, 2014; Albuquerque et al., 2015). The rs9939609 obesity risk A-allele was also associated with an increased vulnerability to Eating Disorders including bulimia nervosa (BN) and anorexia nervosa (AN) (Castellini et al., 2017). Binge Eating Disorder (BED) is marked by regular overly excessive eating episodes accompanied by a sense of lack of control in the absence of regular inappropriate compensatory behaviors (APA, 2013).

As until now, data addressing the association between FTO SNPs and BED are totally lacking, we evaluated the genotype distribution of rs9939609 in a series of BED patients.

Methods

SNP rs9939609 T/A was genotyped by TaqMan assay in 31 overweight/obese females (25≤BMI<50 kg/m^2) (20–57 years old; mean age 30.09) diagnosed with BED and in a sex matched group of 60 overweight/obese females (26<BMI<45.2 kg/m^2) (22–58 years old; mean age 42.85) without signs of BED psychopathology. A normal weight group of 105 females (15<BMI<25 kg/m^2) (21–36 years old; mean age 23) was also enrolled in the study. Clinical data were collected through a face-to-face structured clinical interview and self-reported questionnaires assessing eating psychopathological symptoms. BED diagnosis was establish using the DSM-5 criteria (APA, 2013). To determine the existence of a BED, the Eating Disorders Examination Interview (Fairbun et al., 2008) and the Binge Eating Scale (BES) (Duarte et al., 2015) total score were used. The overall association between the *FTO* genotypes (*AA*, *AT*, *TT*) and BED was tested by logistic regression. Statistical analysis was performed using the PLINK software (http://zzz.bwh.harvard.edu/plink/). Written informed consent was obtained from all individuals prior to enrollment. The study was conducted in accordance with Declaration of Helsinki and with ethical guidelines of the University of Coimbra.

Results and Discussion

Frequency of obesity risk A-allele was 0.242 in overweight/obese females classified as BED (G1), 0.40 in overweight/obese subjects with no BED symptomatology (G2) and 0.329 in the normal weight group (G3) (Table 1). Genotype distributions are according HWE in G1 (p=1), G2 (p=0.07) and G3 (p=0.67) (Table 1).

Genetic comparison between the BED group (G1) vs. group with no BED symptomatology (G2), showed a marginal significant association between T-allele and BED (OR=1.873; p=0.056 in the additive model), in concordance with a lower A-allele frequency in G1 (0.24 vs. 0.4) (Table 1).

No significant differences were found between the normal-weight group G3 and the overweight/obese BED group G1 (OR=0.641; p=0.19 in the additive model) (Table 1), meaning that the rs9939609 A-allele should not explain the obese phenotype of BED individuals.

Comparing the normal-weight group G3 and the overweight/obese group with no BED symptomatology G2, a significant association was observed in the recessive model, between the rs9939609 A-allele and obesity risk (OR=2.628; p=0.034), in concordance with general studies.

Table 1: Allele and genotype frequencies of the FTO rs9939609 polymorphism in overweight/obese females with BED and without BED psychopathology and in normal weight females.

Group	Alleles	Frequency	Genotypes	N (%)	p HWE	OR	CI95%	p-value
G1: BED (OB/OW) N=31	T	0.758	TT	18 (58.07)	1			
			TA	11 (35.48)				
	A	0.242	AA	2 (6.45)				
G2: No BED (OB/OW) N=60	T	0.60	TT	25 (41.67)	0.07			
			TA	22 (36.67)				
	A	0.40	AA	13 (21.66)				
G3: Normal weight N=105	T	0.671	TT	46 (43.81)	0.67			
			TA	49 (46.67)				
	A	0.329	AA	10 (9.52)				
G1: BED vs. G2: no BED								
additive						0.533	0.279-1.018	0.056
recessive						0.249	0.052-1.185	0.080
G1: BED vs. G3: normal weight								
additive						0.641	0.330-1.246	0.19
recessive						0.655	0.135-3.162	0.598
G2: no BED vs. G3: normal weight								
additive						1.34	0.850-2.112	0.206
recessive						2.628	1.073-6.434	**0.034**

Abbreviations: OB, obese; OW, overweight; CI95%, 95% confidence interval; OR, odds ratio.
Logistic regression was used to compare genotype distribution between groups.
p-values (asymptotic p-value for t-statistic) shown are for an additive (AA vs. AT vs. TT) and recessive (AA vs. AT+TT) genetic models.
OR is shown for the minor allele A. p-values significant (p<0.05) are in bold.

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Conflicts of interest: none.

Conclusions

In conclusion, the marginally significant lower frequency of the rs9939609 A-allele in individuals with BED when comparing with overweight/obese subjects with no BED psychopathology suggest that the FTO obesity risk A-allele has no potential role in BED.

References

- Albuquerque D et al. (2015) Current review of genetics of human obesity: from molecular mechanisms to an evolutionary perspective. Mol Genet Genomics 290(4):1191-221.
- American Psychiatric Association (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
- Castellini G et al. (2017) Fat mass and obesity-associated gene (FTO) is associated to eating disorders susceptibility and moderates the expression of psychopathological traits. PLoS ONE 12(3): e0173560.
- Duarte, C., Pinto-Gouveia, J., & Ferreira, C. (2015) Expanding binge eating assessment: Validity and screening value of the Binge Eating Scale in women from the general population. *Eating Behaviors, 18,* 41–47.
- Fairburn, C.G., Cooper, Z., & O'Connor, M. (2008) Eating Disorder Examination (Edition 16.0D) In Fairburn, CG. Cognitive Behavior Therapy and Eating Disorders. Guliford Press, New York.
- Loos, R. J. F. & Yeo, G. S. H. (2014) The bigger picture of FTO—the first GWAS-identified obesity gene. *Nat. Rev. Endocrinol.* 10, 51–61.