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Impact of Fat Mass and Obesity Associated (FTO) Gene Variants and Lifestyle Factors on Obesity Traits in A Turkish Population

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Studies have shown that the effect of the fat mass and obesity-associated gene(*FTO*) on obesity is modulated by dietary factors in several populations[(1)]; however, to date, there has been only one study that has been conducted in the Turkish population[(2)]. Hence, we aimed to determine whether two single nucleotide polymorphisms (SNPs) in the *FTO* gene (rs9939609 and rs10163409) are associated with obesity-related traits and to assess whether these associations were modified by lifestyle factors including physical activity and macronutrient intake in the Turkish population.

The study included 200 obese and 200 non-obese individuals in Turkey. Dietary intakes were assessed using 24-hour dietary recall. Levels of physical activity were measured based on self-report questionnaires. Statistical analysis was performed using the SPSS software. Logistic and general linear models were used to determine the independent and joint, genetic risk score (GRS), effect of *FTO* SNPs on the risk of obesity and its related traits, respectively. Furthermore, interactions were tested by including the interaction terms in the regression models.

The SNP rs9939609 and GRS were significantly associated with body mass index (BMI) and fat mass index (FMI), after correction for multiple testing. Carriers of the risk allele 'A' of the SNP rs9939609 had significantly higher BMI and FMI compared to 'TT' homozygotes ($P = 0.001$ and $P = 0.002$, respectively). In the GRS analysis, carriers of two or more risk alleles of the *FTO* variants had higher BMI and FMI compared to individuals carrying less than two risk alleles ($P = 0.002$ and $P = 0.003$, respectively). A significant interaction was observed between the SNP rs9939609 and physical activity levels on adiponectin concentrations ($P_{interaction} = 0.027$). Among individuals with low physical activity levels, carriers of the risk allele 'A' of this SNP had significantly lower adiponectin concentrations than homozygous individuals for 'TT' genotype ($P = 0.006$). Furthermore, there was a significant interaction between the SNP rs10163409 and protein intake on increased waist circumference (WC) ($P_{interaction} = 0.044$). Among individuals in the highest tertile of protein intake, carriers of the minor allele 'T' of the SNP rs10163409 had a significantly higher risk of increased WC than those with 'AA' genotype ($P = 0.027$).

Our study in this Turkish population has demonstrated that the risk allele 'A' of the *FTO* SNP rs9939609 and GRS were significantly associated with higher BMI and FMI. It also suggests that the effect of the *FTO* SNPs, rs9939609 and rs10163409, on adiponectin concentrations and WC is potentially influenced by physical activity levels and dietary protein intake, respectively. However, these findings warrant a replication in other large cohorts.

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