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LETTERS

Lack of association between a new tag SNP in the *FTO* gene and BMI in Czech–Slavonic population

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We read with great interest the recent article by Tönjes *et al*[1] published in the European Journal of Human Genetics. In the last 2 years, the association between variants within the first intron of the *FTO* ('fat mass and obesity related') gene and obesity was recognized and widely replicated.[2] Despite recent data suggesting that FTO has a DNA demethylase activity[3] and non/heme dioxygenase activity,[4] the exact role of *FTO* genetic variants in BMI determination are yet to be identified. Tönjes *et al*[1] performed a genome-wide association study in the Sorbian population (isolate of Slavonic origin resident in eastern part of Germany) and detected an independent *FTO* signal, mapping to a region in introns 2/3 and about 40–60 kb away from the originally reported SNPs (rs9939609, rs1421085, and rs17817449). There, the strongest effect on BMI values was associated with rs17818902. As the signal has not so far been confirmed in independent populations, we have genotyped this *FTO* SNP in a group of 2559 unrelated Caucasians (1191 males and 1368 females, aged 25–65 years), a 3-year cohort of the selected 1% Czech–Slavonic population sample from nine districts. The individuals were recruited in 1997–1998 and reinvited in 2000–2001, according to the WHO protocol (*Multinational monitoring of trends and determinants in cardiovascular diseases: 'MONICA Project'.* Manual of operations WHO/MNC 82.2, Nov. 1983). Further, 556 university students (both males and females) with known birth length and birth weight were genotyped.

The frequencies of the individual genotypes were in Hardy–Weinberg equilibrium (P=0.49) and did not differ between the Czechs (TT – 63.8%; TG – 31.7%; GG – 4.5%) and the Sorbs (TT – 66.4%; TG – 30.6%; GG – 2.9%). All statistical analyses were performed separately for both the measurements obtained at the 1997/8 and 2000/1 surveys and for the means of these analyses. The results were not significant for either survey. Namely, we did not confirm the original association between *FTO* rs17818902 SNP and BMI, despite the fact that the slight similar trend (like in Sorbs) in BMI was detected at least in females (data from 2000/01 survey: males, TT – 28.2 ± 3.9 kg/m^2; TG – 28.3 ± 4.1 kg/m^2; GG – 28.1 ± 4.0 kg/m^2; females, TT – 27.6 ± 5.7 kg/m^2; TG – 27.5 ± 5.4 kg/m^2; GG – 28.0 ± 5.4 kg/m^2). Further, neither waist–hip ratio (males, TT – 0.93 ± 0.07; TG – 0.93 ± 0.07; GG – 0.93 ± 0.06; females, TT – 0.81 ± 0.07; TG – 0.81 ± 0.07; GG – 0.80 ± 0.06) nor plasma levels of total cholesterol (males, TT – 5.76 ± 1.03 mmol/l; TG – 5.75 ± 1.08 mmol/l; GG – 5.78 ± 1.14 mmol/l; females, TT – 5.78 ± 1.14 mmol/l; TG – 5.82 ± 1.12 mmol/l; GG – 5.49 ± 1.32 mmol/l), LDL and HDL cholesterol, triglycerides, glycaemia, nor hsCRP levels were associated with the newly detected *FTO* rs17818902 variant in Czechs. Also birth length and weight were independent in *FTO* rs17818902 variant. Discrepancies between the studies could not be easily explained. First, both in Sorbs[1] and in Czechs,[5,6] SNPs in intron 1 are associated with BMI and we also don't suppose some major differences in general genetic background between the two neighboring middle-European Slavonic populations,[7] despite the fact that recent neighbors could have different historical ancestry.[8] Also, the common cause of non-replication in genetic association studies – different definitions of the analyzed populations – is most probably not the cause as both analyzed groups are based on general populations. However, it is still possible that the SNP in intron 3 tagged a causal novel variant on an existing haplotype in the Sorbian population, or the BMI effect of rs17818902 is the result of interaction with environmental factors and/or genetic variant(s) outside the *FTO* region which is/are specific to the Sorbian isolate.[1] Our results underline the importance of detailed analyses of the gene–gene and/or gene–environmental interactions, which could clarify the exact role of this variant in pathogenesis of obesity in different populations.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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