Homocysteine levels are associated with the fat mass and obesity associated gene FTO(intron 1 T>A) polymorphism in MS patients

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Background. High homocysteine levels have been associated with obesity and multiple sclerosis (MS). Obesity is also a significant risk factor for development of early-onset MS. The fat mass and obesity associated (FTO) gene has not previously been studied in relation to MS and homocysteine, an important marker of dysfunctional methylation. This study evaluated the influence of vascular risk factors, including body mass index (BMI), total cholesterol levels and the FTO rs9939609 (intron 1 T>A) single nucleotide polymorphism (SNP) in relation to homocysteine levels.

Methods. A total of 108 white MS patients and 197 control individuals were genotyped for FTO rs9939609 using real-time polymerase chain reaction (RT-PCR). Homocysteine levels were subsequently measured in a subgroup of 60 patients and 87 controls and correlated with selected vascular risk factors.

Results. A statistically significant association (p=0.006) was observed between homocysteine levels and FTO rs9939609, with a 15% increase in the presence of each risk-associated A allele. Homocysteine levels were significantly higher in males than females (p<0.001) as expected, with a 15% increase associated with the A allele after adjustment for gender. Total cholesterol levels (p=0.049) and BMI (p=0.046) correlated significantly with increased homocysteine levels in the age-, gender- and MS-status adjusted group and in age- and MS-adjusted females respectively, with no difference noted between MS patients and controls.

Conclusion. This study provides evidence for FTO rs9939609 as a genetic link between obesity and MS. Increased homocysteine levels, associated with both MS and vascular risk factors in our study population, may identify a new disease pathway in MS mediated by genetic variation in the FTO gene.